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Non-Elective Surgery for Acute Complicated Diverticulitis. Primary Resection-Anastomosis or Hartmann's Procedure? A Systematic Review and Meta-Analysis

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Abstract

Background: The use of Primary Resection-Anastomosis with or without protective ileostomy

(PRA) or Hartmann's Procedure (HP) in the surgery of complicated acute diverticulitis is still an open question. The latest published meta-analyses were limited to the most severe stages (Hinchey III and IV). Our systematic review aimed to compare PRA with the HP in all non-elective surgical patients with complicated acute diverticulitis (perforation or obstruction).

Methods: A computerized literature search was performed on Medline databases until July 2014. The studies included in the meta-analysis were 24 with a total of 4,062 patients. Study outcomes included postoperative surgical complications, reintervention, 30-day mortality, overall mortality as well as the length of stay as secondary outcome. The pooled effects were estimated using a fixed effect model or random effect model based on the heterogeneity test. Results were expressed as odds ratio (OR) and 95% confidence interval (CI) for dichotomous outcomes and as mean difference (MD) with 95% CI for continuous outcomes. Subgroup analyses by study type were performed.

Results: The PRA group had a lower rate of postoperative surgical complications (OR=0.525, 95% CI 0.387-0.713), reintervention (OR=0.688, 95% CI 0.525-0.902), 30-day mortality (OR=0.389, 95% CI 0.259-0.586), overall mortality (OR=0.467, 95% CI 0.272-0.803) and length of stay (MD=9.129, 95% CI 2.391-15.867) compared to the HP group.

Conclusion: Our meta-analysis shows that the PRA technique is better than HP for all considered outcomes. Due to the high variability of the included studies, further randomized controlled trials would be required to confirm these results.

Keywords: Acute complicated diverticulitis; Primary resection-anastomosis; Hartmann's procedure

Introduction

Colonic diverticulosis is a common condition in the Western world and its incidence increases substantially with age. It was estimated that in patients older than age 60 years, 50% have diverticulosis [1,2]. Surgeons' interest for this disease is related to the treatment of the complications of diverticulitis (perforation, occlusion, bleeding). About 25% of patients hospitalized for diverticulitis will require a non-elective surgical intervention, in most cases for perforation [3,4]. The surgical management of emergencies for diverticulitis progressed over the past years. The three stage procedure (stoma without resection of the diseased segment as first stage) only maintains a historical value. The two stage procedure, better known as Hartmann's procedure (HP), includes the resection of the perforated or stenotic segment with terminal colostomy (first stage) and the subsequent restoration of the bowel continuity (second stage). Most recently a one stage surgical approach was proposed including resection of involved colon and primary anastomosis realized in the same setting, with or without protective ileostomy (PRA). Many studies demonstrated no differences between HP and PRA in terms of morbidity and mortality [5,6]. Nevertheless, most surgeons still prefer HP in the emergency setting to treat perforation or obstruction from acute colonic diverticulitis [3,7,8]. Most retrospective studies and the only two prospective trials [6,9] are focused only on patients operated for perforated diverticulitis and peritonitis (Hinchey stage III and IV). Our systematic review aimed to evaluate the literature comparing PRA (with or without protective ileostomy) with HP in all non-elective surgical patients with complicated acute diverticulitis (perforation

or obstruction) to assess the effectiveness and safety of the one-stage technique.

Methods

Data sources and search strategy

A comprehensive computerized literature search was performed until July 2014 on Medline databases using the following search terms: "Hartmann", "primary anastomosis", "perforated diverticulitis", and "acute diverticulitis". Only papers published in English were considered while no publication date restrictions were applied. The computer search was supplemented with a manual search of reference lists for all available review articles and meta-analyses to identify further relevant works not found by the computer search. We followed the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) guidelines for systematic reviews and meta-analyses.

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Eligibility criteria

Eligible studies were those comparing PRA (with or without protective ileostomy) with HP in non-elective surgical patients with acute diverticulitis complicated by peritonitis or bowel obstruction. The laparoscopic techniques were not considered in the present review. Peritonitis and bowel obstructions caused by inflammatory bowel diseases or cancer were also excluded. Surgical interventions on acute colonic diverticulitis meeting the above criteria had also to include at least one of the following primary outcomes: (i) postoperative surgical complications, (ii) reintervention, (iii) 30-day mortality and (iv) overall mortality. Postoperative surgical complications included wound infection, wound dehiscence, intra-abdominal infection/abscess, rectal stump dehiscence, sepsis, multiorgan failure, stoma complications, bowel occlusion and intra-abdominal hemorrhage. The number of events for each study was obtained by summing all postoperative surgical complications occurred while the number of possible complications was calculated multiplying the number of patients by 9, which expressed the number of complications. This method was applied to estimate the postoperative complications occurred after the first intervention as well as to sum the complications occurred after the first and the second intervention, when the restoration of the bowel continuity was indicated. Reintervention was defined as any surgical procedure required in a postoperative patient within a few days/weeks following the initial surgical procedure and related to the initial surgery. The 30-day mortality expressed the number of deaths from any cause within 30 days from the first hospital admission for non-elective surgery in patients with complicated diverticular disease. Overall mortality recorded the number of deaths occurred after both the first intervention and the second intervention of recanalization. The overall mortality coincided with 30-day mortality, for patients who underwent PRA without diverting loop ileostomy. Secondary outcome considered the length of stay (LOS) in days for first admission in both groups. Randomized controlled trials (RCT), prospective non randomized trials (PNR) and retrospective studies (R) were included in this study.

Data extraction

Original articles were reviewed and the variables of interest were abstracted, where reported. When discrepancies occurred between

reviewers, the reasons were identified and a final decision was made based on the reviewers' agreement. Quality score was assigned to each study by the Jadad scale assessing 3 major criteria: reporting and handling of randomization and blinding and handling of withdrawals. The maximum possible score was 5 while studies with extensive flaws were those with a ≤ 2 score. The validity assessment was performed by the same two reviewers who extracted data from the full text articles.

Statistical analysis

For dichotomous outcomes formal statistical tests for heterogeneity of the odds ratios (ORs) were performed with the Cochrane Q test, heterogeneity being assumed with a p value ≤ 0.05 . When a Q test indicated substantial heterogeneity, a random-effects model weighted by the DerSimonian-Laird method was used. A fixed-effects model weighted by the Mantel-Haenszel method was used for pooling the ORs. Results were expressed as OR and 95% confidence interval (95% CI). For continuous outcomes, the mean difference (MD) with 95% CI was calculated. The pooled effects were estimated using a fixed effect model or random effect model based on the heterogeneity test.

We performed subgroup analyses to assess the effect of the study type (RCT, PNR or R) on the association between surgical technique and outcomes.

All meta-analytical data were analyzed according to intention-to treat analyses. All procedures and calculations used in the meta-analyses were made following the methodology reported elsewhere [10].

Results

A total of 372 potentially eligible studies were identified, as reported in Figure 1. Study titles and abstracts were screened for inclusion. 307 were excluded and the remaining 65 possibly relevant studies were retrieved as full text articles. Based on the full text assessment, 41 studies were excluded for the following reasons: elective surgery (n=9), outcomes not reported or not available (n=25), other surgical techniques (n=1), data included in previous or more complete studies (n=4), Italian language (n=2). The USA national survey conducted by Masoomi et al. [11] was excluded to avoid a selection bias because the authors compared 56,866 HP patients with 3,361 patients treated

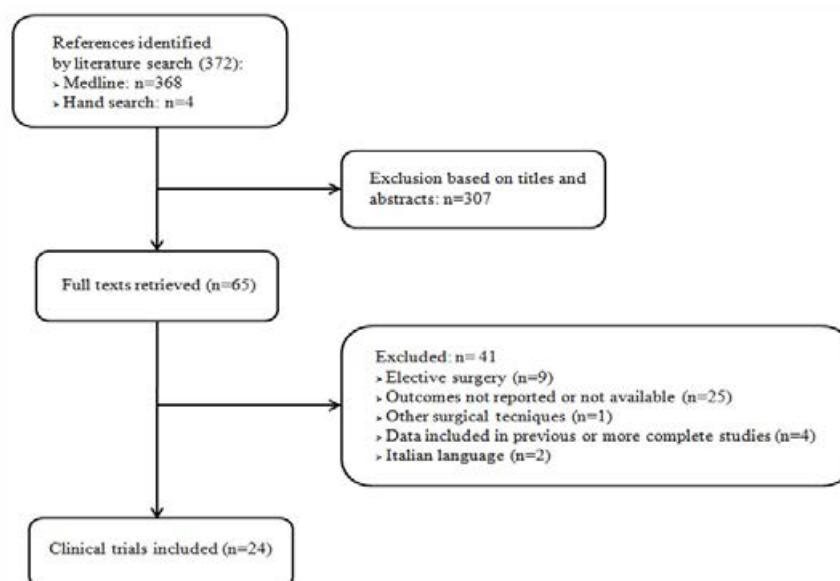


Figure 1: Systematic review PRISMA flow diagram.

Abbreviations: HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; REM: Random Effect Model; FEM: Fixed Effect Model

with PRA and proximal diversion, excluding from the analysis 39,032 patients treated with PRA without diversion. A total of 24 studies met our eligibility criteria and were included in the meta-analysis, yielding a total of 4,062 non-elective surgical patients with acute complicated diverticulitis. 1,184 patients underwent PRA (with or without protective ileostomy) while 2,878 patients were submitted to HP. The selected study characteristics are summarized in Table 1 [12-33]. Two randomized controlled trials [6,9] were included in the meta-analysis and ranked as high quality studies with a Jadad's score of 3, while four were prospective non randomized studies and eighteen followed a retrospective design. The inherent lower methodological quality of retrospective and prospective non randomized designs suggested us to perform subgroup analyses by study type (Figures 2-6).

Postoperative surgical complications

Patients who underwent to PRA had a substantial lower risk to develop postoperative surgical complications compared to HP (OR=0.525, 95% CI 0.387-0.713; heterogeneity: Q value=49.364; P<0.0001). The observed heterogeneity is mainly due to the retrospective studies in which, however, the average effect went in the same direction of the other two groups that, instead, did not show heterogeneity. For this reason we considered the random effect model used strong enough.

The PRA group also showed lower postoperative surgical complications in all study types analyzed (R, PNR and RCT) (Figure 2). Although few studies [6,9,17-25] reported the complications occurred after the second intervention planned to restore the bowel continuity, the same results were found considering the sum of the complications occurred after the first and the second intervention (OR=0.490; 95% CI 0.361-0.664; heterogeneity: Q value=50.716; P<0.0001) (data not shown). The previous considerations about heterogeneity could also be applied in this case.

Reintervention

HP patients showed a higher risk to be submitted to reintervention

compared to PRA (OR=0.688, 95% CI 0.525-0.902; heterogeneity: Q value=33.027; P=1.000). Such result was confirmed in the R and PNR subgroups but not in the only RCT considered (Figure 3). Despite the absence of heterogeneity, in our opinion this result should be interpreted with caution and further studies would be required to confirm it. The complications that led to perform a reintervention were reported only by six studies and amounted to 18.0% for HP and 9.7% for PRA. In the HP group, the main causes of reintervention were related to wound complications (41.8%), stoma complications (27.3%) and intraabdominal abscess (14.5%) while patients submitted to PRA were reoperated for anastomotic leak (57.9%), wound complications (21.1%) and resuturation of abdominal incisions (21.1%).

30-day mortality

Statistical heterogeneity was present among the 24 studies considered (Q value=50.548; P= 0.001). By using a random effect model, pooled analysis showed a statistically significant advantage in the PRA group in terms of lower 30-day mortality rate (OR=0.389, 95% CI 0.259-0.586), which was confirmed in the three subgroups considered (Figure 4).

Overall mortality

The overall mortality rate was 8.5% (19/224) in the PRA group and 16.9% (50/295) in the HP group, respectively (Figure 5). Data were pooled from 8 studies and demonstrated a significant lower overall mortality risk in the PRA group (OR=0.467, 95% CI 0.272-0.803), which was confirmed in the three subgroups considered. Heterogeneity among the studies was no significant (Q value=6.247; P=0.511), allowing us to use a fixed effect model.

Length of hospital stay

The trend was in favor of the PRA technique with a pooled MD of 9.129 (95% CI 2.391-15.867), in spite of the presence of significant heterogeneity among the 4 considered studies (Q value= 25.730; P<0.0001). The quantitative aspect of this analysis (hospital days saved)

Table 1: Characteristics of included studies.

Author	Region	Year	Study type	Number of patients	
				HP	PAR
Alanis et al. [12]	USA	1989	R	26	34
Alizai et al. [13]	Germany	2013	R	72	26
Berry et al. [14]	England	1989	R	47	27
Binda et al. [9]	Multicenter	2012	RCT	56	34
Blair et al. [15]	Canada	2002	R	64	33
Gawlick et al. [16]	USA	2012	R	1678	340
Gooszen et al. [17]	Netherlands	2001	R	28	32
Herzog et al. [18]	Germany	2011	R	19	21
Hold et al. [19]	Austria	1990	R	76	99
Kourtesis et al. [20]	USA	1988	R	10	23
Mäkelä et al. [21]	Finland	2005	R	93	64
Mueller et al. [22]	Germany	2011	R	26	47
Oberkofler et al. [6]	Switzerland	2012	RCT	30	32
Pasternak et al. [23]	Switzerland	2010	R	65	46
Regenet et al. [24]	France	2003	PNR	33	27
Richter et al. [25]	Germany	2006	R	5	36
Saccomani et al. [26]	Italy	1993	R	8	26
Schilling et al. [27]	Germany	2001	PNR	42	13
Smirniotis et al. [28]	Greece	1992	R	18	6
Stumpf et al. [29]	USA	2007	R	30	36
Tabbara et al. [30]	USA	2010	R	176	18
Trenti et al. [31]	Spain	2011	PNR	60	27
Tudor et al. [32]	England	1994	PNR	77	76
Vermeulen et al. [33]	Netherlands	2007	R	139	61

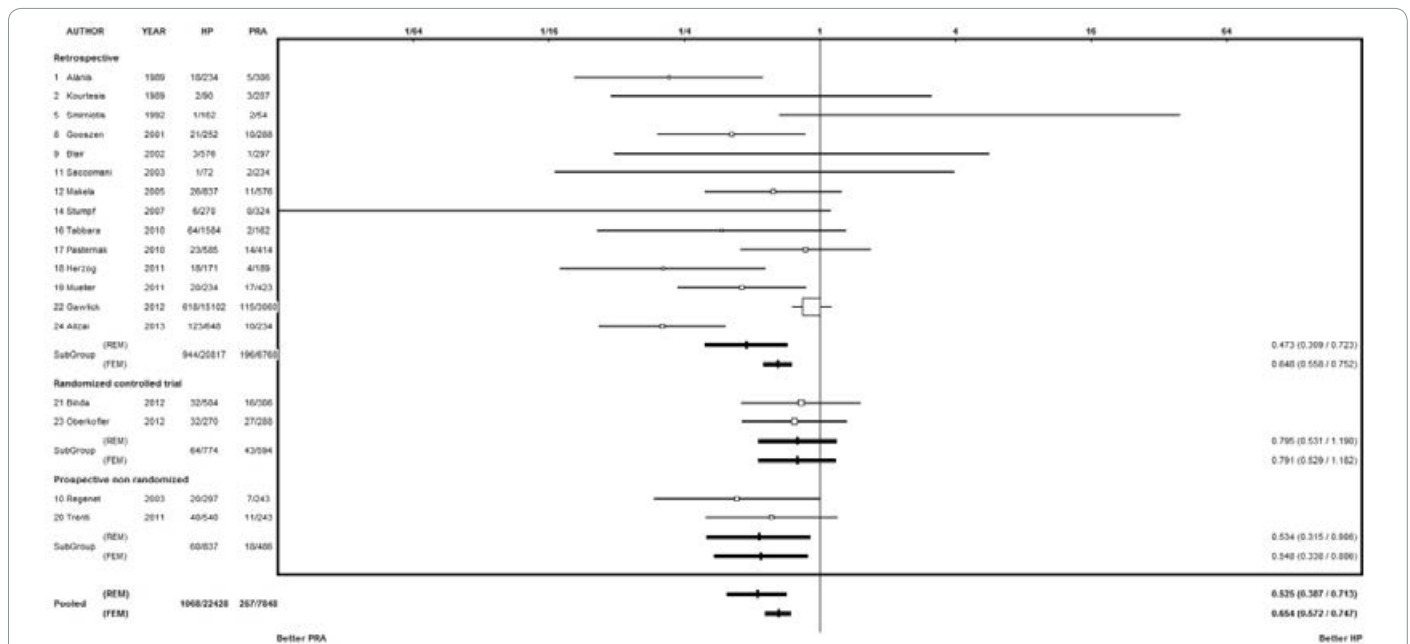


Figure 2: Forest plot for postoperative surgical complications by study type and results of meta-analysis.

Abbreviations: HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; REM: Random Effect Model; FEM: Fixed Effect Model

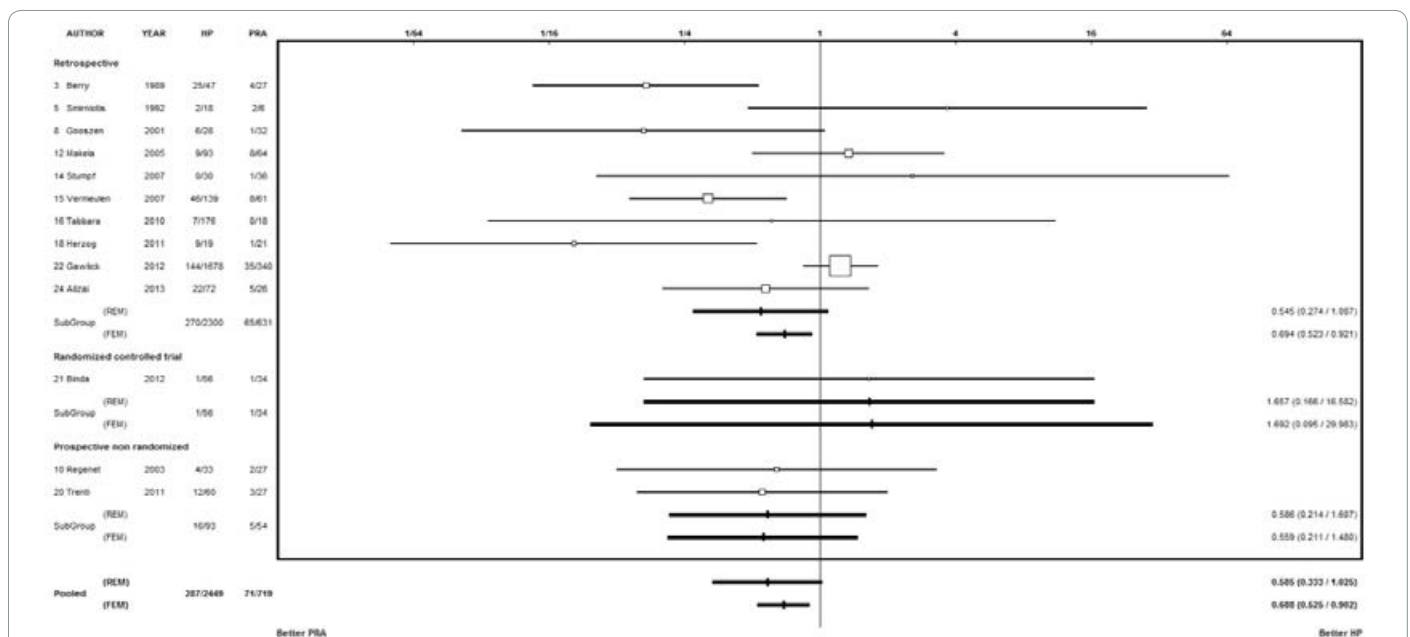


Figure 3: Forest plot for reintervention by study type and results of meta-analysis.

Abbreviations: HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without protective ileostomy; REM: Random Effect Model; FEM: Fixed Effect Model.

must be interpreted with caution due to the significant heterogeneity between prospective and retrospective studies (Figure 6).

Discussion

Worldwide, HP is still the most common procedure performed in emergency surgery for complications of acute diverticulitis. This tendency was also reflected in the data collected in our meta-analysis: excluding the two RCT, out of a total of 3,910 patients 2,792 (71.4%) patients were submitted to HP while only 1,118 (28.6%) patients underwent PRA (with or without protective ileostomy). Emergency colorectal resection is an independent risk factor for anastomotic leak

(relative risk 4.6, 95% CI 1.9-9.8) and the presence of peritonitis and/or bowel obstruction is also a predictive factor [34]. This is the reason why, in patients with a diffuse peritonitis or occlusion in a colon not prepared, most surgeons commonly avoid the anastomosis for the high risk of dehiscence with major complications for the patient [25,35]. However, many studies, including the only completed randomized clinical trial and four systematic reviews, have demonstrated the feasibility of anastomosis for peritonitis due to perforated diverticulitis so that nowadays the colorectal anastomosis is not absolutely contraindicated in emergency surgery for this disease [5,6,8,36,37]. In particular, the above mentioned studies showed that morbidity and mortality

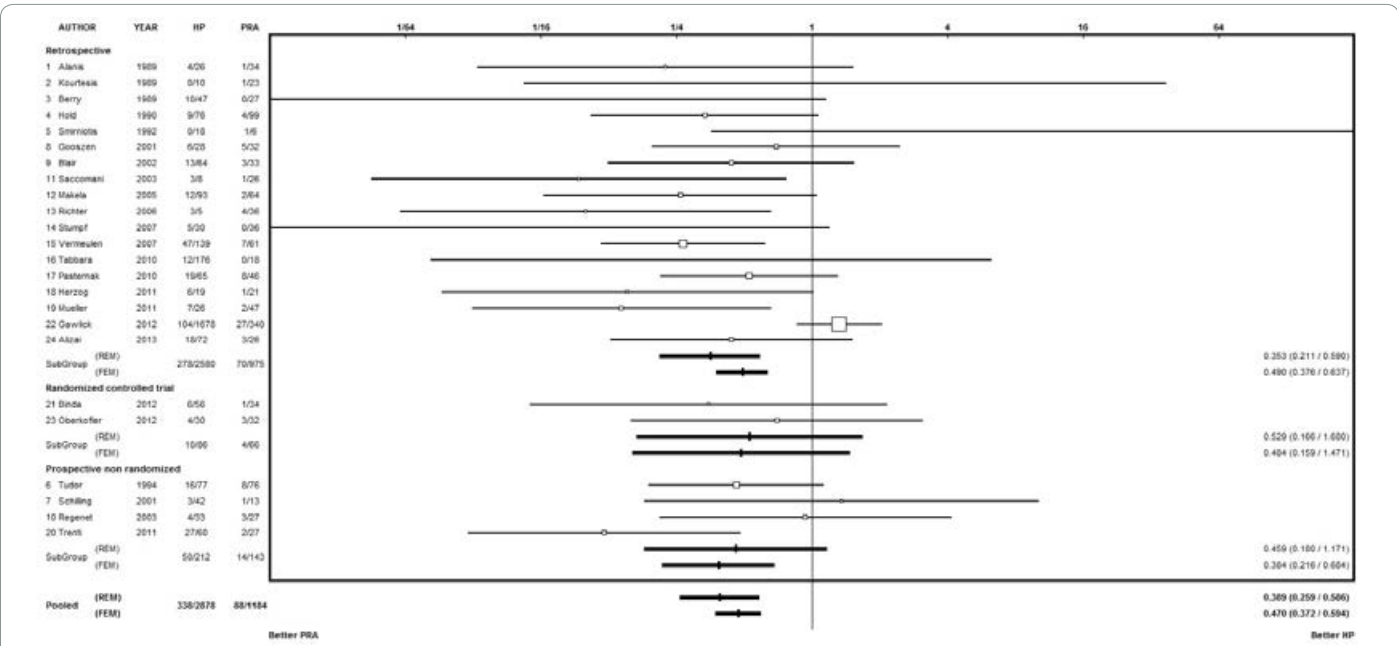


Figure 4: Forest plot for 30-day mortality by study type and results of meta-analysis.

Abbreviations: HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; REM: Random Effect Model; FEM: Fixed Effect Model.

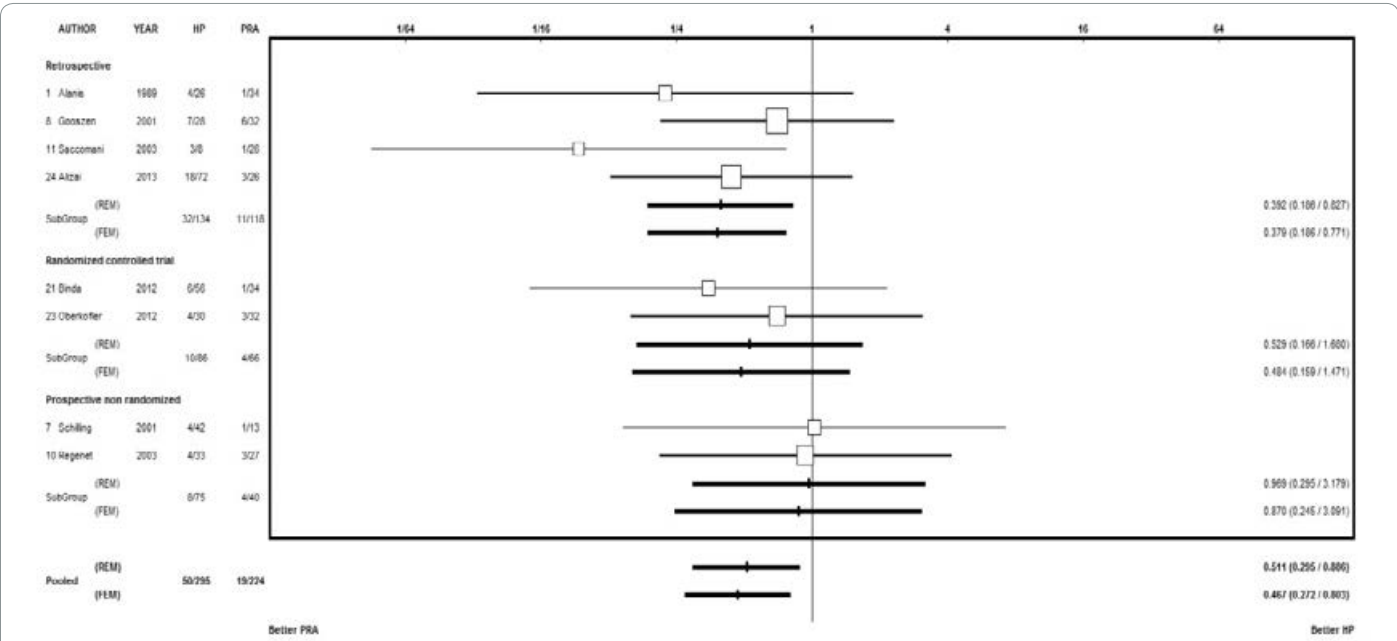


Figure 5: Forest plot for overall mortality by study type and results of meta-analysis.

Abbreviations: HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; REM: Random Effect Model; FEM: Fixed Effect Model.

rates were similar for PRA and HP, but for the second intervention (recanalization) hospital costs, length of stay, operative time and the likelihood of stoma reversal all favored the PRA group [6,38]. Almost all of the studies reviewed, including the two randomized controlled trials and three out of four systematic reviews [5,8,37], considered only patients with peritonitis secondary to perforated diverticulitis (Hinchey stage III-IV). Our review, instead, together with the review performed by Constantinides et al. [36], is the only one that considered all non-elective surgical patients with complicated acute diverticulitis (perforation or bowel obstruction). Indeed, we consider common practice to perform HP also for acute intestinal obstruction secondary

to diverticular sigmoid stenosis with dilated and unprepared proximal colon. Constantinides et al. [36] reported in their review a significantly decreased mortality for emergency operations with PRA vs HP (7.4% vs. 15.6%; OR=0.44). Also the incidence of wound infection and postoperative abscess or peritonitis was significantly lower in the PRA group (OR=0.42 and 0.43, respectively). The results of our review are in agreement with those of Constantinides. In fact, our meta-analysis shows that the 30-day mortality rate is significantly lower in the PRA group vs. the HP group. Also the overall mortality (number of deaths occurred after both the first intervention and the second intervention of recanalization, when indicated) was 8.5% in the PRA group and

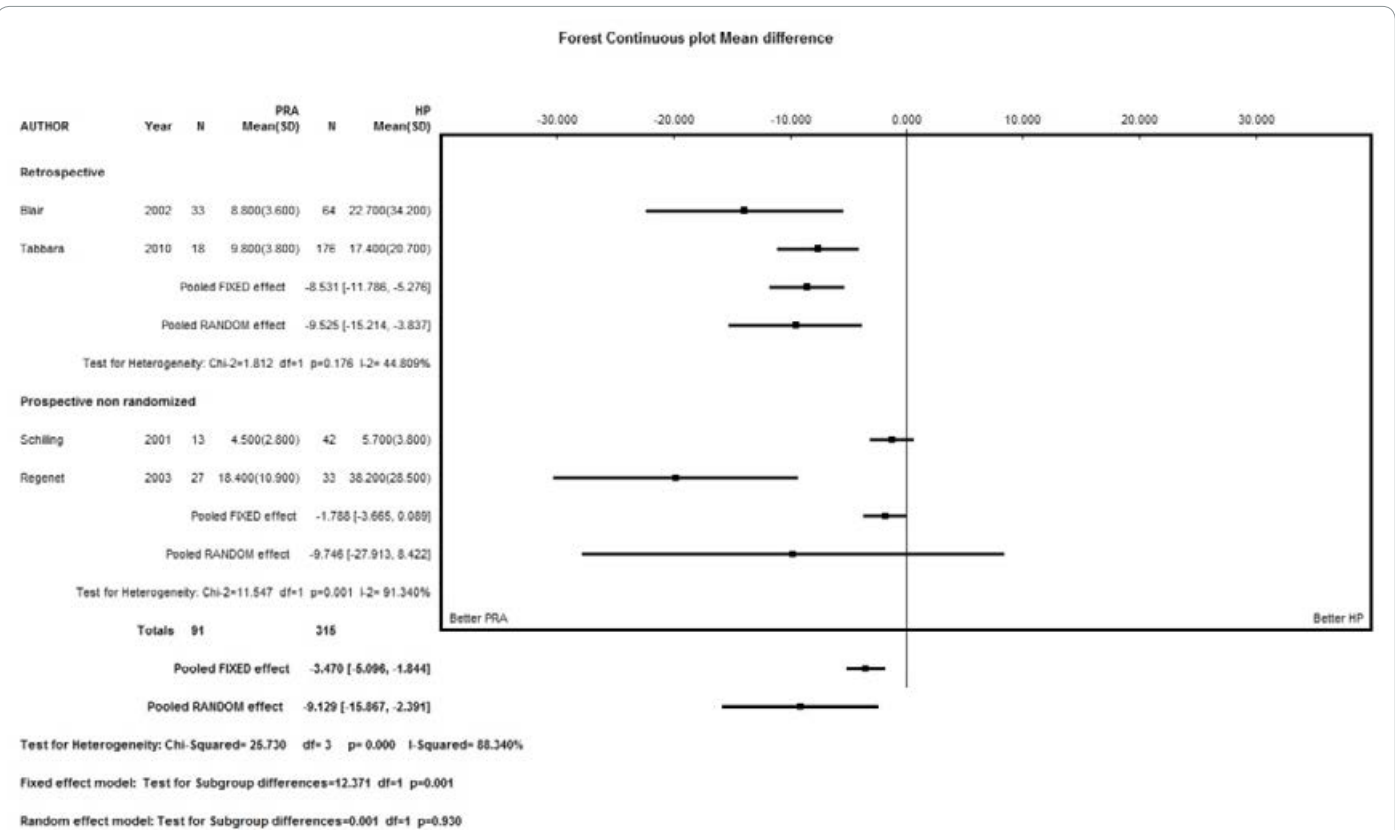


Figure 6: Forest plot for length of hospital stay (days) by study type and results of meta-analysis.

Abbreviations : HP: Hartmann procedure; PRA: Primary resection-anastomosis with or without diverting ileostomy; SD: Standard Deviation; N: Numerosity

16.9% in the HP group. Our study also shows that patients undergoing PRA have a lower risk of reintervention compared to HP group. However, it should be noted that the first cause of reintervention in the PRA group was the anastomotic leak (57.9% of reinterventions). Some of the results of our meta-analysis should be interpreted with caution for several biases related to the variability of the studies, the inclusion of only two RCT of which one was stopped early [39], the wide span of time in which the trials were conducted (1988-2014) and, above all, the patients' selection bias which definitely influenced the results. As previously highlighted, in the retrospective and prospective non randomized studies included in our meta-analysis, the PRA technique was performed only in 28.6% of cases, suggesting that surgeons followed rigorous criteria, such as most favorable clinical conditions, to define the indication to the PRA technique. This could explain the better outcomes shown in this group, in terms of both morbidity and mortality. However, the two randomized controlled trials, of which only one was, concluded [6], and the prospective studies showed average values in favor to the PRA technique, encouraging the promotion of further studies to confirm the hypothesis that the PRA technique is more effective and safer in emergency setting for acute complicated diverticulitis. Furthermore, based on the results of our review, we can assert that the HP is not the only technique to perform in non-elective surgical patients with acute complicated diverticulitis and that, in selected cases; PRA can be executed without increased morbidity and mortality, even obtaining in some cases better results. The surgeon will choose, case by case, the most appropriate technique, taking into account his own experience in colorectal surgery [40] and considering that the anastomotic leak risk is based on the patient's risk factors (severe comorbidities, significant intraoperative hemorrhage, shock, sepsis) [34].

Highlights

- Best surgical technique for complicated acute diverticulitis is an open question.

- Included studies didn't provide strong evidence to define the best surgical technique.
- Primary Anastomosis was better than Hartmann's procedure for all included outcomes.
- Further well-designed studies should be performed to confirm our evidences.

Conclusion

The available studies do not provide strong evidence to define the best surgical technique in non-elective patients with complicated acute diverticulitis (perforation or obstruction). However, in selected cases, the PRA technique may be preferred to HP for the lower morbidity and postoperative mortality. Further randomized controlled trials are required to assess if the PRA technique could be routinely executed, leaving the Hartmann's procedure for particularly severe cases.

Conflicts of interest

Authors have no conflict of interest to disclose.

References

1. Wong WD, Wexner SD, Lowry A, Vernava A 3rd, Burnstein M, et al. (2000) Practice parameters for the treatment of sigmoid diverticulitis--supporting documentation. The Standards Task Force. The American Society of Colon and Rectal Surgeons. Dis Colon Rectum 43: 290-297.
2. Weizman AV, Nguyen GC (2011) Diverticular disease: epidemiology and management. Can J Gastroenterol 25: 385-389.
3. Masoomi H, Buchberg BS, Magno C, Mills SD, Stamos MJ, et al. (2011) Trends in diverticulitis management in the United States from 2002 to 2007. Arch Surg 146: 400-406.
4. Schwesinger WH, Page CP, Gaskill HV 3rd, Steward RM, Chopra S, et al. (2000) Operative management of diverticular emergencies: strategies and outcomes. Arch Surg 135: 558-562.

5. Salem L, Flum DR (2004) Primary anastomosis or Hartmann's procedure for patients with diverticular peritonitis? A systematic review. *Dis Colon Rectum* 47: 1953-1964.
6. Oberkofler CE, Rickenbacher A, Raptis DA, Lehmann K, Villiger P, et al. (2012) A multicenter randomized clinical trial of primary anastomosis or Hartmann's procedure for perforated left colonic diverticulitis with purulent or fecal peritonitis. *Ann Surg* 256: 819-826.
7. Salem L, Anaya DA, Roberts KE, Flum DR (2005) Hartmann's colectomy and reversal in diverticulitis: a population-level assessment. *Dis Colon Rectum* 48: 988-995.
8. Abbas S (2007) Resection and primary anastomosis in acute complicated diverticulitis, a systematic review of the literature. *Int J Colorectal Dis* 22: 351-357.
9. Binda GA, Karas JR, Serventi A, Sokmen S, Amato A, et al. (2012) Study Group on Diverticulitis. Primary anastomosis vs nonrestorative resection for perforated diverticulitis with peritonitis: a prematurely terminated randomized controlled trial. *Colorectal Dis* 14: 1403-1410.
10. Leandro G (2004) *Meta-analysis in Medical Research*. Oxford, Blackwell Publishing, UK.
11. Masoomi H, Stamos MJ, Carmichael JC, Nguyen B, Buchberg B, et al. (2012) Does primary anastomosis with diversion have any advantages over Hartmann's procedure in acute diverticulitis? *Digest Surg* 29: 315-320.
12. Alanis A, Papanicolaou GK, Tadros RR, Fielding LP (1989) Primary resection and anastomosis for treatment of acute diverticulitis. *Dis Colon Rectum* 32: 933-939.
13. Alizai PH, Schulze-Hagen M, Klink CD, Ulmer F, Roeth AA, et al. (2013) Primary anastomosis with a defunctioning stoma versus Hartmann's procedure for perforated diverticulitis—a comparison of stoma reversal rates. *Int J Colorectal Dis* 28: 1681-1688.
14. Berry AR, Turner WH, Mortensen NJ, Kettlewell MG (1989) Emergency surgery for complicated diverticular disease. A five-year experience. *Dis Colon Rectum* 32: 849-854.
15. Blair NP, Germann E (2002) Surgical management of acute sigmoid diverticulitis. *Am J Surg* 183: 525-528.
16. Gawlick U, Nirula R (2012) Resection and primary anastomosis with proximal diversion instead of Hartmann's: evolving the management of diverticulitis using NSQIP data. *J Trauma Acute Care* 72: 807-814.
17. Gooszen AW, Gooszen HG, Veerman W, Van Dongen VM, Hermans J, et al. (2001) Operative treatment of acute complications of diverticular disease: primary or secondary anastomosis after sigmoid resection. *Eur J Surg* 167: 35-39.
18. Herzog T, Janot M, Belyaev O, Sülberg D, Chromik AM, et al. (2011) Complicated sigmoid diverticulitis—Hartmann's procedure or primary anastomosis? *Acta Chir Belg* 111: 378-383.
19. Hold M, Denck H, Bull P (1990) Surgical management of perforating diverticular disease in Austria. *Int J Colorectal Dis* 5: 195-199.
20. Kourtesis GJ, Williams RA, Wilson SE (1988) Surgical options in acute diverticulitis: value of sigmoid resection in dealing with the septic focus. *Aust N Z J Surg* 58: 955-959.
21. Mäkelä JT, Kiviniemi H, Laitinen S (2005) Prognostic factors of perforated sigmoid diverticulitis in the elderly. *Digest Surg* 22: 100-106.
22. Mueller MH, Karpitschka M, Renz B, Kleespies A, Kasperek MS, et al. (2011) Co-morbidity and postsurgical outcome in patients with perforated sigmoid diverticulitis. *Int J Colorectal Dis* 26: 227-234.
23. Pasternak I, Dietrich M, Woodman R, Metzger U, Wattchow DA, et al. (2010) Use of severity classification systems in the surgical decision-making process in emergency laparotomy for perforated diverticulitis. *Int J Colorectal Dis* 25: 463-470.
24. Regenet N, Pessaux P, Hennekinne S, Lermite E, Tuech JJ, et al. (2003) Primary anastomosis after intraoperative colonic lavage vs. Hartmann's procedure in generalized peritonitis complicating diverticular disease of the colon. *Int J Colorectal Dis* 18: 503-507.
25. Richter S, Lindemann W, Kollmar O, Pistorius GA, Maurer CA, et al. (2006) One-stage sigmoid colon resection for perforated sigmoid diverticulitis (Hinchey stages III and IV). *World J Surg* 30: 1027-1032.
26. Saccomani GE, Santi F, Gramegna A (1993) Primary resection with and without anastomosis for perforation of acute diverticulitis. *Acta Chir Belg* 93: 169-172.
27. Schilling MK, Maurer CA, Kollmar O, Büchler MW (2001) Primary vs. secondary anastomosis after sigmoid colon resection for perforated diverticulitis (Hinchey Stage III and IV): a prospective outcome and cost analysis. *Dis Colon Rectum* 44: 699-703.
28. Smiriotis V, Tsoutsos D, Fotopoulos A, Pissiotis AC (1992) Perforated diverticulitis: a surgical dilemma. *Int Surg* 77: 44-47.
29. Stumpf MJ, Vines FY, Edwards J (2007) Is primary anastomosis safe in the surgical management of complications of acute diverticulitis? *Am Surg* 73: 787-790.
30. Tabbara M, Velmahos GC, Butt MU, Chang Y, Spaniolas K, et al. (2010) Missed opportunities for primary repair in complicated acute diverticulitis. *Surgery* 148: 919-924.
31. Trenti L, Biondo S, Golda T, Monica M, Kreisler E, et al. (2011) Generalized peritonitis due to perforated diverticulitis: Hartmann's procedure or primary anastomosis? *Int J Colorectal Dis* 26: 377-384.
32. Tudor RG, Farmakis N, Keighley M (1994) National audit of complicated diverticular disease: analysis of index cases. *Br J Surg* 81: 730-732.
33. Vermeulen J, Akkersdijk GP, Gosselink MP, Hop WC, Mannaerts GH, et al. (2007) Outcome after emergency surgery for acute perforated diverticulitis in 200 cases. *Digest Surg* 24: 361-366.
34. McDermott FD, Heeney A, Kelly ME, Steele RJ, Carlson GL, et al. (2015) Systematic review of preoperative, intraoperative and postoperative risk factors for colorectal anastomotic leaks. *Br J Surg* 102: 462-479.
35. Belmonte C, Klas JV, Perez JJ, Wong WD, Rothenberger DA, et al. (1996) The Hartmann procedure. First choice or last resort in diverticular disease? *Arch Surg* 131: 612-615.
36. Constantinides VA, Tekkis PP, Athanasiou T, Aziz O, Purkayastha S, et al. (2006) Primary resection with anastomosis vs. Hartmann's procedure in nonelective surgery for acute colonic diverticulitis: a systematic review. *Dis Colon Rectum* 49: 966-981.
37. Cirocchi R, Trastulli S, Desiderio J, Listorti C, Boselli C, et al. (2013) Treatment of Hinchey stage III-IV diverticulitis: a systematic review and meta-analysis. *Int J Colorectal Dis* 28: 447-457.
38. Khalil HA, Yoo J (2014) Colorectal emergencies: perforated diverticulitis (operative and nonoperative management). *J Gastrointest Surg* 18: 865-868.
39. Leandro G (2013) How to interpret a randomized controlled study stopped early. *Intens Care Med* 39: 1642-1643.
40. Jafferji MS, Hyman N (2014) Surgeon, not disease severity, often determines the operation for acute complicated diverticulitis. *J Am Coll Surgeons* 218: 1156-1161.

Carpal Tunnel Release: Avoiding Complications with Layer Shield Matrix

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Abstract

Study design

To evaluate the role played by the Layershield matrix (L.S.M.) in avoiding scar tissue and adhesion of the median nerve after decompression in carpal tunnel syndrome.

Objective

Prospective randomized trial to examine this technique. The idea was to investigate the potential benefits when dealing with complications (adherence of the flexor tendons and severing or scarring of the median nerve using the two-inch matrix as an adhesion barrier following mini-open carpal tunnel release).

Summary of background

The study cohort (L.S.M group) consisted of consecutive patients (200 patients) treated with L.S.M. Patients in the standard procedure group (200 patients in all) underwent operations using the same technique in carpal tunnel surgery in both groups, completing follow-up evaluations at no less than 3 to 6 months post-operation. The male to female ratio was 1:6. In twenty patients, there was bilateral involvement.

Method

All operations were conducted by the author at the Hospital General Universitario de Valencia, and the Clínica La Salud, Valencia, Spain, between 2012 and 2013. All patients complained of numbness and/or sensory disturbance or weakness in the median nerve distribution of the hand. Tinel and Phalen sign tests were positive in about two-thirds of patients. EMG studies were performed in all patients and were positive, ranging from mild to severe.

Results

Numbness and paresthesia were relieved in 95% of patients in the L.S.M. group and 89% in the control group (CG). Pain was relieved in 95% DG and 90% CG. Motor weakness was relieved in 95% DG and 92% CG. Normal grip strength was evident in 93% DG and 91% had normal pinch strength.

Re-operation rate

Adherence of the flexor tendons in 3 CG patients and 8 patients due to scarring involving the median nerve, with the L.S. matrix group undergoing re-operation for the following reasons: recurrent pain (3 patients due to scarring around the median nerve). The difference in the re-operation rate between the collagen matrix group and the standard procedure group is statistically significant ($p < 0.01$).

Conclusion

Findings in this study (reduced pain and lower incidence of adhesions) are consistent with the L.S. matrix acting as an effective adhesion barrier. By preventing median nerve adhesions, the L.S. matrix may significantly reduce the incidence of disabling pain associated with re-operation. Ultimately, the prophylactic use of the Layershield Matrix to prevent adhesions may result in improved patient outcomes.

Keywords: Carpal tunnel release; Carpal tunnel syndrome; Short incision; Physical barrier

Introduction

Carpal tunnel syndrome (CTS), or compressive median neuropathy at the transverse carpal ligament, is the mononeuropathy most commonly encountered in clinical practice. It has an estimated prevalence of 125 cases per 100,000 populations [1], although other surveys indicate that the prevalence may be as high as 1% of the population [2]. The clinical signs and symptoms include hand paresthesia, upper-extremity pain, Tinel's sign on percussion over the median nerve at the wrist, Phalen's sign, median distribution sensory loss, and thenar muscle weakness and atrophy. Many of these clinical features are not unique to CTS and distinguishing among the several causes of upper-extremity signs and symptoms often has important therapeutic implications. Electrodiagnostic testing, including motor and sensory nerve conduction studies and needle electromyographic

(EMG) studies, plays an important role in the evaluation of patients with possible CTS. Electrodiagnostic testing has been shown to have a high degree of sensitivity and specificity in evaluation of CTS [3]. In addition, it may help to identify superimposed or alternative neuropathic conditions mimicking CTS, such as cervical

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radiculopathy, brachial plexopathy, proximal median neuropathy or other upper limb mononeuropathies, as well as peripheral neuropathy. When electrodiagnostic testing is normal, this may suggest that non-neuropathic conditions, such as arthritis or tendinitis, are responsible for the patient's symptoms. Despite the clear value of nerve conduction and EMG studies in the evaluation of patients with possible CTS, the tests may be underutilized in clinical practice. Since CTS has become an important public health problem because of its frequent occurrence in workplace settings leading to repetitive stress injury, its diagnosis and treatment have attracted the attention of organized medicine and governmental agencies. At least nine medical specialty societies have published position papers of various kinds, and three governmental agencies have issued statements on the subject [4]. There is an increasing debate related to the proper setting for electrodiagnostic testing, and some attempt has been made to limit its use in the diagnosis of CTS. Much of this debate has been based on the opinions of individuals or groups with varying degrees of expertise in the field, little on actual data. We carried out this study in order to determine the actual real-life experience of a clinical neurophysiology laboratory in the evaluation of CTS. Surgical division of the transverse carpal ligament (TCL) has been performed since 1933 and is usually a relatively simple procedure [5]. A recent report on a microsurgical carpal tunnel release (CTR) technique, performed on an outpatient basis, documented excellent results equal to those obtained by using minimally invasive techniques such as the retinaculotomy or the endoscope [6]. The reported advantage of the minimally invasive techniques is a small-sized incision, which allows for a short operating time and an early return to work for the patient.

A thorough knowledge of the anatomy of the carpal tunnel is essential in order to avoid complications and to ensure optimal patient outcome. There are many strong arguments for open (short 2-cm incision) vs. conservative treatment. Nerve conduction studies (NCS) potentially have great value in selecting patients for a specific treatment and in objectively assessing the efficacy of treatment for carpal tunnel syndrome. Release of the transverse carpal ligament can be performed safely under local anaesthetic without requiring a tourniquet (bupivacaine 0.5% without adrenaline) and bipolar diathermy. The local anaesthetic was injected into the carpal tunnel and into the subcutaneous tissue under the skin incision, from proximal to distal, in order to make infiltration more comfortable.

Purpose

The objective of this prospective clinical study was to investigate the potential benefits when dealing with complications (adherence of the flexor tendons and severing or scarring of the median nerve) using the Layershield Matrix (Suprofilm™) as an adhesion barrier following mini open carpal tunnel release.

Patients and Setting

The study cohort (L.S matrix group) consisted of consecutive patients (200 patients) treated with Suprofilm. Patients in the standard procedure group (200 patients in all) underwent operations without using the matrix. Patients underwent carpal tunnel surgery (Figure 1) using the same technique in both groups and completed follow-up evaluations at no less than 12 to 24 months post-operation. The male to female ratio was 1:6. Twenty patients were found to have bilateral involvement. All operations were conducted by the author (2012-2013). All patients complained of numbness and/or sensory disturbance or weakness in the median nerve distribution of the hand. Tinel and Phalen sign tests were positive in about two-thirds of patients. EMG studies were performed in all patients and were positive, ranging from mild to severe.

Study Design and Technique

To evaluate the role played by the L.S matrix in avoiding scar tissue

and adhesion of the median nerve after decompression in carpal tunnel syndrome (Figure 2).

Results

Numbness and paresthesia were relieved in 95% of patients in the L.S.M group and 89% in the control group (CG). Pain was relieved in 95% DG and 90% CG. Motor weakness was relieved in 95% DG and 92% CG. Normal grip strength was evident in 93% DG and 91% had normal pinch strength.

Re-operation Rate

Adherence of the flexor tendons in 3 CG patients and 8 patients due to scarring involved the median nerve, with the L.S matrix group undergoing re-operation for the following reasons: recurrent pain (3 patients for scarring around the median nerve). The difference in re-operation rate between the L.S matrix group and the standard procedure group is statistically significant ($p < 0.01$). There were no infections or complications due to the L.S matrix. After 8 weeks the matrix became endogenous tissue, meaning that fibrosis was over at this point.

Discussion

Long-term persistent pain is a major determinant for the success or failure of open carpal tunnel release (OCTR). The complication of long-term persistent pain may arise from any of the following causes: hypertrophic skin scarring, intra- and perineural scarring, adherence of the nerve to the skin, subcutaneous tender nerve secondary to



Figure 1: Short incision for a carpal tunnel release.



Figure 2: Suprofilm matrix in place to avoid complications: scarring of the median nerve.

superficial position, adhesions between flexor tendons and the median nerve, pillar pain at the thenar and hypothenar eminences, and reflex sympathetic dystrophy (RSD) [7]. Hypertrophic scars are often the result of an incision that transverses the flexion crease at a right angle. If a painful hypertrophic scar should occur despite all attempts to prevent this, scar revision should be performed [8]. Intra- and perineural scarring sometimes produces dysesthesia, pain and hypersensitivity. Proper hemostasis is important to prevent perineural scarring [9]. If intra- and perineural scarring should develop despite the surgeon's best efforts to prevent it, the hypersensitivity and dysesthesia respond to coverage of the nerve with a L.S matrix (Figure 1).

The superficial position of the median nerve and adherence of the nerve to the skin are usually consequences of an improper skin incision directly above the nerve, rather than toward the ulna. Splinting the wrist in a slightly dorsiflexed position for the first 3 to 5 postoperative days may lessen the likelihood of superficial nerve position [10]. Three common methods of insulating the nerve from the skin surface include: rotation of a hypothenar fat-pad flap; rotation of local muscle pedicle flaps, such as the pronator quadratus and abductor digiti minimi; and Z-plasty with underlying temporary silicone sheeting, or the easy way [11] is to use L.S matrix to prevent scar adherence. Tendon adhesions may result from poor hemostasis during conventional OCTR surgery or from bleeding associated with tenosynovectomy. Resection of the synovium is usually indicated only in cases of an extremely bulky synovium, such as those associated with rheumatoid arthritis, because of the propensity of tenosynovectomy to cause bleeding and scar formation with subsequent adhesions between tendons or between tendons and the median nerve [12]. Using the matrix may reduce this point. Preoperatively, patients should be informed about the expected clinical course following carpal tunnel release. They should be specifically warned about tenderness around the incision for up to 8-12 weeks after the operation. Although night-time symptoms are often relieved immediately, other symptoms, such as persistent numbness, weakness or clumsiness are due to nerve damage. These will be very gradually resolved, and recovery may be incomplete [13]. The patient should be counselled regarding activity modification and the possible impact on his/her employment. The patient should also be instructed on the isolated tendon-gliding exercises to be initiated postoperatively.

Gentle exercise and light use of the hand is encouraged from the day after surgery. The bandage and stitches are removed about a week after surgery. The palm is tender for at least four to six weeks after the procedure. Golf and hand-related sports are usually too uncomfortable for up to six to eight weeks postop.

Patients planning to return immediately to strenuous activities may do so in a short arm cast or strong clamshell splint, 30 degrees wrist dorsiflexion, basal joint immobilized, worn for one month.

The effects of scar tissue shrinking and maturing result in adhesions which pull on the median nerve and often result in brief shooting or electrical pains with motion, particularly when the patient stretches his or her hand out to reach something at arm's length. Sudden shooting or electrical shock pains may also occur spontaneously while the patient is inactive. Both of these are normal occurrences and improve with time [14]. The shrinking and swelling associated with scar maturation results in the feeling of a lump at the base of the palm at the proximal end of the incision. This is most noticeable when the patient leans on the hand while changing from a sitting to a standing position. This is normal and improves over time and with massages. Patients are given therapy to make their hands less tender. Grip strength is normally reduced for two to three months following surgery, but full recovery can be expected. The mid-proximal palm is normally the most sensitive and tender to the touch during the interval from two to six weeks following surgery. The patient is given clearance to resume light activities within their own tolerance level, including driving, as soon as they feel comfortable

enough to do so. They are encouraged to use common sense and avoid activities that may cause pain. They are normally seen for a follow-up visit four to six weeks after surgery.

Conclusion

Findings in this study (reduced pain and lower incidence of adhesions) are consistent with the Suprofilm Matrix acting as an effective adhesion barrier. By preventing median nerve adhesions, the collagen dural matrix may significantly reduce the incidence of disabling pain associated with re-operation. Ultimately, the prophylactic use of the L.S Matrix to prevent adhesions may result in improved patient outcomes.

Conflict of interest

Authors have no conflict of interests to declare

References

- Dayican A, Unal VS, Portakal S, Utkan A, Tumor MA (2004) Carpal tunnel release: using a short vertical incision above the flexor crease of the wrist. *Mt Sinai J Med* 71: 401-404.
- Jugovac I, Burgic N, Micovic V, Ralojovic L, Stanic MF, et al. (2002) Carpal tunnel release by limited incision vs. traditional open technique; randomized controlled trial. *Croat MED J* 43: 33-36.
- Schuh A, Schuh R (2002) Experience with 925 outpatient operations of carpal tunnel syndrome. *Zentralbl Chir* 127: 224-227.
- Bradley MP, Hayes EP, Weiss AP, Akelman E (2003) A prospective study of outcomes following mini-open carpal tunnel release. *Hand Surg* 8: 59-63.
- Klein RD, Kotsis SV, Chung KC (2003) Open carpal tunnel release using a 1-centimeter incision: technique and outcomes for 104 patients. *Plast Reconstr Surg* 111: 1616-1622.
- Rotman MB, Donovan JP (2002) Practical anatomy of the carpal tunnel. *Hand Clin* 18: 219-230.
- Hallock, Geoffrey G, Lutz, Debra ARN (1995) Prospective comparison of minimal incision "open" and two-portal endoscopic carpal tunnel release. *Plast Reconstr Surg* 96: 941-947
- Jacobsen MB, Rahme H (1996) A prospective, randomized study with an independent observer comparing open carpal tunnel release with endoscopic carpal tunnel release. *J Hand Surg* 21: 202-204.
- Jakab E, Ganos D, Cook FW (1991) Transverse carpal ligament reconstruction in surgery for carpal tunnel syndrome: a new technique. *J Hand Surg* 16: 202-206.
- Kelly CP, Pulisetti D, Jamieson AM (1994) Early experience with endoscopic carpal tunnel release. *J Hand Surg* 19: 18-21.
- Kluge W, Simpson RG, Nicol AC (1996) Late complications after open carpal tunnel decompression. *J Hand Surg* 21: 205-207.
- Kuschnier SH, Brien WW, Johnson D, Gellman H (1996) Complications associated with carpal tunnel release. *Orthop Rev* 4:346-352.
- Kuschnier SH, Ebramzadeh E, Johnson D (1992) Tinel's sign and Phalen's test in carpal tunnel syndrome. *Orthopedics* 15:1297-1302.
- Nathan PA, Meadows KD, Keniston RC (1993) Rehabilitation of carpal tunnel surgery patients using a short surgical incision and an early program of physical therapy. *J Hand Surg (Am)* 18: 1044-1050.

Anorectal Malformations in a Tertiary Pediatric Surgery Center from Romania: 20 Years of Experience

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Abstract

Introduction: The main goal of surgery and multidisciplinary behavioral therapy in anorectal malformations (ARMs) is to achieve good anatomical and functional outcomes and a better quality of life.

Material and Methods: A retrospective analysis of 146 patients with ARMs was conducted over a 20 years period in our pediatric surgery department. The clinical and demographical data, operative protocols, short and long term outcomes were subject to assessment.

Results: The patient series included 85 boys and 61 girls aged between one day and two years, of which 82.19% were diagnosed in the first few days of life by means of clinical examination and current imaging tests. In 26.02% of cases we found associated congenital abnormalities. A total of 142 (97.25%) cases of all our series underwent surgical treatment; four patients died before surgery. For 131 children the definitive treatment involved posterior sagittal anorectoplasty (PSARP) respectively 11 posterior sagittal anorectovaginourethroplasty (PSARVUP). Long-term follow-up in 115 patients showed good clinical continence in 82 cases (71.30%) but more than half of the teenagers had body dissatisfaction and social difficulties.

Conclusions: Through this review of 20 years of experience our findings are consistent with other reports regarding male predominance, low birth weight, clinical and imaging diagnosis. We found however a lower incidence of associated abnormalities. The most frequent surgical intervention was posterior sagittal anorectoplasty (PSARP) or posterior sagittal anorectovaginourethroplasty (PSARVUP), both followed by satisfactory functional outcome reporting nevertheless moderate social insertion. Our experience in ARMs proved the effectiveness of the consecrated surgical strategy; long-term assistance for patients and their families should be improved.

Keywords: Rectum; Anorectal malformations; Anorectoplasty; Anorectovaginourethroplasty

Introduction

Anorectal malformations (ARMs) are a group of commonly encountered congenital anomalies in pediatric surgery practice, with an incidence of 2 in 1000 to 1 in 5000 live births, but with significant variations between different regions throughout the world, as reported in the literature [1,2]. According to Peña and Bechit there is a wide spectrum of presentation, ranging from low perineal fistula to high anomalies with complex surgical management [3,4]. As Stoll and Moore discussed, ARMs are often associated with a complex range of another anomalies i.e. esophageal atresia, and central nervous system, cardiovascular, urogenital, gastrointestinal and skeletal defects [5,6]. In his report, Holschneider stated that the advances in imaging techniques and improvements in the knowledge of embryology, anatomy and physiology of ARM cases have refined both diagnosis and surgical therapy [7]. Other authors found that the classical approach to this pathology have moved towards PSARP and minimally invasive techniques with a clear goal of improving anatomical and functional outcomes and quality of life [8]. However constipation and fecal incontinence are still the main concerns regarding the long-term outcomes in these patients, as was discussed by de Blaauw et al. [9]

Material and Methods

We performed a retrospective study by analyzing the clinical records of all the ARMs patients managed in the Pediatric Surgery Department of "St. Mary" Children Emergency Hospital of Iași, Romania over a 20 years period (1996-2015). The collected data included demographic and social

characteristics of the mother and child, birth weight, type of ARMs, clinical features including associated malformations, imaging tests, initial and definitive surgical approach and postoperative outcomes, comprising a long term follow-up with respect to functional aspects, psychological modifications associated with chronic disabilities, social insertion, and quality of life.

Results

The patient series included 146 children, 85 boys and 61 girls, with ages between 1 day and 2 years old, with a mean age of 46.4 ± 5.7 days. Our report showed male predominance (58.21% vs 41.78%) along with a higher frequency in neonates with low birth weight (68.4% of all the patients, N = 100). A significant percentage of these children came from rural areas (64.4%, N = 94) and from families with low incomes (75.34%, N = 110). Mothers' age ranged from 16 to 42 years old, with a mean age of 21.3 ± 2.3 years old. The initial diagnosis was made

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in the first four days of life by means of a full physical examination in 120 patients (82.19%), within the first year of life in 14 cases (9.58%), and after one year in 12 children (8.21%) respectively. In the cases with delayed diagnosis, the main presenting complaint was chronic constipation. Although most of the patients admitted in our department were usually diagnosed at birth, some of them the anomaly correctly diagnosed beyond the early newborn period. All these cases were patients with perineal fistula, both males and females, or girls with vestibular fistula, in which a superficial examination of the perineal area and the presence of feces evacuation through the fistula in the first days of life led to a delay in establishing the diagnosis. These children subsequently developed constipation that consistently coincided with a change in their diet from breast milk to formula, or at the time of switching to solid food, so they were admitted for a pediatric surgical examination which identified the malformation. In the neonatal period, the anomaly presented most frequently with abdominal distension, vomiting and failure to pass meconium, associated with an abnormal aspect of the perineum (with or without the presence of an orifice). Upon perineal inspection, the most frequent clinical sign that we identified was the absence of a normal anal opening. Other frequently encountered findings upon physical examination included a bulge in the perineum or an anterior anal opening, meconium in urine and stool passing through the vestibule or, in the case of girls, through the vagina. Older patients presented with constipation and/or narrow anal opening (Table I).

Clinical diagnosis of so called “low” ARMs was made in almost all of the male and female patients, while the more complex cases required further explorations. However, all the patients underwent plain thoracic and abdominal X-Ray, as well as cardiac and abdominal ultrasound to assess cardiac, genitourinary, vertebral and other associated anomalies. Invertography was performed in 27 cases (18.49%) to determine the location of the rectal pouch in patients without visible fistula (Figure 1).

Other imaging contrast studies such as rectal pouch examination, fistulography and urethrography were performed in 40 cases (27.39%), while voiding cystography was conducted in 15 cases (10.27%) in order to detect the rectal urethral fistula or associated vesicoureteral reflux. Endoscopic evaluation of the genitourinary tract was performed in 62 patients (42.46%), including 11 cases of cloaca, in order to assess the complexity of the malformation. In 8 of these cases the length of the common channel was less than 3 cm. Other endoscopic findings included the presence of a septate vagina (2 cases) and the identification of recto-urethral fistula (3 cases). In two cases perineal ultrasound measured the distance between the rectal pouch and perineal skin. None of the patients underwent CT or MRI explorations. As far as the type of ARMs according to Peña's classification is concerned, there were 87 perineal fistulas (59.58%), 26 cases (17.80%) of imperforate anus without fistula, 14 vestibular fistulas (9.58%), 11 cases (7.53%) of cloaca, 6 rectourethral fistulas (4.10%), and two patients with rectal atresia (1.36%) (Table II and Figure 2).

Associated abnormalities were found in 38 patients (26.02%), some of them having two or even three congenital defects. The most common were genitourinary lesions in 14 patients (9.58%), including congenital hydronephrosis, hypospadias, renal agenesis, undescended testis, and Mayer-Rokitansky syndrome. Cardiovascular anomalies were reported in 11 cases (7.53%), including tetralogy of Fallot (TOF), ventricular or atrial septal defect, coarctation of the aorta or left ventricle hypoplasia. We noticed a significant incidence of Down syndrome (12 cases; 8.21%), esophageal atresia (8 cases; 5.47%), vertebral anomalies (myelomeningoceles) (6 cases; 4.10%) and omphalocele, cloacal exstrophy, imperforate anus and spinal defects complex (OESI) (2 cases; 1.36%).

Surgical treatment was performed in 142 out of 146 patients; four patients died before surgery due to multiple associated congenital anomalies. The surgical approach and timing were dictated by the

type and anatomy of the malformation, general condition at the time of presentation, and additional pathology (Table III). A total of 33 patients (23.23%) underwent colostomy; in 30 children, the colostomy was placed on the transverse colon, while the other three were fitted with a divided colostomy placed at the end of the descending colon. All the female patients with cloaca and vestibular fistula received an ostomy, and all the rectourethral fistulas in male patients were managed in the same way. Also, the colostomy as the first surgical procedure was performed on the two patients with rectal atresia. The preliminary colostomy was part of three stage repair, as all cases subsequently underwent posterior sagittal anorectoplasty (PSARP) or posterior sagittal anorectovaginourethroplasty (PSARVUP), and finally colostomy closure. All the patients with imperforate anus or perineal fistula (109 patients) underwent a mini PSARP or PSARP procedure, without requiring a colostomy, so in 76.76% of the cases the original and preferred surgical protocol was a definitive anorectal reconstruction (Figure 3). The definitive treatment in 131 children (92.25%) was PSARP, with an additional abdominal access in 4 cases due to a high placed rectal pouch. All cloacal cases underwent a PSARPVUP procedure (7.74%) with abdominal access in 4 cases. Early postoperative complications were minor, including perineal wound infection (4 patients), and colostomy related complications – prolapse (4 cases) and stenosis (1 case); all such complications were treated conservatively. We also reported three postoperative obstructions which required surgical therapy. Patient follow-up was carried out on a regular basis for all the patients every 1, 3, 6 and 12 months, and then annually. In patients over the age of three, periodic monitoring included clinical continence, social insertion and their quality of life. The functional outcome was assessed in 115 patients over the age of three, and the results were as follows: good in 82 cases (71.30%) – presence of voluntary defecation, no or occasionally soiling, absent or mild constipation; acceptable in 25 cases (21.73%) – presence of bowel movement, rare soiling, moderate constipation; and poor in 8 cases (6.95%) – absence of voluntary defecation, moderate to severe soiling and any degree of constipation. Three of these cases required additional surgery for continence purposes. In the follow-up group, 39 children (33.91%) presented with constipation, which was more prevalent in the group with perineal, vestibular fistula and imperforate anus, but it

Table I: Associations of clinical findings in children with ARMs.

Clinical Findings	N (%)
Vomiting, abdominal distension	69 patients (47.26%)
Failure to pass meconium	63 patients (43.15%)
Bulge in perineum with absent anus	42 patients (28.76%)
Anterior anal opening	33 patients (22.60%)
Constipation/narrow anal opening	26 patients (17.80%)
Meconium in urine	21 patients (14.38%)
Passing meconium through the vagina / vestibule	20 patients (13.69%)

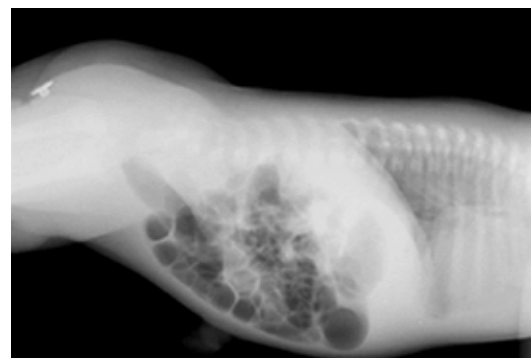
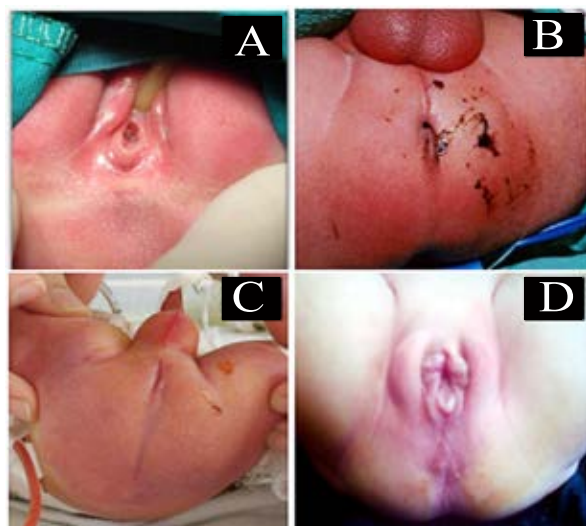


Figure 1: Invertography: Holding the baby upside down, a lateral radiography is performed to observe the distance between the level of gas in the distal rectum and a metal piece placed over the expected anus

Table II: ARM type; case distribution (according to Peña's classification).

Males	N/%	Females	N/%
Perineal fistula	57/39.04	Perineal fistula	30/20.54
Imperforate anus without fistula	21/14.38	Imperforate anus without fistula	5/3.42
Rectourethral fistula	6/4.1	Vestibular fistula	14/9.58
Rectal atresia	1/0.68	Cloaca	11/7.53
		Rectal atresia	1/0.68

**Figure 2:** Anorectal malformation—clinical aspects. A: Perineal fistula; B: Vestibular fistula; C: Rectourethral fistula; D: Cloaca.

was associated with good bowel control. On the other hand, cases with severe malformations (cloaca, recto-urethral fistula, rectal agenesis) were found to have a high prevalence of soiling (8 cases, 6.95 %). A small group of 44 children (24 males and 20 females) remained in our database until the age of 18; psychological assistance was provided in all cases, along with short psychotherapy meetings. Standardized interviews were used to assess the patients' school performances and behavior, while validated tests and questionnaires were used to evaluate their intelligence, attention, self-esteem and quality of life. The majority of the patients (35 cases, 79.54%) have normal intelligence (for IQ, $M = 92$) with no statistically significant difference between boys and girls. All patients were enrolled in normal schools. Psychological distress and emotional difficulties were identified in teenagers (32 cases, 72.72%) together with a low level of body-consciousness and self-confidence, as well as a relatively reduced autonomy and social contacts (28 cases, 63.63%). Over half of these children (26 patients, 59.09%) avoided participating in activities that are specific for their age.

Discussion

Malformations of the anus, anal canal and rectum are relatively common congenital defects, often coexisting in a significant percentage of cases with other congenital anomalies, but as different authors reporting their incidence has major differences in terms of worldwide geographic distribution [1-3,7]. Researchers such as de Blaauw and Wijers found that the causes of ARMs are unknown, but some studies demonstrated a genetic predisposition to these conditions [9,10]. ARMs include a wide spectrum of inborn defects ranging from perineal fistulas that require a relatively simple modality of treatment to major defects that require complex management. The multiple taxonomy of these lesions (Wingspread, Peña, Kirkenbeck) proposed in the literature is rather confusing, most practitioners currently favoring a classification based on the anatomical criteria depending on the position of the rectal pouch relative to the puborectal sling, associated

abnormalities ("syndromic" forms) and the presence or absence of fistulas [2,10,11]. Advances in imaging techniques along with improvements in embryology, morphology and pathogenesis of these lesions have refined both diagnosis and management, moving from classical procedures to PSARP (VUP) and even minimally invasive methods, as discussed by different authors [12-18]. In our report we noticed a male predominance and a higher frequency in male neonates with low birth weight. The median age of the mothers was 21.3 ± 2.3 years, lower than the national average reported by the National Statistics Institute for that period, i.e. 22.5-26.0 years [19]. These findings are consistent with Vermes' report, which suggested that the male gender and intrauterine growth restriction, together with mother's age and low socioeconomic conditions may have an impact on the risk of ARMs [20]. In our series, the majority of ARMs were diagnosed at or soon after birth upon routine postnatal examination. Evident features of these anomalies included the absence of the anus or an abnormal appearance of the perineum, i.e. lack of or minimal passage of meconium, but evidence of perineal, vestibular, recto-urethral fistula or persistent cloaca (as a frequent deformity in female patients). In addition to this, clinical signs in the neonatal period included vomiting, abdominal distension, and failure to pass meconium. We performed VACTERL (Vertebral anomalies, Anal atresia, Cardiac defects, Tracheoesophageal and/or Esophageal atresia, Renal and Radial anomalies, and Limb defects) screening in all newborn with a diagnosis of ARMs upon the first perineal inspection. However, we have identified a number of 26 cases (17.80%) with a late diagnosis in children with perineal fistula or vestibular fistula misdiagnosed in the neonatal period and referred to us due to severe constipation or narrow anal opening. We consider that a correct physical examination of the perineal area is crucial in the neonatal period in order to avoid a delay in the diagnosis of these cases. In a quarter of the cases, ARMs presented with associated abnormalities, the most common of which were urinary tract and cardiovascular defects. Our findings are not consistent with other authors' research that finds an association between anorectal malformations and other inborn defects ranging from 68% to 78%. As far as the types of associated congenital defects are concerned, the literature reports a variety of multisystemic conditions associated with ARMs including MURCS (Müllerian duct aplasia, Renal aplasia, Cervicothoracic Somite dysplasia), trisomy 13, 18, 21 or cat-eye, caudal regression, facio-auriculo-vertebral and fetal alcohol syndromes [21]. Authors like Bălănescu and Nah found an increased incidence of gastrointestinal and urogenital defects, while others found more genitourinary and spinal anomalies [14,22]. The most frequent associations in our study were genitourinary malformations and Down syndrome, followed by cardiovascular anomalies and esophageal atresia. The diagnosis of ARMs in our series was mainly clinical, including routine imaging (thoracic, abdominal, pelvic and spinal X-rays) and invertography, abdominal ultrasound and contrast studies, along with endoscopic evaluation that aimed to evaluate the topography and extent of the lesion. The recent ARM-Net meeting brought minor changes to the preoperative management of ARMs regarding the 24 hours re-evaluation and cross-table lateral X-ray, compared to Levitt and Peña's flow chart [23,24]. It was suggested that in a newborn male with a perineal fistula, a cross-table lateral X-ray is unnecessary, this procedure being recommended only in cases of normal buttocks, normal spine, normal sacrum, and negative urinalysis on meconium; this protocol was extended to female neonates with visible fistula. Early diagnosis was essential for short and long term prognosis. Almost all our patients underwent surgery, except for a few patients (4 cases, 2.73%) with delayed admission, major comorbidities and impaired general condition, who died shortly after presentation. Neonates with low-type ARMs benefit from minimal PSARP, with good short and long term results. PSARP was performed in male patients with cases of high-type ARMs, preceded by a protective colostomy. All cloaca cases were treated in the neonatal period by

Table III: Types of surgical procedures in patients with ARM.

Arm Type	First Surgical Procedure	Definitive Surgery
Perineal fistula	(mini)-PSARP – 85 cases	
Rectourethral fistula	Colostomy – 6 cases	PSARP – 4 cases PSARP + abdominal approach – 2 cases
Vestibular fistula	Colostomy – 14 cases	PSARP – 14 cases
Imperforate anus without fistula	(mini)-PSARP – 24 cases	
Rectal atresia	Colostomy – 2 cases	PSARP + abdominal approach – 2 cases
Cloacal malformation	Colostomy – 11 cases	PSARVUP – 7 cases PSARVUP + abdominal approach – 4 cases

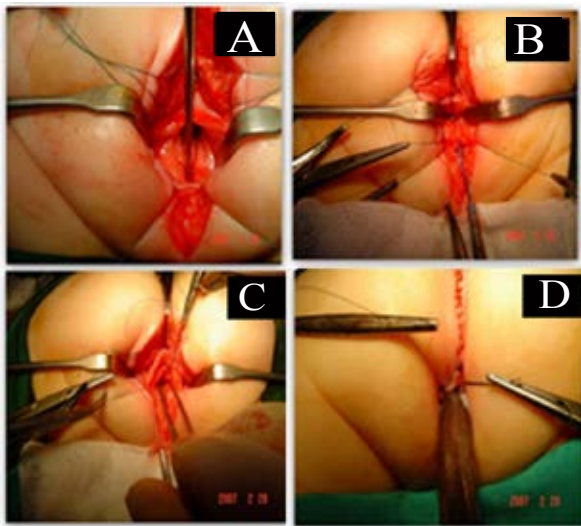


Figure 3: Rectourethral fistula: PSARP procedure; A: Identification of the rectourethral fistula (with metal probe inside); B: Isolation of the fistula with multiple sutures; C: Closure of the fistula and complete separation of the rectum; D: Final aspect of the anoplasty.

placing a colostomy, and a PSARVUP procedure was later used as final surgery, sometimes requiring an associated abdominal approach. As far as the treatment alternatives for female patients with vestibular fistula are concerned, the literature argues for either a one or a three stages surgery. The supporters of perineal surgery in the neonatal period champion the idea of one stage surgery for the purpose of reducing possible anesthesia and morbidities-related colostomy complications. However, this type of surgery requires good bowel preparation, as there is a great risk of infection. We preferred to do a three stages surgery (colostomy, followed by PSARP and then colostomy closure) in a more cautious approach, although there are studies like Adeniran's and Liu's showing no significant differences in functional outcomes between a one stage and three stage operation [25,26]. The final goal of the surgical treatment in ARMs is to obtain an anus placed within the muscular complex, by separating the rectum from the genital or urinary tract and also to gain continence without any social impairment. The long term functional outcome is essential for these patients' quality of life. During our follow up period, we noted that 71.30% of the cases acquired voluntary bowel movements, these results being similar to those previously reported by Sohyun Nam (84.8%) or Peña (75%) [8,27]. Almost half (42.10%) of the children with high anomalies like cloaca, recto-urethral fistula and rectal atresia presented with moderate and severe soiling (i.e. 6.95 % of patients in the follow-up group), a result that also seemed similar to other series, as Rintala reported a rate of 30% soiling in these patients [28]. The majority of patients that remained in our database until the age of 18 had a normal intelligence, but their sustained attention was below the norm. This data is consistent with Hondel's studies, which also suggest that these patients should benefit from special education or remedial teaching [29,30]. All the children from our sample were enrolled in

normal schools. Due to educational policies in Romania of the last two decades, we have no cases of children integrated in a special institution. We found that 63.63% of teenagers were dissatisfied with their body and 59.09% were having difficulties in social activities; our results are consistent with Grano's reports on self-perception and social insertion in children with ARMs [31]. Schmiedeke considers that multidisciplinary behavioral treatment (MBT) should offer psychological assistance both for the parents and the child, as well as physical therapy, thus reducing psycho-social distress. There is still an open discussion regarding the possibilities of accurate quantification of the short and long term outcomes. Despite our sometimes limited possibilities to investigate these children, we succeeded in taking a correct approach to our cases, with promising short and long term results of definitive surgery; reduced morbidity and lack of postoperative mortality come to support our approach to surgical treatment of this pathology. This study has several limitations as it is a single center report and it only provides limited data regarding the long-term monitoring of the patients. We intend to focus our future research on vestibular fistula dilation in selected patients. (Low birth weight <2,000 g or severe associated congenital anomalies).

Conclusion

A better understanding of pathogenesis with more accurate pre- and intraoperative diagnosis together with continuous perfectible practice of established operative techniques appear to be the keys to success in ARMs management, aligning our team experience and expertise toward reputed centers. We support a multidisciplinary approach to these cases, using complex teams that include neonatologists, pediatrics, surgeons, pediatricians, psychologist and family doctors, together with a monitored transition towards adult gastroenterology centers.

Conflict of interest

Authors have no conflict of interests to disclose. All the authors had a significant contribution to this paperwork.

References

- Levitt MA, Pena A (2010) Imperforate anus and cloacal malformations. *Ashcraft's Pediatr Surg* 468-490.
- Gangopadhyay AN, Pandey V (2015) Anorectal malformations. *J Indian Assoc Pediatr Surg* 20: 10-15.
- Levitt MA, Pena A (2007) Anorectal malformations. *Orphanet J Rare Dis* 2: 33.
- Bechit E, Murphy F, Puri P, Hutson JM (2006) The Clinical Features and Diagnostic Guidelines for Identification of Anorectal Malformations. In: *Anorectal Malformations in Children*. Springer Berlin Heidelberg 185-200.
- Stoll C, Alembik Y, Dott B, Roth MP (2007) Associated malformations in patients with anorectal anomalies. *Eur J Med Genet* 50: 281-290.
- Moore SW (2013) Associations of anorectal malformations and related syndromes. *Pediatr Surg Int* 29: 665-676.
- Holschneider A, Hutson J, Pena A, Beket E, Chatterjee S, et al. (2005) Preliminary report on the International Conference for the Development of Standards for the Treatment of Anorectal Malformations. *J Pediatr Surg* 40: 1521-1526.
- Nam SH, Kim DY, Kim SC (2015) Can we expect a favorable outcome after surgical treatment for an anorectal malformation? *J Pediatr Surg* 51: 421-424.

9. de Blaauw I, Wijers CH, Schmiedeke E, Holland-Cunz S, Gamba P, et al. (2013) First results of European multi-center registry of patients with anorectal malformations. *J Pediatr Surg* 48: 2530-2535.
10. Wijers CH, van Rooij IA, Marcellis CL, Brunner HG, de Blaauw I, et al. (2014) Genetic and nongenetic etiology of nonsyndromic anorectal malformations: a systematic review. *Birth Defects Res C Embryo Today* 102: 382-400.
11. Endo M, Hayashi A, Ishihara M, Maie M, Nagasaki A, et al. (1999) Analysis of 1,992 patients with anorectal malformation over the past two decades in Japan. *J Pediatr Surg* 34: 435-441.
12. Zouaoui W, Maaoui W, Hellal Y, Chammachi J, Brn Hassen I, et al. (2009) RP-WD-27 Imagerie et evaluation pre-operatoire des malformations ano-rectale. *J Radiol* 89: 1622-1623.
13. Le Bayon AG, Carpentier E, Boscq M, Lardy H, Sirinelli D (2010) Imaging of anorectal malformations in the neonatal period. *J Radiol* 91: 475-483.
14. Balanescu RN, Topor L, Moga A (2013) Anomalies associated with anorectal malformations. *Chirurgia* 108: 38-42.
15. Upadhyaya V, Gangopadhyay A, Sinvastava P, Hasan Z, Sharma S, et al. (2007) Evolution of management of anorectal malformation through the ages. *Internet J Surg* 17: 1.
16. Bischoff A, Levitt MA, Pena A (2013) Update on the management of anorectal malformations. *Pediatr Surg Intern* 29: 899-904.
17. Iwai N, Furmino S (2013) Surgical treatment of anorectal malformations. *Surg Today* 43: 955-962.
18. Georgeson KE, Inge TH, Albanese CT (2000) Laparoscopically assisted anorectal pull-through for high imperforate anus – a new technique. *J Pediatr Surg* 35: 927-931.
19. National Statistics Institute (2012) Evolution of birth and fertility in Romania.
20. Vermes G, Laszlo D, Czeizel AE, Acs N (2016) Birth outcomes of patients with isolated anorectal malformations: A population-based case-control study. *Congenit Anom (Kyoto)* 56: 41-45.
21. Alamo R, Meyrat BJ, Mewly JY, Meuli RA, Gudinchet F, et al. (2013) Anorectal Malformations: Finding the Pathway on the Labyrinth. *Radiographics* 33: 491-512.
22. Nah SA, Ong CC, Lakshmi NK, Yap TL, Jacobsen AS, et al. (2012) Anomalies associated with anorectal malformations according to the Krickbeck anatomic classification. *J Pediatr Surg* 47: 2273-2278.
23. Van der Steeg HJJ, Schmiedeke E, Bagolan P, Broens P, Demirogullari B, et al. (2015) European consensus meeting of ARM-Net members concerning diagnosis and early management of newborns with anorectal malformations. *Tech Coloproctol* 19: 181-185.
24. Levitt MA, Pena A (2005) Outcomes for the corrections of anorectal malformations. *Curr Opin Pediatr* 17: 394-401.
25. Adeniran JO (2002) One-stage correction of imperforate anus and rectovestibular fistula in girls: Preliminary results. *J Pediatr Surg* 37: 16-19.
26. Liu G, Yuan JG, Wang C, Li T (2004) The treatment of high and intermediate anorectal malformations: one stage or three procedures? *J Pediatr Surg* 39: 1466-1471.
27. Pena A, Hong A (2000) Advances in the management of anorectal malformations. *Am J Surg* 180: 370-376.
28. Rintala RJ, Lindahl H (1995) Is normal bowel function possible after repair of intermediate and high anorectal malformations? *J Pediatr Surg* 30: 491-494.
29. van den Hondel D, Aarsen FK, Wijnen R, Sloots C, IJsselstijn H, et al. (2015) Children with congenital colo-rectal malformations often require special education or remedial teaching, despite normal intelligence. *Acta Paediatr* 105: e77-e84.
30. Grano C, Bucci S, Aminoff D, Lucidi F, Violani C, et al. (2015) Transition from childhood to adolescence: Quality of life changes 6 years later in patients born with anorectal malformations. *Pediatr Surg Int* 31: 735-740.
31. Schmiedeke E, Busch M, Stamatopoulos E, Lorenz C (2008) Multidisciplinary behavioural treatment of fecal incontinence and constipation after correction of anorectal malformation. *World J Pediatr* 4: 206-210.

Giant Condyloma Acuminatum (Buschke-Lowenstein Tumor): A Case Report and Review of the Literature

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Abstract

Giant condyloma acuminatum (GCA) commonly known as Buschke-Lowenstein tumor is a rare, aggressive, slow growing; fungating variant of condyloma that is usually found in the genital and perianal regions but may affect any portion of the anogenital region. Although clinically malignant, its histology is benign without distant metastases. The incidence is 0.1% in the general population and while the prognosis is generally good with early diagnosis and proper treatment, mortality rates as high as 20% have been reported. Human papilloma virus (HPV) types 6 and 11 are implicated as etiologic factors in the development of GCA. Radical surgical excision with clear histologic margins and plastic reconstruction remains the cornerstone treatment of choice, while preventing the incidence of recurrence. Topical agents and local destructive methods can be helpful for smaller lesions and immunotherapy as an alternative for widespread and relapsed cases. The authors report the case of a 51-year-old male patient with a perianal 8 × 7 cm Buschke-Lowenstein tumor who underwent total excision and plastic reconstruction with V-Y flap technique.

Keywords: Giant condyloma acuminatum; Buschke-Lowenstein tumor; V-Y flap technique; Case report; Review

Introduction

Surgery, Condyloma acuminata is the most common sexually transmitted disease found in young, sexually active population and mostly seen in the colorectal practice. Condylomas have been well known in history with physicians of ancient Roman Empire calling them as “figs” which were thought to result from excessive sexual exploits [1]. The term “acuminatum” means “pointed” and was used to distinguish condyloma acuminatum from condyloma lata, the “broad” condyloma of syphilis [2].

Giant condyloma acuminatum or Condylomata gigantea (commonly known as Buschke-Lowenstein tumor) is a rare, aggressive, slow growing; fungating variant of condyloma that is usually found in the genital and perianal regions but may affect any portion of the anogenital region.

While the tumor was first clinically described by Buschke in 1896, both Buschke and Lowenstein first discovered the histological features in 1932 and hence the name, Buschke-Lowenstein tumor. Although benign in nature, the GCA is also sometimes known as “verrucous carcinoma” because of its tendency to deeply invade the underlying tissues. It has been also described as a rare variant of genital warts [3]. Some authors, however, consider GCA as an intermediate form between benign condyloma acuminata and malignant verrucous carcinoma [3].

While there is no standard treatment due to its biological behavior, surgical excision remains the method of choice to achieve local control of the disease. Most of the authors recommend radical excision with clear histological margins and eventual abdominoperineal resection for perianal and anal canal invasion or malignant transformation [4-6]. The use of a temporary loop colostomy before excision, to avoid a possible contamination of the wound is rarely applicable. On the other hand, skin reconstruction can be performed with the use of different plastic procedures. S-plasty grafts (right or left gluteus and posterior leg flaps) and V-Y advancement flap technique have been commonly used [7,8]. We represent a case report of a perianal and anal GCA treated by radical local excision and reconstruction with the V-Y plasty technique and a review of the literature.

Case Report

A 51 years old homosexual man was admitted to the surgical department in October 2010 for a lesion located in the perianal and anal region. The patient was complaining of a painful palpable mass for the last year and also of itching and constipation. The last month he noticed a foul smell, bleeding and mucopurulent perianal discharge.

On physical examination an enormous, exophytic, cauliflower-like tumor was found with irregular surface, eventually exceeding 10 cm in length and 8 cm in diameter. All the patients' blood tests were normal, while he was found HIV negative and HbsAg positive. The tumor was totally excised. The entire specimen was sent for histological examination to ensure clear margins and the absence of a malignant verrucous carcinoma.

Skin defect reconstruction was achieved with a bilateral V-Y fasciocutaneous advancement flap. The skin incision was closed with a stapler and the medial edge of the flap was sutured to the anal area by a 3/0 ployglactin material. The histological report of the specimen revealed the presence of a giant condyloma acuminatum (Buschke-Lowenstein tumor) with clear surgical margins and no evidence of malignant transformation. An HPV analysis was also performed by PCR technique, demonstrating the presence of HPV types 16 and 18, something less common in giant condyloma acuminatum. A non-fiber diet and loperamide (12mg/day) were administered for 4 days to avoid wound infection.

There were no postoperative complications and the patient was discharged. After 2 years the patient is doing well without any evidence of recurrence (Figures 1-6).

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Discussion

The incidence of GCA is probably 0.1% in the general population and about 2 to 3 million newly reported cases each year have been estimated [9]. While the prognosis is generally good with early diagnosis and proper treatment, mortality rates as high as 20–30% has been reported.

Most frequently, Human papillomavirus (HPV) types 6 and 11 are implicated as etiologic factors [10] in the development of GCA. However, an immunologic aberration of the cell-mediated immune system and/or the combined synergistic effect of viral or environmental carcinogens may all contribute to the formation of the tumor. In addition, one of more of the risk factors may have a significant contributory role in the development or aggravation of the disease process.

Gender: Buschke-Lowenstein tumor is much more common in males than in females. The ratio of males to females is approximately 2.3:1 [11].

Viral infection: The tumor has been found to be frequently associated with the presence of human papillomavirus (HPV) viral infection [11,12]. In fact, almost all cases of GCA are associated with contagious low-risk HPV types 6 and 11 [3].

Condyloma acuminatum: GCA is always preceded by condyloma acuminatum, and the immune system is probably suppressed.

Homosexual men: Common practice of anal receptive intercourse in the homosexual population is also considered a risk and GCA, therefore, is mainly seen in men.

Uncircumcised males: The tumor has also been frequently noticed in uncircumcised men between the ages of 18 and 86 years. According to an estimate, about 5% to 25% of all penile cancers are GCAs [10].

Age: While GCA can occur at any age after puberty, it usually affects young patients in the second and third decades of life. However, its development between the 4th and 6th decades of life is also not uncommon. Various studies have shown that the average age for the occurrence of disease among most patients is 43.5 years [13].

Immunocompromised patients: In some cases, GCA has also been found to be associated with chronic diseases or immunocompromised states such as congenital or acquired immunodeficiency (AIDS), alcoholism, diabetes, or chemotherapy with immunosuppressive therapy [9].

Other associated risk factors include numerous sexual partners (such as common in prostitution), poor hygiene, depression of immune system, smoking and anaerobic infections etc.

Although GCA is a highly differentiated squamous cell tumor of the genital region that is mostly benign, the characteristic thicker stratum corneum, marked papillary proliferation and its tendency to invade deeply displacing the underlying tissues are the histopathological features that differentiate the GCA from ordinary condylomas, and squamous cell carcinomas. It should also be noted that while squamous cell carcinoma and giant condyloma acuminata can coexist in 30% to 56% of patients [14], GCA only rarely presents with histological features of malignancy such as infiltration of the basement membrane, frequent mitotic figures, lymphatic or angioinvasion, and distant metastases. Granular vacuolization is present, and individual keratinocytes have large cytoplasm and a nucleus with prominent nucleolism [15]. The basal membrane is intact, and a lymphohistiocytic inflammatory infiltrate is present in the upper dermis [9].

The penis is the most common site for GCA development [3]

although the perianal region, rectum, scrotum, perineum and bladder may also be involved. In women, however, the tumor usually occurs in the vulva, vagina, or cervix.

Most frequent symptoms include continuous perianal discomfort, anal itching, and painful defecation associated with bleeding and mucopurulent perianal discharge. A clinical study involving review of 51 patients with GCA showed the most frequent clinical features to due to tumor-effect: perianal mass (47%), followed by pain (32%), abscess or fistula (32%), and bleeding (18%) [11].

On physical examination, the tumor presents as an enormous, exophytic, cauliflower-like, white or yellow vegetative growth of papillomatous and irregular surface, eventually exceeding 10 cm [9]. It should be noted, however, that the gross appearance of GCA is not easily differentiated from ordinary condylomas or malignant squamous cell carcinomas as all of these masses appear as large cauliflower-like lesions.



Figure 1: A Buschke-Lowenstein tumor in the perianal area.



Figure 2: The tumor very close to the anus.



Figure 3: Circumferential excision is performed with wide margins, histologically negative for Condyloma acuminatum,



Figure 4: The residual defect will be closed by advancing surrounding V-shaped islands of skin and underlying tissue.



Figure 5: Closure of the flap wounds converts the V-shaped wounds to Y-shaped suture lines.



Figure 6: Follow up after 2 months.

GCA of the penis, for example, appears as a soft, pink, vascular, cauliflower-like warty growth that may be relatively small and localized initially but gradually enlarges to a size greater than 5 cm in diameter. The lesion begins on or around the prepuce and gradually becomes nodular [10]. In many cases, peripheral clinical signs such as inguinal lymphadenopathy have also been observed. The tumor often forms an ulcerating mass with abscesses and necrotic tissue [1].

Although GCA rarely metastasizes, its aggressive nature displaces deeper tissues by downward growth, causing multiple sinuses or fistula tracts that may invade deeply into the fascia, muscle, or rectum. In some cases, extension into the urethra, genitalia, and perineum can occur. This may result in inflammation, secondary bacterial infection, or hemorrhage. The lesion is also often complicated by several deep fissures discharging pus and blood. Improperly treated or unmanaged cases have been even found to be fatal in some cases [15]. One of the complications of GCA is its neoplastic transformation into fully invasive

squamous cell carcinoma because of its highly malignant behavior which often conflicts with its benign nature and histopathological features. In fact, according to some estimates, GCA has a malignant transformation rate as high as 50% [3]. Therefore, while the GCA tumors do not metastasize, clinically they are nevertheless regarded as malignant [16]. Appropriate treatment of GCA provides very good prognosis and low rate of recurrence. Prognosis is specifically considered good with adequate surgical excision [10]. However, good prognosis does not necessarily affect the rate of recurrence of the tumor which is also considered relatively high. Initial diagnosis is based on a detailed clinical history and a thorough, carefully performed physical examination of the patient. In most cases, the pathologic analysis of the specimen confirms the diagnosis of condyloma acuminatum, with moderate degree of dysplasia of the epithelium with koilocytosis atypia, acanthosis, and parakeratosis. For a confirmatory diagnosis of GCA, however, deep biopsy from different points of infected tissue should be performed essentially involving the epidermal/dermal interface as the specimen usually shows presence of koilocytotic cells and the large hyperkeratotic cellular nests propagate deep into underlying stroma [15].

Although the lesion is generally benign, its management is often challenging due to the size, degree of local invasion, young age of the patients and high recurrence rate. In addition, as there are no universally accepted guidelines for the treatment of GCA, therapy is mainly based on individual case reports and degree of severity of the disease.

The following treatment modalities are generally implied in most cases:

Surgical excision: When possible, surgical excision with examination of histologic margins is considered as the cornerstone of treatment and is generally recommended as the treatment of choice in the early stages of the tumor for complete elimination of the tumor and prevention of recurrence. Excision must be wide and the Mohs technique is often used [9]. Lymph node dissection is indicated only in cases of suspected malignant transformation. However, evidence has shown that even surgically excised GCA cases tend to have a recurrence rate of about 50% [11]. In some cases, Cryosurgery has been also found to be successful but only in small, simple lesions.

Medical treatment & chemotherapy: Most of the published studies and documented evidence have shown highly variable response to the medical drug / chemotherapy. Topical application of podophyllin, for example, has shown to be helpful for ordinary condyloma acuminata but is not recommended for the treatment of condylomata gigantea because of its large size. Similarly, topical chemotherapy with 5-fluorouracil has been used for the treatment of genital condylomata, but seems to yield poor outcome with giant lesions. However, administering interferon injection directly in the lesion is considered safe and has an eradication rate of 47% to 62%. It should also be noted that interferon chemotherapy is associated with high cost and a recurrence rate up to 40% [14]. Similarly, systemic interferon therapy may be considered for those very large lesions that cannot be excised surgically because of the immune-modulating, anti-proliferative and antiviral properties of GCA. It is expensive, however, with a high incidence of side effects and a variable response rate. Systemic chemotherapy with methotrexate, 5-FU, bleomycin, mitomycin C, cisplatin, and leucovorin may also be tried in extensive or recurrent GCA. On the other hand, long-term treatment with oral retinoids such as etretinate or acitretin has been reported to be effective in GCA because of their immune-modulating, anti-proliferative and proapoptotic properties. In addition, Imiquimod, a potent antiviral and antitumoral agent known for its protective cytotoxic immune response against HPV acts as a synthetic imidazoquinoline immune-response modifier. As Imiquimod also offers the valuable benefits of

less tissue damage, self-applicability on an outpatient basis and lower recurrence rates, its 5% cream has been approved by the US Food and Drugs Administration for the topic treatment of GCA. It is applied three times a week overnight for up to 4 months [3].

Immunotherapy: Immunotherapy with autologous vaccine from the patient's own condyloma has been reported with good success rates and, therefore, has been suggested for giant condyloma acuminata and recurrent lesions.

Radiotherapy: Evidence has shown radiotherapy as a controversial option (even contraindicated by some) for the treatment of GCA because of high rate of recurrence and appearance of anaplastic transformations in some cases [15]. It should be, therefore, reserved for non resectable or adamantly recurrent lesions [3]. However, there is some evidence that indicates the effectiveness of definitive radiation therapy as used in the Nigro Protocol when a patient with recurrent GCA after four surgical excisions, treated definitively with radiation therapy to 45 Gy, showed total regression, and was biopsy-proven to be disease-free 20 months after radiation [11].

Laser therapy: Recently, CO2 laser therapy as the next step after the surgical excision has been found to have some benefits such as a bloodless field, the least destruction of surrounding tissue, the lesser degree of scarring and hemostasis in a same time [15].

HPV vaccine: The available quadrivalent HPV vaccine which is frequently used in females aged 11 to 26 years for the prevention of cervical cancer has been suggested by some to be used in males as a preventive therapy against condylomas and extensive condylomatosis although, at present, no data is available to support this claim [13].

While the overall rate of recurrence of GCA is variable and depends on the on the modality of treatment, recurrence rates

as high as 67% and mortality rates of 20% to 30% have been reported. High rate of recurrence (over 60%) is characteristic for chronic disease [15].

Conclusion

Condylomata gigantean commonly known as Buschke-Lowenstein tumor or giant condyloma acuminatum (GCA) is a rare but highly aggressive tissue destructing lesion of genital or perianal region that is usually found in men but is also not uncommon in women. Because of its location, severity and high recurrence rates, the disease causes significant psychological morbidity and requires active treatment. However, with no universally defined treatment guidelines, GCA tumor remains a well-known, clinically challenging, entity. To date, surgical excision remains the treatment of choice for most of the cases but other treatment modalities such as chemoradiotherapy and laser have yielded mixed results with variable success and recurrence rates. The tumor also has a strong tendency to recur but is not frequently associated with metastatic potential and yet is known for "behaving in a malignant fashion" despite having no histopathological features of typical malignancy. Post-treatment clinical monitoring is highly recommended.

Conflict of interest

Authors have no conflict of interests to disclose

References

1. Tytherleigh MG, Birtle AJ, Cohen CE, Glynne-Jones R, Livingstone J, et al. (2006) Combined surgery and chemoradiation as a treatment for the Buschke-Lowenstein tumor. *Surgeon* 4: 378-383.
2. Steffen C (2006) The Men Behind the Eponym – Abraham Buschke and Ludwig Lowenstein: Giant Condyloma (Buschke-Loewenstein). *Am J Dermatopathol* 28: 526-536.
3. Erkek E, Basar H, Bozdogan O, Emeksiz MC (2009) Giant condyloma acuminata of Buschke-Lo'wenstein: successful treatment with a combination of surgical excision, oral acitretin and topical imiquimod. *Clin Exp Dermatol* 34: 366-368.
4. Creasman C, Haas PA, Fox TA, Balazs M (1989) Malignant transformation of anorectal giant condyloma acuminatum (Buschke-Lowenstein Tumor). *Dis Colon Rectum* 32: 486-487.
5. Bogomoletz WV, Potet F, Molas G (1985) Condylomata acuminata, giant condyloma acuminatum (Buschke-Lowenstein Tumor) and verrucous squamous cell carcinoma of the perianal and anorectal region: a continuous precancerous spectrum? *Histopathology* 9: 155-169.
6. Chu QD, Vezeridis MP, Libbey NP, Wanebo HJ (1994) Giant condyloma acuminatum (Buschke-Lowenstein Tumor) of the perianal and anorectal region: analysis of 42 cases. *Dis Colon Rectum* 37: 950-957.
7. De Toma G, Cavallaro G, Bitonti A, Polistena A, Onesti MG, et al. (2006) Surgical management of Perianal Giant Condyloma Acuminatum (Buschke-Lowenstein Tumor) Report of three cases. *Eur Surg Res* 38: 418-422.
8. Arif HD, Ali UO, Ferruh B, Nevzat G (2008) Total Excision V-Y plasty technique in the anal area condyloma acuminatum. *Indian J Plast Surg* 41: 67-69.
9. Hicheri J, Jaber K, Dhaoui MR, Youssef S, Bouziani A, et al. Giant condyloma (Buschke-Lowenstein tumor). A case report. *Acta Dermatovenereol Alp Pannonica Adriat* 15: 181-183
10. Sherman RN, Fung HK, Kevin J (1991) Verrucous Carcinoma (Buschke-Lowenstein Tumor). *Int J Dermatol* 30: 730-733.
11. Haque W, Kelly E, Dhingra S, Carpenter LS (2010) Successful treatment of recurrent Buschke-Lowenstein tumor by radiation therapy and chemotherapy. *Int J Colorectal Dis* 25: 539-540.
12. Wietfeldt ED, Thiele J (2009) Malignancies of the Anal Margin and Perianal Skin. *Clin Colon Rectal Surg* 22: 127-135.
13. Sarzo G1, Del Mistro A, Finco C, Frayle-Salamanca H, Marino F, et al. (2010) Extensive anal condylomatosis: prognosis in relation to viral and host factors. *Colorectal Disease* 12: 128-134.
14. Renzi A, Giordano P, Renzi G, Landolfi V, Del Genio A, et al. (2006) Buschke-Lowenstein Tumor Successful Treatment by Surgical Excision Alone: A Case Report. *Surg Innov* 13: 69-72.
15. Perisic Z, Lazic JP, Terzic B, Perisic S, Rasic R, et al. (2003) Condylomata gigantea in anal and perianal region: surgical and CO2 laser treatment. *Arch Gynecol Obstet* 267: 263-265.
16. Boshart and Hausen HZ (1986) Human Papillomaviruses in Buschke-Lowenstein Tumors: Physical State of the DNA and Identification of a Tandem Duplication in the Noncoding Region of a Human Papillomavirus 6 Subtype. *J Virol* 58: 963-966.

Sertoli – Leydig Tumor and Meigs' Syndrome, an Infrequent Association-A Case Report

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Abstract

The Meigs' syndrome, of infrequent presentation in approximately 4% of benign ovarian tumors, is characterized by the association of a benign tumor of gynecological origin with ascites and pleural effusion, which, in the majority of cases, induces the Clinician to suspect a malignant etiology. However, these conditions are resolved after tumor excision. Fewer than 60 cases of Meigs' syndrome have been reported in the literature to date that have a rise in the CA 125 antigen. The first case was documented by Jones and Survit in 1989 in a 70-year-old patient with a fibrothecoma and with an elevation of CA 125 of 226 IU/ml. The association of a Meigs' syndrome with Sertoli-Leydig tumors is extremely rare, we present the second case reported in the literature. The fact of being able to find the association of these two entities renders it evident that the Clinician should bear this in mind at the time of carrying out the evaluation of a patient with a pelvic injury that is bears a resemblance to advanced-stage ovarian cancer, and even more so if it presents with elevations of CA 125, in that Meigs syndrome will present complete resolution after the tumor excision.

Keywords: Sertoli-Leydig; Meigs' syndrome; Ca 125

Introduction

Sertoli-Leydig tumors are extremely rare neoplasms that represent 0.5% of ovarian neoplasms [1]. One third of patients with one of these tumors present clinical and biochemical data of virilization or defeminization [2,3], although they generally have a good prognosis [4]. These tumors were initially called arrhenoblastomas, and in 1958, they were designated Sertoli-Leydig tumors [5]. On the other hand, Meigs' syndrome is characterized by the presence of ascitis and pleural effusion, associated with a benign tumor of gynecological origin [6,7]. The majority of Meigs' syndromes present as associated with fibromas, thecomas, and granulosa cells, or Brenner tumor; the association of a Sertoli-Leydig tumor with Meigs' syndrome is an extremely infrequent event; thus, the importance of reporting a case in which this association is present.

Clinical Case

Patient feminine gender 48 years of age, without antecedents of importance, who initiated with a clinical condition with seven months of evolution, characterized by abdominal distension and edema of the lower extremities without other accompanying symptoms (Figure 1). The patient made an appointment with the physician, who requested abdominal Ultrasound (US), which detected a pelvic tumor, multicystic, heterogeneous, 24.4 × 23.5 × 18.4 cm in size, 5.605 cc in volume, uterus 7 × 7 × 10.8 cm in size, with intramural myomas of 6 × 4 cm, endometrium of 8 mm, ascitic fluid, which the requirement of multiple hospitalizations due to respiratory difficulty, with the performance of three evacuatory paracenteses prior to admission at our institution (Figure 2).

On her admission, the patient exhibited anasarca with paleness and respiratory difficulty, integrating bilateral pleural syndrome, globus abdominalis at the expense of fluid with tense ascites without achieving delimitation of visceromegaly or intra-abdominal tumors, weight = 87 kg, Karnofsky scale = 50.

Paracenteses was carried out, draining 6 L of cetin fluid and with placement of a pleural catheter for lung drainage. Tumoral markers on the patient's admission to the institution were the following: CA 125,

352 IU/ml; Alpha Feto Protein (AFP), 17 ng/ml; Carcinoembryonic antigen (CEA) 0.62 ng/ml; CA 19-9, 2.9 IU/ml, and CA 15.3, 12.9 IU/ml, and hormones were estradiol, 370 pg/ml, progesterone, 0.58 ng/ml, and testosterone, 42.4 ng/dl. Cytology of the ascitic fluid and pleural fluid reported reactive mesothelium without neoplastic cells.

Computer Axial Tomography (CAT) of the thorax, abdomen, and pelvis were performed, considering that the patient was not an initial candidate for cytoreduction; thus, the decision was made to conduct a guided biopsy for diagnosis and to establish norms for treatment behavior. The biopsy was conducted with a cutting needle of the adnexal lesion without complications, reporting an ovarian stromal tumor, complementing the study with the following immunohistochemistry: AFP, negative; CD99, positive; CD10, negative; C7 EMA, negative; inhibin, positive; SALL4, negative; WTQ, negative, and IRE, positive.

Exploratory laparotomy was carried out, finding a multilobulated tumor, septated, multicystic, right ovary-dependent adhered to pelvic cavity, and right parietocolic gutter with myomati uterus and left ovary of normal appearance. The transoperative study of the lesion reported a tumor of 29 cm with integral capsule with tumor of the sex cords.

The patient was in intensive therapy for 7 days due to important bleeding during the surgical procedure, presenting resolution of the pleural effusion and of the ascitic fluid.

The definitive pathological report demonstrated right ovary with Sertoli-Leydig-cell tumor of intermediate differentiation. Tumor size

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Figure 1: Teleradiography of thorax showing total collapse of the right lung at the expense of massive pleural effusion, which conditions displacement to the left of the cardiomediatinum, left lung with compensatory expansion.

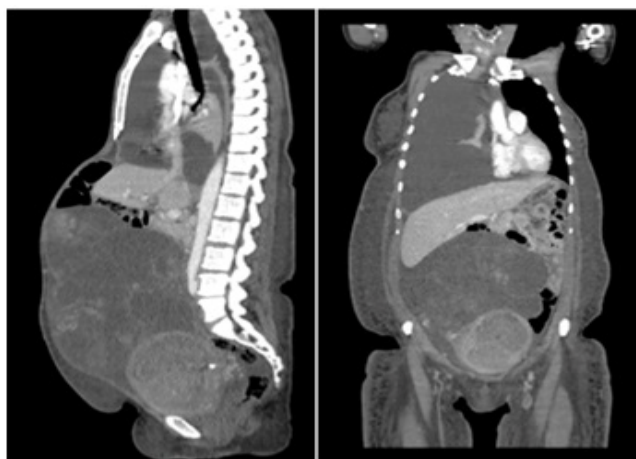


Figure 2: Coronal and sagittal reconstruction of phase-contrast Computer Tomography (CT), in which right pulmonary collapse can be observed at the expense of massive pleural effusion with displacement of the cardiomediatinum to the left. At the level of abdominal cavity and pelvis, occupation of the heterogenous neoformation dependent on right ovary, as well as implants in left mesenterinum due to carcinomatosis and uterus with increase in dimensions due to intramural myomatosis. Edema of soft tissues.

of $29 \times 28 \times 10$ cm with integral capsule (Figure 3). Contralateral ovary with fibrous cystoadenoma and white tissues, fallopian tube with vascular congestion, slight, chronic cervicitis, basal endometrium, and conventional-type, intramural leiomyoma's 1-6 cm in diameter. The patient is found in follow-up without evidence of disease recurrence and a CA 125 marker of 4.75 IU/ml.

Discussion

Sertoli-Leydig tumors represent a very low percentage of ovarian neoplasms at the National Institute of Cancerology (INCan) in Mexico: during the 2000–2004 periods, only five cases occurred among 754 ovarian neoplasms registered [8], corresponding to 0.66%, similar to that reported in the literature [2-5,9,10]. It affects all ages, but mainly women 25 years of age [11]. Are hormonally active with estrogen secretion, which is associated with early puberty, endometrial hyperplasia, and metrorrhagia, while androgen secretion gives rise to amenorrhea, hirsutism, mammary gland atrophy, and clitoral hypertrophy [3,12,13]. Some cases are intensely virilizing, related

with elevations in testosterone of >200 ng/dl. These tumors are solid in consistency and generally unilateral, up to 98%. Only 4% present with ascitis [14] and the majority of patients have pain and abdominal distension. Elevations have been reported of the marker AFP, which have been related with the existence of an intestinal-type component, obliging the performance of differential diagnosis with germinal cell tumor and, although less frequently, with hepatic carcinoma. Immunohistochemistry allowed confirmation of the diagnosis, because it was positive for alpha-inhibin in Sertoli as well as in Leydig cells. Prognosis is general is favorable, due to that 95% of these present confined to ovary [14], with 90% survival; generally, it has a malignancy rate of 13% with intrapelvic and abdominal distension, and recurrence can present in the first 10 years, although its percentage is extremely rare, with only one case of recurrence present in the literature [15]. Poor prognostic factors associated with this neoplasm comprise the heterologous component, the presence of gastric or intestinal epithelium, carcinoid foci, or stromal elements and retiform pattern, which determine to offer of adjuvancy in the treatment [5].

On the other hand, the Meigs' syndrome, also with infrequent presentation in approximately 4% of benign ovarian tumors [16], affects middle-aged women and is characterized by the association of a benign tumor of gynecological origin with ascitis and pleural effusion [17], which, in the majority of cases, induces the Clinician to suspect a malignant etiology. However, these conditions are resolved after tumor excision. Other tumors distinct from fibroma, such as teratomas or uterine leiomyomas are associated with the Meigs' criterion, and the denomination of Pseudo-Meigs' syndrome is preferred. The distinction between Meigs' and Pseudo-Meigs' syndrome is merely academic, because therapeutic treatment is the same [18].

Multiple theories have attempted to explain the pathophysiology of ascitis and of pleural effusion from the publication of Meigs in 1960, in which the author suggests that the ascitis could be associated with the pressure exerted by the tumor itself on the lymphatic vessels, thus the accumulation in the peritoneal cavity, or associated with the exudate of the tumor itself to the peritoneum, and up to the most recent theories, which have related the production of inflammatory cytosine's or of Vascular Endothelial Growth Factors (VEGF) and Fibroblast Growth Factors (FGF), whose values have been documented as elevated pre-operatively, in pleural fluid as well as in ascitic fluid, with a decline in these values after tumor extirpation [19-22].

Fewer than 60 cases of Meigs' syndrome have been reported in the literature to date that have a rise in the CA 125 antigen ranging between 42 and up to 7,000 IU/ml (Table I) [23-63]. The first case was documented by Jones and Survit in 1989 in a 70-year-old patient with

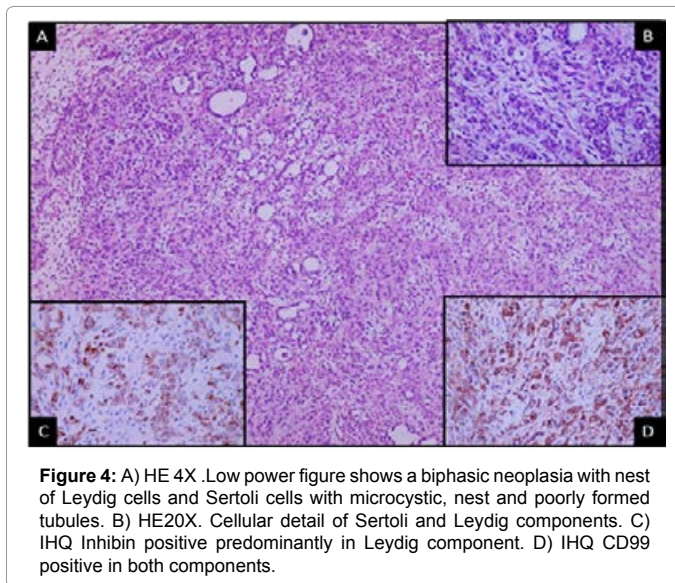


Figure 3: Right ovary with Sertoli-Leydig-cell tumor $29 \times 28 \times 10$ cm on size with integral capsule.

Table I: Summary of reported cases of Meigs' syndrome with elevated CA levels since 1989.

Author	Year	Age	Histopathology	Tumor size (cm/vol)	CA 125 (IU/ml)
Jones and Survit [21]	1989	70	Fibroma/thecoma	11x9x8	226
Hoffman [23]	1989	32	Thecoma	11x11x7	498
Martin et al. [24]	1990	NR	Granulosa cell tumor	NR	307
Walker et al. [25]	1990	52	Cellular fibroma	16x4x8	>5,000
	1990	67	Cellular fibroma	18x15x10	104
Le Bouëdec et al. [26]	1992	66	Fibroma/thecoma	15	645
	1992	76	Fibroma/thecoma	12	286
Williams et al. [27]	1992	74	Luteinized thecoma	15x10x9	329
Lin et al. [28]	1992	74	Fibroma	20x12x12	2,120
	1992	72	Fibroma	14x8x7	7,000
Turan et al. [29]	1993	63	Thecoma	18x9x5	744
Timmerman et al. [30]	1995	71	Fibroma	30x20.5x10	485
	1995	73	Fibroma	19x17x9	42
Aoshima et al. [31]	1995	33	Brenner tumor	NR	71
Siddiqui and Toub [32]	1995	73	Cellular fibroma	15x13x10	1,780
Abad et al. [33]	1999	51	Cellular fibroma	6x5	577
Migishima et al. [34]	2000	51	Uterine leiomyoma	2.3x24.3x 20.5	820
Chan et al. [35]	2000	13	Fibroma	20x19x10	970
Patsner [36]	2000	62	Fibroma	10	185
	2000	57	Fibroma	14	850
	2000	52	Fibroma	16	520
	2000	60	Fibroma	14	64
	2000	72	Fibroma	18	1,200
	2000	58	Fibroma	18	80
Bretelle et al. [15]	2000	71	Fibrothecoma	7x6.6	2610
Abramov et al. [19]	2001	62	Fibroma	12x13	354
Buttin et al. [37]	2001	67	Brenier tumor	11x9x6	759
Massoni et al. [38]	2001	33	Fibrothecoma	17.5x11.5	752
López et al. [39]	2002	78	Fibroma	22x8.5x20	498
	2002	68	Fibroma	18x14x10	265
Huang et al. [40]	2003	31	Sclerosing stromal tumor	7x6x6	396
Vieira et al. [41]	2003	65	Thecoma	14x12x8	319
Bildirici et al. [42]	2003	17	Sclerosing stromal tumor	25x18x15	193
M. Morillo et al. [43]	2003	59	Fibroma	22 x 17 x17	825
Cissé et al. [44]	2004	25	Fibroma	15x11x9.8	482
Salman et al. [45]	2005	56	Fibroma + Takayasu arteritis	15	509
Choi et al. [46]	2005	69	Granulosa cell tumor	6x10x12	82.49
Kurai et al. [47]	2005	79	Ovarian leiomyioma	9x7x7	163
Morán et al. [48]	2006	46	Fibroma	25x23x19	1,808
Boldorini et al. [12]	2006	26	Pure Sertoli	20	1720
Jung et al. [49]	2006	50	Sclerosing stromal tumor	19x13x10	1476.8
Benjapibal et al. [50]	2009	56	Fibroma	13x10x10	1064
Lanitis et al. [51]	2009	56	Cellular fibroma + Breast ductal carcinoma	13.5x10x8	59
Kaur et al. [52]	2009	12	Juvenile granulosa cell tumor	10x10	708
Amorim et al. [53]	2010	63	Right: Sclerosing stromal tumor Left: serous cystadenoma	4.2 x 3.7	2,168
Boufettal et al. [54]	2011	51	Fibrothecoma	7	412
Liou et al. [55]	2011	18	Sclerosing stromal tumor	14.5x13x9.5	4208.3
Monteiro et al. [56]	2012	13	Fibroma (MACF)	19x15x12	453
Su et al. [57]	2013	53	Fibrothecoma	12.2x10.7	222
Riker et al. [58]	2013	54	Fibrothecoma	15 cm	1191
Gomes et al. [59]	2013	17	Pregnancy + Sclerosing stromal tumour	volume 221.3 cm ³	625
Yazdani et al. [60]	2014	50	Fibrothecoma	12 x 10	>600
Cha et al [61]	2014	52	Fibrothecoma	NR	319.2
Park et al. [62]	2015	61	Thecoma	12x11	347

*NR = Not Reported



a fibrothecoma 11 × 9 × 8 cm in size and with an elevation of CA 125 of 226 IU/ml [21]. In our case, the patient also presented with a rise in CA 125 on her admission to our institution of 352 IU/ml. Elevation of CA 125 is considered the responsibility of the mesothelial cells, which produce the rise in response to the mechanical irritation generated by the tumor itself or by the ascitis [22].

The majority of Meigs' syndromes present as tumors, such as fibromas, thecomas, and granulosa cell tumors. Tumor size, to a greater extent than the histology itself, is found in relation to the amount of ascitis, as well as that of the pleural effusion, above all in lesions measuring >13 cm.

The presentation of the Meigs' syndrome associated with a Sertoli-Leydig-cell tumor is extremely infrequent and, on our intentionally searching in the published literature, we found only one case that had occurred prior to our own. This case was reported in 2006 by Boldorini et al., in which the authors presented the case of a young, 26-year-old patient with a pure, 20 cm Sertoli-cell tumor associated Meigs' syndrome with elevated CA 125 levels of 1.720 IU/ml [7].

Sertoli-Leydig cell tumors usually appear as solid masses, however, they may also present as heterogeneous lobulated lesions with both cystic and solid components [64], diagnostic image studies should include pelvic ultrasound and abdominopelvic computed tomography scan in selected cases [65]. Ovarian sex cord-stromal tumors may exhibit characteristic radiologic features with which radiologists should become familiar [66]. Sertoli-Leydig cell tumor are characteristic virilizing neoplasms and can easily be detected using color Doppler US rather than transvaginal US alone, but this presentation is small, no more than 30-50% of cases, the rest of these tumors have nonspecific appearance. On US usually present either as a distinct hypoechoic mass or a heterogeneous mass that is primarily solid with multiple cystic spaces. On CT images a soft-tissue attenuating adnexal mass is usually seen (Figure 4A-D). The solid portions characteristically exhibit avid contrast uptake [67-69]. On MRI strong hypo-intensity on T2-weighted images is not characteristic [70,71], but most of these tumors show a predominantly low signal intensity of the solid components, relating to the fibrous stroma, with some scattered cystic areas of high signal intensity [64].

Conclusion

The association of a Meigs' syndrome with Sertoli-Leydig tumors is extremely rare: this is, to our knowledge, the second case reported in the literature. Tumor size in Meigs' syndrome is related to a greater degree

with the severity of the presentation of ascitis and pleural effusion than with the histology. The diagnosis should include color Doppler US and abdominopelvic computed tomography and is confirmed with immunohistochemistry positive for alpha-inhibin. Meigs syndrome will present complete resolution after the tumor excision.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

References

1. Takafumi W, Hidekazu Y, Yutaka M, Masafumi A, Teiichi M, et al. (2008) Ovarian Sertoli-Leydig cell tumor with heterologous gastrointestinal epithelium as a source of alpha-fetoprotein: a case report. *J Obstet Gynaecol Res* 34: 418-421.
2. Poli UR, Swarnalata G, Maturi R, Rao ST (2009) Recurrent alpha-fetoprotein secreting Sertoli-Leydig cell tumor of ovary with an unusual presentation. *Indian J Cancer* 46: 64-66.
3. Schorge J, Schaffer J, Halvorson L, Hoffman B, Bradshaw K, et al. (2009) Tumores ováricos de células germinales y estromales del cordón sexual.
4. Marie LP, Stephanie M, Pierre L, Florence D, Ghislaine E, et al. (2011) Virilising ovarian tumour: a case associating a Sertoli-Leydig cell tumour and a Brenner tumour. *Gynecol Endocrinol* 27: 345-350.
5. Marianela C, Araceli P, Mario G, Luis Padrón (2011) Tumor del ovario del cordón estromal. Sertoli-Leydig. *Rev Cir Hosp Juárez Mex* 78: 121-123.
6. Lurie S (2000) Meigs' syndrome: the history of the eponym. *Eur J Obstet Gynecol Reprod Biol* 92: 199-204.
7. Griffin J (1996) Dame Mary Page – the first recorded case of Meigs' syndrome?. *J R Coll Physicians Lond* 30: 465.
8. Rizo P, Sierra M, Vazquez G, Cano M, Meneses A, et al. (2007) Registro Hospitalario de Cáncer: Compendio de Cáncer 2000-2004. *Cancerología* 2: 203-287.
9. Huiting X, Bin L, Jing Z, Xiaoli F, Xiaoguang L, et al. (2013) Ovarian Sertoli-Leydig cell tumor: a report of seven cases and a review of the literature. *Gynecol Endocrinol* 29: 192-195.
10. Ting G, Dongyan C, Keng S, Jiaxin Y, Yiwen Z, et al. (2012) A clinicopathological analysis of 40 cases of ovarian Sertoli-Leydig cell tumors. *Gynecol Oncol* 127: 384-389.
11. Young R, Scully R (1985) Ovarian Sertoli-Leydig cell tumors: a clinicopathological analysis of 207 cases. *Am J Surg Pathol* 9: 543-569.
12. Boldorini R, Bozzola C, Ribaldone R, Tosoni A, Monga G, et al. (2006) Pure Sertoli cell tumour of the ovary with Meig's syndrome. *Pathology* 38: 579-581.
13. Wilkinson N, Osborn S, Young R (2008) Sex cord-stromal tumours of the ovary: a review highlighting recent advances. *Diagn Histopathol* 14: 388-400.
14. Bretelle F, Portier M, Boubli L, Houvenaeghel G (2000) Recurrence of Demons-Meigs' syndrome: a case report. *Ann Chir* 125: 269-272.
15. Nemeth AJ, Patel S (2003) Meigs syndrome revisited. *J Thorac Imaging* 18: 100-103.
16. Usandizaga J, Calero F, Contreras F, González A (1998) Patología tumoral del ovario. *Tratado de Obstetricia y Ginecología*. Interamericana, España 2.
17. Barquet-Muñoz SA, Castillo-Ortega AP, López-Árias A, Pérez-Montiel MD, Isla-Ortiz D, et al. (2015) Association of Pseudo-Meigs' syndrome with struma ovarii and high CA125 mimicking ovarian malignancy. *Gynecol Obstet Res Open J* 2: 57-61.
18. Abramov Y, Anteby SO, Fasouliotis SJ, Barak V (2001) Markedly elevated levels of vascular endothelial growth factor, fibroblast growth factor, and interleukin 6 in Meigs syndrome. *Am J Obstet Gynecol* 184: 354-355.
19. Ishiko O, Yoshida H, Sumi T, Hirai K, Ogita S, et al. (2001) Vascular endothelial growth factor levels in pleural and peritoneal fluid in Meigs' syndrome. *Eur J Obstet Gynecol Reprod Biol* 98: 129-130.
20. Jones O, Surwit E (1989) Meigs syndrome with elevated serum CA 125. *Obstet Gynecol* 73: 520-521.
21. Losa EM, Villar M, Pascual A, Gómez T, González G, et al. (2006) Síndrome de Meigs y pseudoMeigs. *Rev Clin Invest Ginecol Obstet* 33: 25-34.
22. Hoffman MS (1989) Peritoneal tuberculosis, large ovarian thecoma, and an elevated serum CA 125 level mimicking ovarian cancer. *J Fla Med Assoc* 76: 388-389.

23. Martin F, Brouche S, Haidar A (1990) Demons-Meigs' syndrome. Report of a case with ovarian tumor of the granulosa. *Rev Pneumol Clin* 46: 123-124.
24. Walker JL, Manetta A, Mannel RS, Liao SY (1990) Cellular fibroma masquerading as ovarian carcinoma. *Obstet Gynecol* 76: 530-531.
25. Le Bouëdec G, Glowaczower E, de Latour M, Fondrinier E, Kauffmann P, et al. (1992) Demons-Meigs' syndrome. A case of thecoma and ovarian fibroma. *J Gynecol Obstet Biol Reprod* 21: 651-654.
26. Williams L, Fleischer A, Jones H (1992) Transvaginal color Doppler sonography and CA-n in a patient with ovarian thecoma and ascites. *Gynecol Oncol* 46: 115-118.
27. Lin J, Angel C, Sickel J (1992) Meigs syndrome with elevated serum CA 125. *Obstet Gynecol* 80: 563-566.
28. Turan Y, Demirel L, Ortac F (1993) Elevated CA 125 in Meigs syndrome. *Int J Gynaecol Obstet* 43: 64-65.
29. Timmerman D, Moerman P, Vergote I (1995) Meigs' syndrome with elevated serum CA 125 levels: two case reports and review of the literature. *Gynecol Oncol* 59: 405-408.
30. Aoshima M, Tanaka H, Takahashi M, Nakamura K, Makino I (1995) Meigs' syndrome due to Brenner tumor mimicking lupus peritonitis in a patient with systemic lupus erythematosus. *Am J Gastroenterol* 90: 657-658.
31. Siddiqui M, Toub DB (1995) Cellular fibroma of the ovary with Meigs' syndrome and elevated CA-125. A case report. *J Reprod Med* 40: 817-819.
32. Abad A, Cazorla E, Ruiz F, Aznar I, Asins E, et al. (1999) Meigs' syndrome with elevated CA125: case report and review of the literature. *Eur J Obstet Gynecol Reprod Biol* 82: 97-99.
33. Migishima F, Toshiko J, Hiroki H, Rinya S, Yasuhiro I, et al. (2000) Uterine leiomyoma causing massive ascites and left pleural effusion with elevated CA 125: a case report. *J Obstet Gynaecol Res* 26: 283-287.
34. Chan Cy, Chan SM, Liauw L (2000) A large abdominal mass in a young girl. *Br J Radiol* 73: 913-914.
35. Patsner B (2000) Meigs syndrome and "false positive" preoperative serum CA-125 levels: analysis of ten cases. *Eur J Gynaecol Oncol* 21: 362-363.
36. Buttin B, Cohn D, Herzog T (2001) Meigs' syndrome with an elevated CA 125 from benign Brenner tumors. *Obstet Gynecol* 98: 980-982.
37. Massoni F, Carbillon L, Azria E, Uzan M (2001) Demons-Meigs syndrome: apropos of 1 case. *Gynecol Obstet Fertil* 29: 905-907.
38. López S, Laforga J, Torregrosa P, García E, Rius J, et al. (2002) Síndrome de Meigs: presentación de dos casos. *Prog Obstet Ginecol* 45: 403-407.
39. Huang S, Chen H, Chang K, Chou C (2003) Ascites and elevated androgen level in a pregnant patient with an ovarian sclerosing stromal tumor. *J Formos Med Assoc* 102: 124-126.
40. Vieira S, Pimentel L, Ribeiro J, de Andrade N, de Santana J, et al. (2003) Meigs' syndrome with elevated CA 125: case report. *Sao Paulo Med J* 121: 210-212.
41. Bildirici K, Yalçın O, Ozalp S, Peker B, Ozden H, et al. (2004) Sclerosing stromal tumor of the ovary associated with Meigs' syndrome: a case report. *Eur J Gynaecol Oncol* 25: 528-529.
42. Morillo M, González-Sicilia E, Martín F, Muñoz V, Calero M, et al. (2003) Síndrome de Meigs con valores elevados de CA 125. Aportación de un caso y revisión de la bibliografía. *Invest Gin Obst Clin* 30: 355-358.
43. Cissé C, Ngom P, Sangare M, Ndong M, Moreau J, et al. (2004) Ovarian fibroma associated with Demons-Meigs syndrome and elevated CA 125. *J Gynecol Obstet Biol Reprod* 33: 251-254.
44. Salman M, Basaran A, Guler T, Gultekin M, Dursun P, et al. (2005) Meigs' syndrome with highly elevated ca. 125 levels in a patient with Takayasu arteritis: a case report. *Arch Gynecol Obstet* 272: 90-92.
45. Choi K, Lee HJ, Pae JC, Oh SJ, Lim SY, et al. (2005) Ovarian granulosa cell tumor presenting as Meigs' syndrome with elevated CA125. *Korean J Intern Med* 20: 105-109.
46. Kurai M, Shiozawa T, Noguchi H, Konishi I (2005) Leiomyoma of the ovary presenting with Meigs' syndrome. *J Obstet Gynaecol Res* 31: 257-262.
47. Morán-Mendoza A, Alvarado-Luna G, Calderillo-Ruiz G, Serrano-Olvera A, López-Graniel CM, et al. (2006) Elevated CA125 level associated with Meigs' syndrome: case report and review of the literature. *Int J Gynecol Cancer* 16: 315-318.
48. Jung N, Kim T, Kim H, Lee K, Lee N, et al. (2006) Ovarian sclerosing stromal tumor presenting as Meigs' syndrome with elevated CA-125. *J Obstet Gynaecol Res* 32: 619-622.
49. Benjapibal M, Sangkarat S, Laiwejpithaya S, Viriyapak B, Chaopotong P, et al. (2009) Meigs' syndrome with elevated serum CA125: case report and review of the literature. *Case Rep Oncol* 2: 61-66.
50. Lanitis S, Sivakumar S, Behranwala K, Zacharakis E, Al Mufti R, et al. (2009) A case of Meigs syndrome mimicking metastatic breast carcinoma. *World J Surg Oncol* 7: 10-16.
51. Kaur H, Bagga R, Saha S, Gainer S, Srinivasan R, et al. (2009) Juvenile granulosa cell tumor of the ovary presenting with pleural effusion and ascites. *Int J Clin Oncol* 14: 78-81.
52. Amorim-Costa C, Costa A, Baptista P, Paiva V (2010) Sclerosing stromal tumour of the ovary associated with Meigs' syndrome and elevated CA125. *J Obstet Gynaecol* 30: 747-748.
53. Boufettal H, Zaghba N, Morad S, Bakhatar A, Yassine N, et al. (2011) Syndrome de Demons-Meigs: à propos d'une nouvelle observation et revue de la littérature. *Rev Pneumol Clin* 67: 121-123.
54. Liou J, Su T, Hsu J (2011) Meigs' syndrome with elevated serum cancer antigen 125 levels in a case of ovarian sclerosing stromal tumor. *Taiwan J Obstet Gynecol* 50: 196-200.
55. Monteiro S, Costa A, Paiva V (2012) Mitotically active cellular ovarian fibroma with Meigs' syndrome and elevated CA-125: towards fertility preservation. *J Pediatr Adolesc Gynecol* 25: 107-109.
56. Su F, Cummings K, Krigman H, Ranganathan P (2013) Meigs' syndrome: a rare cause of recurrent pleural effusion in scleroderma. *Rheumatol Int* 33: 2647-2651.
57. Riker D, Goba D (2013) Ovarian mass, pleural effusion, and ascites revisiting Meigs syndrome. *J Bronchol Interv Pulmonol* 20: 48-51.
58. Gomes D, Vasconcelos R, Carvalho B, Furtado V, Ramos F, et al. (2013) Sclerosing stromal tumor of the ovary associated with a Meigs' syndrome and pregnancy: a case report. *Rev Bras Ginecol Obstet* 35: 331-335.
59. Yazdani S, Alijanpoor A, Sharbatdaran M, Bouzari Z, Abedisamakoosh M, et al. (2014) Meigs' syndrome with elevated serum CA125 in a case of ovarian fibroma/thecoma. *Caspian J Intern Med* 5: 43-45.
60. Cha M, Roh H, You S, Lee S, Cho H, et al. (2014) Meigs' syndrome with elevated serum CA 125 level in a case of ovarian fibrothecoma. *Eur J Gynaecol Oncol* 35: 734-737.
61. Park JW, Bae JW (2015) Postmenopausal Meigs' syndrome in elevated CA-125: a case report. *J Menopausal Med* 21: 56-59.
62. Danilos J, Kwaśniewski M, Mazurek D, Bednarek W, Kotarski J, et al. (2015) Meigs' syndrome with elevated CA-125 and HE-4: a case of luteinized fibrothecoma. *Prz Menopausalny* 14: 152-154.
63. Foti PV, Attina G, Spadola S, Caltabiano R, Farina R, (2016) MR imaging of ovarian masses: classification and differential diagnosis. *Insights Imaging* 7: 21-41.
64. Ray-Coquard I, Brown J, Harter P, Provencher DM, Fong PC (2014) Gynecologic Cancer InterGroup (GCIg) Consensus Review for Ovarian Sex Cord Stromal Tumors. *Int J Gynecol Cancer* 24: S42-47.
65. Mariana Horta, Teresa Margarida Cunha (2015) Sex cord-stromal tumors of the ovary: a comprehensive review and update for radiologists. *Diagn Interv Radiol* 21: 277-286.
66. Outwater EK, Wagner BJ, Mannion C, McLarney JK, Kim B, et al. (1998) Sex cord-stromal and steroid cell tumors of the ovary. *Radiographics* 18: 1523-1546.
67. Outwater EK, Marchetto B, Wagner BJ (2000) Virilizing tumors of the ovary: imaging features. *Ultrasound Obstet Gynecol* 15: 365-371.
68. Yanushpolsky EH, Brow DL, Smith BL (1995) Localization of small ovarian Sertoli-Leydig cell tumors by transvaginal sonography with color Doppler. *Ultrasound Obstet Gynecol* 5: 133-135.
69. Hricak H, Akin O, Sala E, Ascher SM, Levine D, et al. (2007) Fibrothecoma and Sclerosing Stromal Tumor. In *Diagnostic Imaging: Gynecology*, 1st Ed 728-731.
70. Outwater EK, Wagner BJ, Mannion C, McLarney JK, Kim B, et al. (1998) Sex cord-stromal and steroid cell tumors of the ovary. *Radiographics* 18: 1523-1546.
71. Tanaka YO, Tsunoda H, Kitagawa Y, Ueno T, Yoshikawa H, et al. (2004) Functioning ovarian tumors: direct and indirect findings at MR imaging. *Radiographics* 24: S147-166.

Isolated Celiac Trunk Dissection after Cardiac Surgery

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Abstract

The most catastrophic postoperative gastrointestinal complication in cardiac surgery is mesenteric ischemia, which is frequently fatal. This may result from atheroembolization, heparin-induced thrombocytopenia or hypoperfusion. We reported the case of 72 year old man undergone to coronary artery bypass and aortic valve replacement, presented isolated celiac trunk dissection after surgery. CT scan described a dissection flap of the first part of celiac trunk possible due to ulcerative plaque without note of antegrade or retrograde development. Considering patient's hemodynamic, respiratory and general trend, we decided to choose conservative management. The sequent postoperative period was uneventfully, the patient was hemodynamically stable and he was discharged at the 20th postoperative day. The atheroembolization was a life-threatening problem of all vascular districts: a correct CPB pressure and postoperative BP monitoring could help to reduce the incidence of its complications.

Keywords: Complication cardiac surgery; Celiac trunk dissection; Post cardiac surgery

Introduction

Spontaneous dissection of the superior mesenteric and inferior mesenteric arteries and of the celiac artery is uncommon occurrence [1]. Celiac artery dissection (CTD) is rare, and can present with intimal flap, mural thrombus or infiltration of fat around the artery. The causes of CTD are several and different: hypertension, arteriosclerosis, degeneration of the arterial wall, trauma, pregnancy, and arteriopathy, iatrogenic and unknown ones. The evolution of CTD isn't well known: it can be associated with complications like aneurysm formation or occlusion, splenic infarction, intraperitoneal hemorrhage and the intestinal ischemia. There are several management modalities applied by the physicians on a case by-case basis like endovascular repair or interventional radiological approach [2] or conservative treatment options by anticoagulants and anti-platelets besides antihypertensive drug are also applied. The choice of CTD isn't univocal and well-defined: according to the reported scientific paper documented CTD from 1959, the proper treatment is related to celiac trunk lesion, celiac trunk complication and patient's clinical trend. The medical treatment consists of oral anticoagulation therapy and monitoring of the patient. The medical therapy failure or the CTS complicated with widespread bowel ischemia and /or large splenic infarction needs surgery because the life-threatening development. On the contrary, a localized and mild CTD due to malperfusion or with high risk of rupture could be treated by endovascular choice.

Case Report

A 72 year old male with a history of paroxysmal atrial fibrillation and chronic coronary artery disease treated with percutaneous coronary intervention two years earlier, was admitted to our hospital suffering from chest pain (angina) and exercise intolerance. Coronary angiography documented a severe lesion of the main stem (>70%) and mild lesion (50%) of the proximal right coronary artery. A Trans Thoracic Echocardiography (TTE) revealed mildly dilated left ventricle (LVEF 40% and LV-End diastolic Volume 120 ml/m²) and moderate aortic regurgitation (Regurgitation Volume 35 ml/beat).

He underwent double coronary artery bypass surgery and Aortic Valve Replacement (AVR, with bioprosthetic valve). Surgery

was performed with standard approach (median sternotomy) in normothermic (34°C) extracorporeal circulation. The Cardiopulmonary Bypass (CPB) time was 170 minutes and mean blood pressure was maintained at about 70 mm Hg. The perioperative period was free of early complications. Hence, we administered Indobufen (200 mg die) and Warfarin to achieve a International Number Ratio (INR) range between 2 to 3. At the second postoperative day, the patient suffered two episodes of high-rate atrial fibrillation, immediately treated with Amiodarone and Metoprolol. After 48 hours, the patient presented abdominal pain with negative physical examination (the pain was mild and widespread, epigastric tenderness, no organomegaly, no signs of ascites, no abdomen aortic pulsation, normal bowel sounds, Blumberg', Murphy' and Giordano' signs were negative) but mild leukocytosis (WBC 11980/mm³). So we started diagnostic workup: an abdomen X-ray showed small air-fluid levels in the jejunal; abdominal ultrasonography was negative; a 64-slice computed tomography (CT) scan showed dissection of the celiac branch of the abdominal aorta (Figure 1A and B) associated with mesenteric distension. Hereby, an endoscopic exam documented ulceration with necrotic area at the second portion of duodenum without evident bleeding sites. Considering the patient details (Table 1) and the high surgical risk due to recent cardiac surgery and possible mesenteric ischemia, we collegially decided for conservative therapy. The patient was monitored in the intensive care unit, nasogastric tube was positioned and antibiotic prophylaxis was started. Indobufen and Warfarin were stopped and we introduced low molecular weight heparin (Enoxaparin 4000 UI subcutaneous twice daily) with proton pump inhibitors (PPI, Pantoprazole 40 mg die intravenous). Two days later, a 64-slide CT scan was performed and showed no aggravation or modification of the abdominal view (Figure 2). At the 12th

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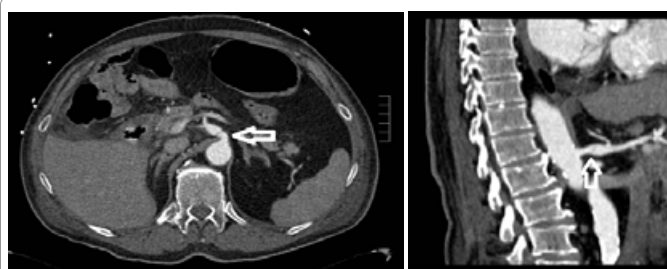


Figure 1A: Axial contrast-enhanced CT image shows celiac trunk proximal partial dissection. **1B:** Sagittal contrast-enhanced CT abdomen/pelvis documents the dissection of celiac trunk.

Table 1: Patient's trend details after the 2nd postoperative day of cardiac surgery.

Celiac Trunk Dissection After CS: Patient's Trend Details	
Mild Symptoms	Widespread and Shallow Abdominal Pain
Mild diagnostic signs	1. Abdomen X-ray showed small air-fluid levels in the jejunal; 2. Abdominal ultrasonography was negative 3. CT scan showed local and limited dissection of the celiac branch of the abdominal aorta 4. Endoscopic exam documented an ulceration with necrotic area at the second portion of duodenum without evident bleeding sites
Stable hemodynamic trend	Optimal blood pressure, PAM (80/85 mmHg)
Optimal respiratory trend	Normal value of PaO ₂ , PCO ₂ , mean pH 7.38, mean HCO ₃ 24 mEq/L, BE -0.6, SaO ₂ 98%, mean CVP 8.
Stable celiac trunk lesion	Documented by: 1. CT scans performing in the 2 nd , 4 th and 12 th postoperative day. 2. No signs and symptoms of sub-ileus and intestinal obstruction 3. No signs and symptoms of gastrointestinal bleeding.

Note: MAP: Mean Arterial Pressure; CVP: Central Venous Pressure; PaO₂: Partial Arterial Pressure of Oxygen; PaCO₂: Partial Arterial Pressure of Carbon Dioxide; CT: Computed Tomography; SaO₂: Arterial Oxygen Saturation

postoperative day, the endoscopy showed worsening and increasing of the ulcerations at the second segment of the duodenum with an evident bleeding site, ulcerations were treated with endoclips and local therapeutic injection of Epinephrine (1:10,000, 8 ml). The subsequent course was uneventful and with stable haemoglobin at laboratory test. At the 20th postoperative days, the US-ECHO did not detect the intimal flap of celiac branch (Figure 3A and B). The endoscopy showed a regression of ulcerative lesions of the duodenum (re-epithelialisation). The patient was discharged and the 1 year and 3 year follow up was free of long-term complication. He didn't refer any abdominal symptoms, the control CT scan and echography didn't showed alteration of the abdomen vascularisation (Figure 4).

Discussion

Gastrointestinal complications after cardiac surgery are rare but carry significant morbidity and mortality even when recognized early and treated appropriately. Reviewing the scientific literature these complications are rare (0.53%-2.1%) but often fatal (13.9%-63%) [3]. According to Mangi et al. [4], the documented or suspected postoperative mesenteric ischemia is a life-threatening fatal complication (death in the 68% of the cases). The outcome in mesenteric ischemia is closely dependent on the elapsed time to diagnosis and treatment. The diagnosis is typically difficult and delayed due to nonspecific results of biological and radiological tests. The etiology of mesenteric ischemia may also be conceptually classified into two distinct subsets: low flow and low perfusion states and embolic related events. Mangi et al. [4] observed that CPB had been implicated in the development of mesenteric ischemia modifying the regional intestinal blood flow, by pulsating to continuous flow. Tao et al. [5]

demonstrated that normothermic CPB may cause a diversion of the blood flow in the splanchnic district away from the ileum and colon. These changes accompanied dysfunction of mesenteric endothelial cells causing hyper-reactivity of alpha agonists [6]. Survival from the insult of mesenteric ischemia depends partially upon the early diagnosis. The most sensitive indicators of mesenteric ischemia after cardiac surgery are abdominal pain (continuous, not local), increasing of lactate and base excess (BE) and spreading of metabolic acidosis. As the majority of cases of mesenteric ischemia occur during the initial hours to days following operation, fast-track extubation pathways and or minimal sedation theoretically may enable earlier recognition of a catastrophic gastrointestinal complication. When intestinal ischemia is clinically suspected, diagnostic imaging studies should be performed even if peritoneal signs are absent.

Acute mesenteric ischemia is considered a vascular emergency; if treated during its initial stage, its mortality rate is less than 30% but if treatment is begun more than 6 to 8 hours after symptom onset, the mortality rate increases exponentially. Various treatment options are currently available, including conservative management, anticoagulation, endovascular stenting, and surgical repair. A review of current literature show that endovascular treatment techniques should be preferred, in order to place less of an additional burden on patients, most of whom have multiple morbidities [7,8]; immediate laparotomy must be performed for acute abdomen and revascularization of the intestine is the primary aim of treatment. Irreversibly damaged portions of the intestine must be resected.

Carefully analyzing our reported case report (Table 1), we decided collegially (cardiac surgeon, cardiologist, cardiovascular anaesthetist and general surgeon) to choose the conservative management. Our conservative management consisted of: strict blood pressure monitoring, every day blood gas analysis and diuresis balance, daily control of bowel function and abdomen physical exam, performing control CT scan and abdomen echography periodically with a maximum interval time of 48 hours. Following this management, we have controlled closely the patient, every possible variables and changes, and the patient was successfully discharged after 20th day.

Conclusion

Acute mesenteric ischemia is a life-threatening surgical emergency in which the outcome is closely dependent on the elapsed time to diagnosis and treatment. Some studies have undertaken systematic analyses of preoperative, intraoperative, and postoperative variables to define the risk stratification to influence cardiac surgeons to



Figure 2: Axial contrast-enhanced CT abdomen/pelvis showing no worsening of celiac trunk dissection.

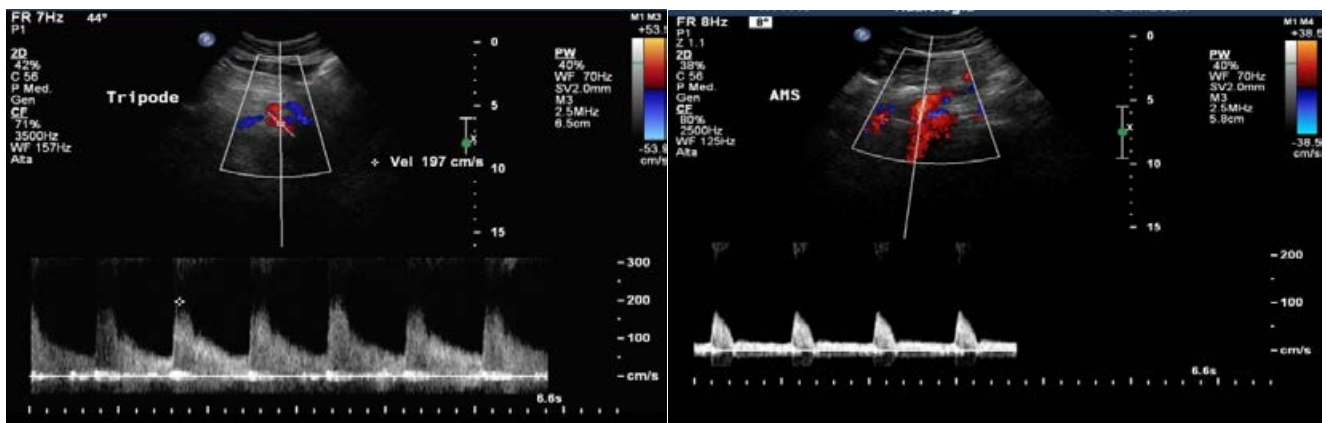


Figure 3A: Duplex Doppler sonography of celiac trunk. **3B:** Duplex Doppler sonography of superior mesenteric artery.



Figure 4: Axial contrast-enhanced CT abdomen/pelvis showing normal celiac trunk and abdomen perfusion.

alter their operative strategy or early postoperative management decisions. Identification of risk factors for death after gastrointestinal complications provides general surgeons with clinically relevant features indicating subsets of patients most likely to benefit from laparotomy. The outcome is closely dependent on the elapsed time to diagnosis and treatment. Conservative management consisted of strict blood pressure control, bowel rest, and close observation, without the use of anticoagulation or antiplatelet agents. Patients with a symptomatic dissection of the superior mesenteric artery should initially undergo conservative management without anticoagulation and antiplatelet therapy if bowel perfusion is not compromised and if the superior mesenteric artery is not likely to rupture. Surgery is indicated in patients with superior mesenteric artery thrombosis; questionable bowel viability, bowel necrosis or severe haemorrhage. Patients initially treated with conservative management should be monitored closely and should undergo a follow-up CT scan.

Conflict of Interest

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

References

1. D'Ambrosio N, Friedman B, Siegel D, Katz D, Newatia A, et al. (2007) Spontaneous isolated dissection of the celiac artery: CT findings in adults. *Am J Roentgenol* 188: 6-11.
2. Fenoglio L, Allione A, Scalabrino E, Alberto G, Benedetti V, et al. (2004) Spontaneous dissection of the celiac artery: a pitfall in the diagnosis of acute abdominal pain. Presentation of two cases. *Dig Dis Sci* 49: 1223-1227.
3. Tsiotos GG, Mullany CJ, Zietlow S, van Heerden JA, (1994) Abdominal complications following cardiac surgery. *Am J Surg* 167: 553-557.

4. Mangi AA, Christison-Lagay ER, Torchiana DF, Warshaw AL, Berger DL, et al. (2005) Gastrointestinal complications in patients undergoing heart operation. *Ann Surg* 241: 895-904.
5. Tao W, Zwischenberger JB, Nguyen TT, Vertrees RA, McDaniel LB, et al. (1995) Gut mucosal ischemia during normothermic cardiopulmonary bypass results from blood flow redistribution and increased oxygen demand. *J Thorac Cardiovasc Surg* 110: 819-828.
6. Abboud B, Daher R, Boujaoude J (2008) Acute mesenteric ischemia after cardio-pulmonary bypass surgery. *World J Gastroenterol* 14: 5361-5370.
7. Oh S, Cho YP, Kim JH, Shin S, Kwon TW, et al. (2011) Symptomatic spontaneous celiac artery dissection treated by conservative management: serial imaging findings. *Abdom Imaging* 36: 79-82.
8. Sparks SR, Vasquez JC, Bergan JJ, Owens EL (2000) Failure of nonoperative management of isolated superior mesenteric artery dissection. *Ann Vasc Sur* 14: 105-109.

Giant solitary Peutz-Jeghers-Type Hamartomatous Polyp in the Duodenum Presenting as Gastric Outlet Obstruction

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Abstract

Solitary Peutz-Jeghers type hamartomatous polyp is a variant of PJS characterized by the presence of hamartomatous polyps in the absence of other manifestations of PJS. It is quite rare with only 19 cases reported in English literature. These cases present in older individuals are usually asymptomatic and carry increased risk of malignant transformation. Hamartomatous polyps are characterized histologically by tree-like branching of smooth muscle fibres covered by mucosal tissue of near normal appearance. Endoscopically, they are characterized by a lobular or nodular surface and whitish colour. We are presenting a case of giant Solitary Peutz-Jeghers type hamartomatous polyp of the duodenum who presented with symptoms of gastric outlet obstruction that was treated with pylorus preserving pancreaticoduodenectomy.

Keywords: Peutz-jeghers; Hamartomatous polyp; Giant polyp; Gastric outlet obstruction

Introduction

Peutz-Jeghers syndrome (PJS), first described by Peutz in 1921 is a rare, autosomal dominant disorder characterized by multiple gastrointestinal hamartomatous polyps and muco cutaneous pigmentation around the lips and oral cavity [1-3]. A germline mutation of the STK11 gene located on chromosome 19p13.3 is responsible for development of PJS [4]. A solitary Peutz-Jeghers type hamartomatous polyp is a variant of PJS characterized by the presence of hamartomatous polyps in the absence of other manifestations of PJS [5]. These patients present with nonspecific symptoms with most diagnosed incidentally during endoscopy. We are reporting a case of giant solitary Peutz-Jeghers-type hamartomatous polyp in the duodenum in a young girl presenting as gastric outlet obstruction.

Case Report

An 18 year old girl presented with history of recurrent non bilious vomiting of 4 month duration associated with vague upper abdominal pain. On abdominal examination, she had a mass in right hypochondrium with features suggestive of mass arising from the pancreas. She didn't have any peri oral muco cutaneous pigmentation. Oesophago gastro duodenoscopy (OGD scopy) revealed a polypoidal mass of about 10 × 6 cm arising from the medial wall of second part of duodenum close to ampulla of vater (Figure 1A). Biopsy from the mass was reported as villous adenoma with severe dysplasia. Contrast Enhanced Computed Tomography (CECT) of the abdomen revealed mass of size arising from the second part of duodenum with loss of fat planes with pancreatic head (Figure 1B). The mass was abutting superior mesenteric vein and right renal vein (Figure 1C). Patient underwent pylorus preserving pancreaticoduodenectomy (Figure 1D). Post operatively she developed post-operative pancreatic fistula (POPF) grade B which was managed conservatively. Histopathological examination of the specimen revealed solitary Peutz-Jeghers-type hamartomatous polyp arising from the 2nd part of duodenum involving the ampulla of vater (Figure 1E and F). There was mild dysplasia, however no evidence of invasive malignancy. All the resection margins were free and lymph nodes were reactive. After recovery she underwent colonoscopy which was within normal limits. On retrospective enquiry, patient's parents had 2nd degree consanguineous marriage though there

was no family history of any hereditary disorders. At 8 months follow up, patient is disease free and in good health. At last follow up, patient underwent colonoscopy to rule out any other polyps.

Discussion

A solitary Peutz-Jeghers type hamartomatous polyp in the duodenum was first described in 1986 by Bott et al. [6]. This disorder differs from Peutz-Jeghers Syndrome (PJS) in following characteristics: Diagnosis at a more advanced age, absence of mutation of the STK11/LKB-1 gene and family history as well as lack of muco-cutaneous pigmentation [5]. However in many cases it is difficult to determine whether these polyps are a separate variant or initial clinical manifestation of PJS. Present patient had no significant family history except for 2 degree consanguineous marriage among her parents and no muco cutaneous pigmentation around the oral cavity.

Literature review by Suzuki et al revealed only 19 cases of solitary Peutz-Jeghers type hamartomatous polyp of the duodenum reported in English literature [7]. Age at diagnosis ranged from 23-89 years. Most common site affected was second portion of the duodenum followed by the duodenal bulb. Size of the polyp ranged from 5-70 mm. Present patient had a solitary hamartomatous polyp of size 80×30×30 mm [7]. The present case represents the largest polyp of this subtype reported in English literature. In addition, unlike previous reported cases she presented at the age of 18 years.

Although most of these patients are asymptomatic with polyp being detected incidentally some may present with features of cholangitis or bleeding [7-9]. Present patient presented with features suggestive

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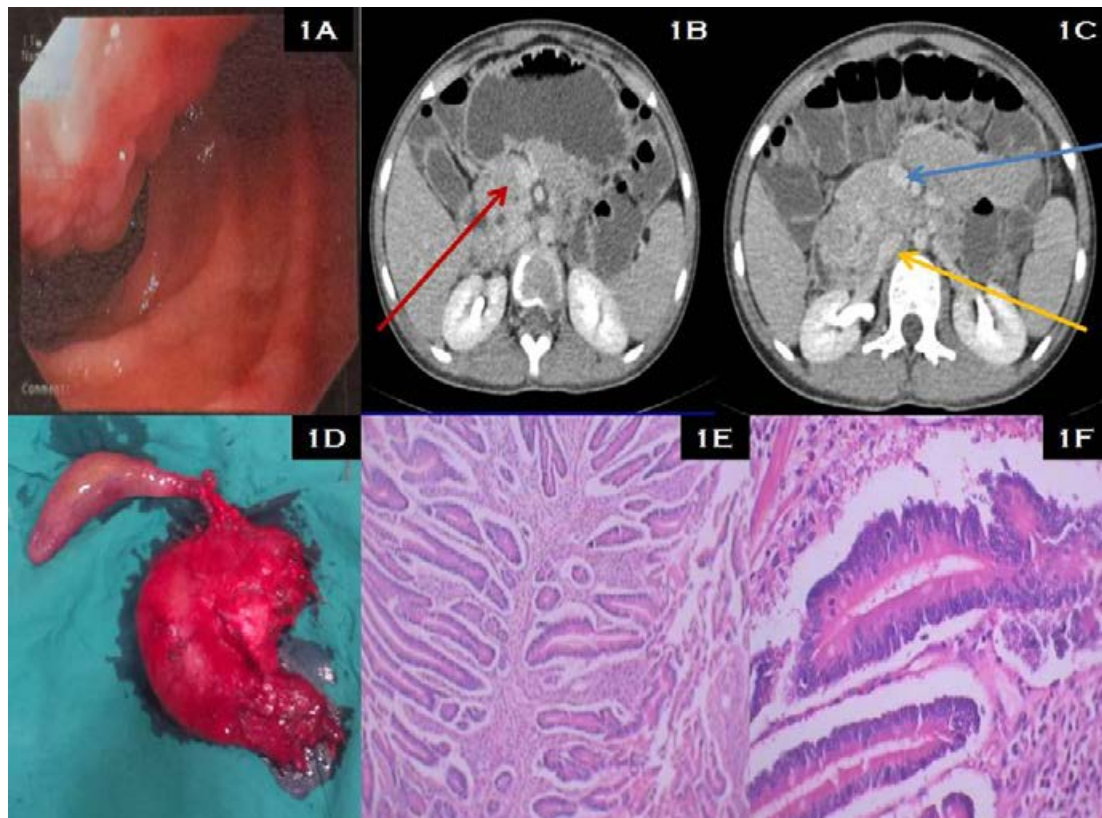


Figure 1A: OGD scopy picture showing a polypoid mass arising from the medial wall of second part of duodenum. **1B.** CECT abdomen showing the duodenal polypoid mass abutting the head of the pancreas (Red arrow). **1C.** CECT abdomen showing the duodenal mass abutting the superior mesenteric vein (Blue arrow) and right renal vein (Yellow arrow). **1D.** Pancreaticoduodenectomy specimen. **1E and F.** Histomicrograph showing the hamartomatous polyp.

of gastric outlet obstruction probably owing to the size of the mass. Hamartomatous polyps are characterized histologically by tree-like branching of smooth muscle fibres covered by mucosal tissue of near normal appearance [10]. Endoscopically, they are characterized by a lobular or nodular surface and whitish colour [11]. Whitish colour is because of the presence of diffusely scattered white spots on the surface of the polyps [12]. However, as diagnosis by morphologic features is difficult, endoscopic biopsies must be performed to establish the diagnosis and hence guide treatment.

There is no consensus on the management of Peutz-Jeghers type hamartomatous polyp of the duodenum. In general, hamartomatous polyps are considered to have very low malignant potential compared to adenomatous polyps [13]. However, malignant transformation has been reported in 3%-6% of the polyps in Peutz-Jeghers syndrome [14,15]. Although, it is a general belief that solitary Peutz-Jeghers type hamartomatous polyp of the duodenum have low malignant potential, 4 of the 19 patients included in the review by Suzuki et al had malignant transformation [7]. In this review, it was observed that higher age of presentation was associated with increased risk of malignancy. In addition, in one of the cases reported by Sekino et al, there were extra duodenal malignancies involving 6 other viscera [16]. In view of these findings, it is reasonable to consider resection of these tumors. The present patient had mild dysplasia in the polyp and hence warranted resection.

Conclusion

Purpose of reporting this case is because of

Rarity of solitary Peutz-Jeghers type hamartomatous polyp.

Giant size and varied presentation with symptoms of gastric outlet obstruction

Conflict of Interests

The authors declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

References

1. Peutz JLA (1921) Very remarkable case of familial case of polyposis of mucous membrane of intestinal tract and nasopharynx accompanied by peculiar pigmentations of skin and mucous membrane. *Ned Maandschr Geneesk* 10: 134-146.
2. Jeghers H, McKusick VA, Katz KH (1949) Generalized intestinal polyposis and melanin spots of the oral mucosa, lips and digits; a syndrome of diagnostic significance. *N Engl J Med* 241: 1031-1036.
3. Tomlinson IP, Houlston RS (1997) Peutz-Jeghers syndrome. *J Med Genet* 34: 1007-1011.
4. Hanks SK, Quinn AM, Hunter T (1988) The protein kinase family: conserved features and deduced phylogeny of the catalytic domains. *Science* 241: 42-52.
5. Kitaoka F, Shiogama T, Mizutani A, Tsurunaga Y, Fukui H, et al. (2004) A solitary Peutz-Jeghers-type hamartomatous polyp in the duodenum. A case report including results of mutation analysis. *Digestion* 69: 79-82.
6. Bott SJ, Hanks JB, Stone DD (1986) Solitary hamartomatous polyp of the duodenum in the absence of familial polyposis. *Am J Gastroenterol* 8: 993-994.
7. Suzuki K, Higuchi H, Shimizu S, Nakano M, Serizawa H, et al. (2015) Endoscopic snare papillectomy for a solitary Peutz-Jeghers-type polyp in the duodenum with ingrowth into the common bile duct: Case report. *World J Gastroenterol* 21: 8215-8220.
8. Ichiyoshi Y, Yao T, Nagasaki S, Sugimachi K (1996) Solitary Peutz-Jeghers type polyp of the duodenum containing a focus of adenocarcinoma. *Ital J Gastroenterol* 28: 95-97.
9. Oncel M, Remzi FH, Church JM, Goldblum JR, Zutshi M, et al. (2003) Course and follow-up of solitary Peutz-Jeghers polyps: a case series. *Int J Colorectal Dis* 18: 33-35.
10. Nakayama H, Fujii M, Kimura A, Kajihara H (1996) A solitary Peutz-Jeghers-type hamartomatous polyp of the rectum: report of a case and review of the literature. *Jpn J Clin Oncol* 26: 273-276.

11. Seiyuu Suzuki, Shoji Hirasaki, Fusao Ikeda, Eiichiro Yumoto, Hiromichi Yamane, et al. (2008) Three cases of Solitary Peutz-Jeghers-type hamartomatous polyp in the duodenum. *World J Gastroenterol.* 14:944-947.
12. Sugimoto K, Shinohara Y, Katakami T, Abe K, Ueda K, et al. (2005) [A case of Peutz-Jeghers type polyp of the duodenum treated by endoscopic resection]. *Nihon Shokakibyo Gakkai* 102: 1039-1044.
13. Bartholomew LG, Moore CE, Dahlin DC, Waugh JM (1962) Intestinal polyposis associated with mucocutaneous pigmentation. *Surg Gynecol Obstet* 115: 1-11.
14. Perzin KH, Bridge MF (1982) Adenomatous and carcinomatous changes in hamartomatous polyps of the small intestine (Peutz-Jeghers syndrome): report of a case and review of the literature. *Cancer* 49: 971-983.
15. Narita T, Eto T, Ito T (1987) Peutz-Jeghers syndrome with adenomas and adenocarcinomas in colonic polyps. *Am J Surg Pathol* 11: 76-81.
16. Sekino Y, Inamori M, Hirai M, Suzuki K, Tsuzawa K, et al. (2011) Solitary Peutz-Jeghers type hamartomatous polyps in the duodenum are not always associated with a low risk of cancer: two case reports. *J Med Case Rep* 5: 240.

To Investigate the Impact of Laparoscopic Resection of Colorectal Carcinoma on the Peritoneal Metastases of Cancer

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Abstract

Objective: To explore the effect of laparoscopy on cancer cells and the expressions of adhesion molecules (ICAM-1, CD44v6 & integrin β 1) in peritoneal tissue and abdominal rinse in patients with colorectal carcinoma (CC).

Methods: A total of 65 CC cases undergoing radical resection at our hospital were analyzed. They were divided into two groups of LAP (laparoscopy, n=35) and OP (open surgery, n=30). Peritoneal tissues were collected at incision and beyond. Also abdominal rinse was collected before tumor resection and abdomen closure. The expressions of adhesion molecules (ICAM-1, CD44v6 & integrin beta 1) in peritoneal and abdominal cavities of two groups were detected by immunohistochemistry and double-antibody sandwich ABC-ELISA. And cancer cells in abdominal rinse were detected by peritoneal lavage cytology (PLC) for comparing two surgical methods.

Results: In LAP group, PLC was positive in 3 cases (8.6%) before tumor resection and 8 cases (22.9%) before abdominal closure. In OP group, PLC was positive in 4 cases (13.3%) before tumor resection and 8 cases (26.7%) before abdominal closure. No inter-group difference existed in PLC ($P>0.05$). The expressions of CD44v6, ICAM-1 and integrin beta 1 in abdominal cavity (before tumor resection & abdomen closure) were compared for LAP and OP groups. And there was no statistically significant difference ($P>0.05$). The expressions of CD44v6, ICAM-1 and integrin beta 1 in peritoneal tissues (at incision and beyond) were compared between LAP and OP groups. And there was no statistically significant difference ($P>0.05$).

Conclusion: Compared with CC patients undergoing traditional open surgery, the risk of exfoliated cancer cells in abdominal cavity shows no increase. And there is no impact upon the expressions of adhesion molecules.

Keywords: Laparoscopic surgery; Peritoneal metastases

Introduction

In China, colorectal cancer is one type of gastrointestinal carcinoma with relatively high occurrence in the population. While surgical resection has been an effective way of getting rid of colorectal carcinoma, laparoscopic resection offers the benefits including shorter hospitalization, rapid recovery, and smaller incisions, and thus has been widely used in removing the colorectal carcinoma. For colorectal cancer, migration of tumor cells to distant organs leading to the metastases of cancer is the main cause of death in colorectal cancer patients [1,2]. Currently, there have been efforts in understanding whether the surgical resection and laparoscopic resection result in significant differences in the peritoneal metastases of cancer [3,4]. This paper reports a study assessing the impact of surgical resection and laparoscopic resection on the peritoneal metastases of cancer in colorectal cancer patients.

Study Design and Methods

A cohort study design

A total of 66 colorectal cancer patients treated between August 2013 and August 2015 were enlisted in a cohort study in which they were equally divided in random into two groups: a control group (33) and an observation group (33).

Patient selection was based on the following criteria: (1) The absence of distant metastasis based on preoperative images including CT, ultrasound, and X-ray; (2) No dysfunction of the liver, kidney, heart, and brain; (3) No history of operation for gastrointestinal carcinoma; (4) Patients' age between 40-65 years old.

Patients were excluded in the study based on the following criteria: (1) Abandoned operation due to tumor spreading to

peritoneal cavity and peritoneum; (2) palliative operation. The control group had 11 females and 22 males, with ages ranging from 40 to 64, and an average age of 53.23 ± 10.33 years old. In this group the average tumor size was 3.56 ± 1.54 cm. Based on the Dukes classification of tumors, there were 8 cases in Stage A, 15 cases in Stage B, and 10 cases in Stage C. The observation group had 10 females and 23 males, with ages ranging from 40 to 65, and an average age of 53.09 ± 10.13 years old. In this group the average tumor size was 4.10 ± 1.65 cm. Based on the Dukes classification, there were 9 cases in Stage A, 12 cases in Stage B, and 12 cases in Stage C. Comparison of the patients' sex, age and Dukes classification between these two groups demonstrated no statistical differences ($P>0.05$).

Treatment

Patients in the control group were subject to surgical resection. Please refer to the Surgical Procedures section for colorectal tumor separation, dissection, removal and digestive tract repair. Patients in the observation group were subject to laparoscopic resection, with the procedures detailed as below.

Tumor site locationing: Place the patient under a general anesthetic through endotracheal intubation and use carbon dioxide

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(CO₂) gas to establish the pneumoperitoneum. Make a 10 mm Trocar incision around the navel to insert the laparoscope inside. Make a 10 mm and 5 mm Trocar incision at the lower left and right pneumoperitoneum respectively to insert the intestinal forceps. Pass the colonoscopy camera into the rectum and colon through the anus to locate the tumor site and determine the section to be surgically removed. Mark the tumor with a titanium forceps, and tie both ends of the colon approximately 10-15 cm from the tumor with cotton tapes. For rectal cancer, tie the proximal end first, followed by tying up the distal end during operation.

Surgical procedures: For transverse colon cancer, use Harmonic scalpel to cut and separate mesentery from the transverse colon. Based on the location of the tumor, clamp off the colic arteries, and make the hepatic flexure and the splenic flexure free. Remove the CO₂ pneumoperitoneum, and extend the middle-left Trocar incision up to 4-5 cm, take out the transverse colon, remove the tumor. Perform the colonic anastomosis, and put the colon back into the peritoneal cavity. Close off the incisions and reestablish CO₂ pneumoperitoneum to finish the operation. For ascending colon cancer, use Harmonic scalpel to cut and separate mesentery from the ascending colon. Make the hepatic flexure, ascending colon, and ilium free. Clamp off the right colic artery and right colic vein. Separate and cut the mesentery from the colon to the root of the right colonic artery. Remove the CO₂ pneumoperitoneum, and extend the middle-right Trocar incision up to 4-5 cm, take out the ascending colon, remove the tumor. Perform the ileum and transverse colon anastomosis, and put the colon back into the peritoneal cavity. Close off the incisions and reestablish CO₂ pneumoperitoneum to finish the operation. For sigmoid colon and rectum cancer, use Harmonic scalpel to cut and separate the mesentery from the sigmoid colon. Clamp off the artery roots of the mesentery. Make a ligation at the region 3-5 cm distal of the tumor using a cotton thread. Make a cut in the rectum. Extend the middle-left Trocar incision up to 4-5 cm, take out the colon, and remove the tumor. Suture the surgical ends together, and put the colon back into the peritoneal cavity. Close off the incisions and reestablish CO₂ pneumoperitoneum, insert the round stapler through the anus, and perform the rectal end anastomosis to complete the operation.

Measurement: Tumor cytology analysis: Collect the rinsing liquid of the peritoneal cavity and centrifuged for 10 minutes. Collect the precipitated cells, followed with H&E staining, fixing and conventional smearing under sterile conditions. Analyze the tumor cells under the light microscope. Tumor cytology analysis for the rinsing liquid of the surgical tools: At the end of the operation, rinse the surgical tools with SSPS (150 ml), collect and store the rinsing liquid under sterile conditions. Tumor cytology analysis of the CO₂ gas filtrate: When the CO₂ pneumoperitoneum was initially established draws the CO₂ through the Trocar, and pass it through the filter bottle with 150 ml SSPS until the end of the operation. Store the filter bottle under sterile conditions. Tumor cytology analysis for shedding tumor cells in the pneumoperitoneum rinsing liquid: Prior to the operation, rinsing the pneumoperitoneum cavity with tumor using 200 ml SSPS, and collect 100 ml rinsing liquid using a sterilized syringe. Post the operation, rinsing the pneumoperitoneum cavity with 500 ml SSPS, and collect 200 ml rinsing liquid using a sterilized syringe. Store the samples under sterile conditions.

Statistical analysis

Data were analyzed using SPSS 15.0 Software. The counting data were analyzed by χ^2 test and expressed in percentages. The measurement data were analyzed by t test and expressed in $\bar{x} \pm s$. Data showed statistic difference whenever $P < 0.05$.

Results

In this study, a comparison of the patients' sex, age and Dukes classification between the two groups (control group and observation group demonstrated no statistical differences ($P > 0.05$).

A comparison of the tumor-positive percentages in the pneumoperitoneum rinsing liquid before and after the operation

No positive tumor cells were found in the CO₂ filtrate. In the observation group, the tumor-positive percentages in the pneumoperitoneum rinsing liquids before the operation and after the operation were 63.64% and 60.61%, respectively. Also in the observation group, the tumor-positive percentages in the pneumoperitoneum rinsing liquids where tumor was found to be negative prior to the operation but positive post the operation was 6.06%. In the control group, the tumor-positive percentages in the peritoneum rinsing liquids before the operation and after the operation were 69.70% and 45.45% respectively. Also in the control the tumor-positive percentages in the peritoneum rinsing liquids where tumor was found to be negative prior to the operation but positive post the operation was 9.09%. This two groups showed no statistical differences with $P > 0.05$. The results of the tumor-positive percentage in the pneumoperitoneum rinsing liquids before and after the operation were summarized in Table 1. In the observation group, the tumor-positive percentage in the device-rinsing liquid was 12.12%, in comparison to that of 9.09% in the control group. There is no statistical difference between these two groups ($P > 0.05$). The results of the tumor-positive percentage in the device-rinsing liquids between the observation group and control group were summarized in Table 2.

Discussion

It has been a clinical hot topic in understanding whether laparoscopic resection of colorectal cancer would result in the peritoneal metastases of cancer [5-7]. Related studies have found that during the laparoscopic surgery, the cancer cells might exist in vaporized form when the CO₂ pneumoperitoneum is established [8-10]. In our study, results showed the absence of positive tumor cells in the CO₂ filtrate, suggesting that the CO₂ pneumoperitoneum during the operation could not increase the rate of cancer metastases. Despite of the wide use of Harmonic scalpel in the laparoscopic surgery to remove cancerous tissues, whether the vaporization of the cancer tissue could increase the peritoneal metastases of the cancer remains to be controversial. When using Harmonic scalpel to remove gastric cancers, the resulting aerosol also contained some living cancer cells. The number of cancer cells is directly proportional to the cutting power and cutting time. Having a cutting time $< 10s$ could prevent the peritoneal metastases of cancer cells [11]. Besides, the Harmonic scalpel may seal off the cutting end, causing the veins to be closed off. This would minimize the avenues of cancer cell metastases, preventing the peritoneal migration of cancer cells. This study also demonstrated that the tumor-positive percentage in the device-rinsing liquid from the observation group was 12.12%, in comparison to that of 9.09% in the control group. There was no statistical difference between these two groups. These results suggested that the devices contaminated with cancer cells might be one of the reasons for peritoneal metastases. However there was no significant difference in the metastatic rates between the surgical resection and laparoscopic resection.

Post the surgery, the shed cancer cells within the abdomen is one of the main reasons for peritoneal cancer metastases. This study compared the tumor shedding levels from the surgical resection and laparoscopic resection of colorectal cancer patients, and assessed their impact of these two surgical operations on the peritoneal cancer metastases. The study demonstrated no statistical differences in the peritoneal rinsing liquids between the control group and the observation group regarding

Table I: Tumor-positive percentages in the peritoneal rinsing liquid before and after the surgery

Groups	Patient Number	Preoperative tumor negative and post-operative tumor-positive rate	Tumor positive rates post-surgery	Tumor -positive rates prior to surgery
Observation Group	33	2 (6.06%)	17 (51.52%)	21 (63.64%)
Control Group	33	3 (9.09%)	15 (45.45%)	23 (69.70%)
χ^2		0.216	0.243	0.273
P		>0.05	>0.05	>0.05

Table II: Tumor-positive rates in the device-rinsing liquid from the control group and observation group

Groups	Patient Number (N)	Tumor-positive Rate
Observation Group	33	4 (12.12%)
Control Group	33	3 (9.09%)
c2		0.16
P		>0.05

the preoperative tumor-positive rates, post-operative tumor-positive rates, and preoperative tumor-negative and postoperative tumor-positive rates. These results suggested that both surgical resection and laparoscopic resection could impact the peritoneal cancer metastases. The postoperative peritoneal rinsing liquids had a lower tumor-positive rate than the preoperative peritoneal rinsing liquids, suggesting that repeated peritoneal rinsing could decrease the tumor cell shedding and cancer metastases. Laparoscopic operation through changing the patient body position could decrease the pulling and dragging on the tumor and surrounding tissues, expand the operative view, lessen the injury to the peritoneal tissues, and avoid the stimulation of the lesions, thus lowering the cancer metastases. Overall, there is no significant difference in the peritoneal cancer metastases between the surgical resection and laparoscopic resection of the colorectal cancer. The application of CO₂ pneumoperitoneum does not increase the rate of peritoneal cancer metastases. Based on this study, we concluded that the laparoscopic resection of the colorectal cancer is safe, effective, and valuable for its clinical applications.

Conclusion

The surgical resection and laparoscopic resection had no significant difference in their impact on the peritoneal cancer metastases.

Conflict of Interest

Authors have no conflict of interest to disclose.

References

- Rong S, Jian Y, Zhi Y, Jun W, Ma Jun, et al. (2015) Clinical characteristics and prognostic factors of 52 patients with colorectal cancer. *Chinese Journal of clinical oncology and rehabilitation* 12: 1420-1422.
- Haiyan W, Chunwei X, Yongfang W, Zhangbo, Shaoyun, et al. (2015) The molecular pathological detection and analysis of KRAS and BRAF gene mutation in tumor tissues of colorectal cancer patients. *Guizhou medicine* 8: 67-69.
- Sun TY, Wei Y, Yongliang W, Peiwu Z (2010) A clinical study on the impact of laparoscopic surgery of gastric tumor on the peritoneal cancer metastases. *The Chinese General Surgery Journal* 4: 109-112.
- Wei Z, Lei K, Jun C (2015) Effects of laparoscopic resection of colorectal cancer on the expression of adhesion molecules in cancer cells and peritoneal and peritoneal washing fluids. *Medical clinical research* 4: 123-124.
- Haisong Y, Qimou L (2014) Impact of laparoscopic surgery and open surgery on postoperative colorectal cancer recurrence and metastases. *Chinese medical guidelines* 05: 162-163.
- Shengqian S, Yunfeng L (2013) The effect of laparoscopic surgery on colorectal cancer metastasis. *Medical review* 19: 4280-4282.
- Zhenxing H, Liyong, L, Liang Z, Wang Yu, Wei ZQ, et al. (2010) CK20 mRNA expression in peripheral blood of patients with gastrointestinal carcinoma and its clinical significance. *Medical information management* 6: 34-35.

- Yanhui L (2012) Research progress of peritoneal tumor migration after laparoscopic resection of colorectal cancer. *Chinese Journal of modern medicine* 50: 27-28.
- Chunxiu D, Bo P, Yue L, Binghong X, Yong C (2010) Study on the effect of laparoscopic resection of colorectal cancer on blood circulation in patients with colorectal cancer. *Chongqing Journal of medicine* 39: 1056-1058.
- Xiao Yi, Liu Senlin, Liu Peihua, Ma Kang (2015) Effects of laparoscopic resection of colorectal cancer on the tumor cells migration through blood circulation. *Journal of Qiqihar Medical School* 12: 3123-3125.
- Jie Hu, Liming Yang (2012) The impact of laparoscopic surgery on the re-implanting and invasion of gastric cancer cells in the peritoneum leading to tumor metastasis. *Journal of Laparoscopic Surgery* 11: 877-880

Abdominal Compartment Syndrome – Severe Complication of Giant Abdominal Tumor: Case Report and Literature Review

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Abstract

Introduction: Giant abdominal tumors, as a result of volume mass and dimensions, even benign being, can develop serious complications. The differential diagnosis includes cystic or solid disorders of the female genitals, ascites, cysts or hydronephrosis, pancreatic cysts or pseudocysts, gastrointestinal stromal tumors.

Case presentation: A 44 years old patient, was hospitalized for an giant abdominal tumor formation, pain, weight loss, nausea and vomiting. Laboratory data show changes in the sense of acute renal failure. Ultrasound examination reveals layout of carcinomatous ascites and native CT scanning, a giant cyst, without being able to specify their organ affiliation. The central venous pressure monitoring showed low values (less than 1 cm water), and intra-abdominal pressure, measured indirectly using the urinary catheter, revealed an increased value (25 mmHg). Patient undergone a midline laparotomy and it was found a giant cyst developed from the left ovary. It was performed cystectomy associated with hysterectomy and controlateral ovariectomy. The postoperative course was favorable and the patient discharged on day 6. Histopathology confirmed a mucinous cystadenoma

Conclusions: Abdominal compartment syndrome is a severe complication of giant abdominal tumors, which must be solved immediately by medical therapy and/or surgery. Choosing the type of surgery (open or laparoscopic) depends on tumor size and the possibility and establishing the preoperative histopathological diagnosis.

Keywords: Abdominal compartment syndrome; Abdominal tumor; Ovarian tumor

Introducere

Chisturile ovariene voluminoase, de tip seros sau mucinos, datorită dimensiunilor și compresiunii exercitate pe organele învecinate, necesită extirpare chirurgicală ca singura soluție terapeutică [1,2]. Abordul laparoscopic al acestora este din ce în ce mai utilizat, însă limitat de dimensiunile chistului, care, dacă depășește 20 de cm face extrem de dificilă sau chiar imposibilă crearea pneumoperitoneului [3,4]. Diagnosticul preoperator nu este întotdeauna cert, ele putând fi interpretate ca ascită în cadrul cirozei hepatice, chisturi epiploice sau mezoteliiale, glob vezical, diverticuli ai vezicii urinare, hidronefroze voluminoase sau utere fibromatoase [5]. Prezentăm cazul unei paciente cu un chist ovarian voluminos, de 25 de kg, dezvoltat din ovarul stâng, care a determinat apariția sindromului de compartiment abdominal.

Prezentare de caz

Pacienta NL, în vârstă de 44 de ani, se prezintă în serviciul de urgență pentru dureri abdominale, grețuri, vărsături. La examenul clinic al abdomenului se constată creșterea imensă în volum a acestuia, sensibil la palpare, de consistență elastică, cu matitate la palpare și zgomote intestinale absente (Figura 1). Datele de laborator indică o creștere a ureei și a creatininei (120 mg/dL, 2,3 mg/dL), leucocitoză (12.000/mm³) și anemie microcitară. Examenul ecografic efectuat în urgență, evidențiază prezența de lichid în întreaga cavitate peritoneală, mai puțin interhepatofrenic și un ficat cu ecogenitate normală, ridicându-se suspiciunea unei ascite paraneoplazice. Pentru elucidarea diagnosticului se efectuează CT nativ, la care se infirmă ascita și se confirmă prezența unei formațiuni polichistice lichidiene gigante, care ocupă întreaga cavitate peritoneală și comprimă toate organele cavității peritoneale, dar și vena cavă inferioară și ureterele, în prezent fără hidronefroză (Figura 2). Explorarea CT nu poate preciza o apartenență de organ a formațiunii chistice și nici nu evidențiază leziuni care să

pledeze pentru determinări secundare. Având în vedere statusul hemodinamic alterat al bolnavei, cu tahicardie marcată și hipotensiune, bolnava este mai întâi preluată de serviciul de terapie intensivă pentru reechilibrare volemică, hidroelectrolitică și pregătire preoperatorie. Presiunea venoasă centrală (PVC) a fost 1 cm apă, iar măsurarea presiunii intraabdominale pe cale transvezicală a înregistrat o valoare mult ridicată, de 25 mmHg. După reechilibrarea pacientei, se intervine chirurgical prin anestezie generală cu intubație orotraheală. La deschiderea cavității peritoneale prin laparotomie mediană ombilicopubiană, se constată prezența unei formațiuni tumorale chistice, fără aderențe la peretele abdominal, însă dimensiunile foarte mari, 30 × 30 × 25 cm face imposibilă explorarea întregii arii tumorale motiv pentru care se prelungește incizia superior (Figura 3). Având noul abord, tumora este complet mobilizată de organele adiacente și exteriorizată. La acest moment se poate identifica formațiunea ca fiind ovarul stâng, transformat chistic (Figura 4 and 5). Având în vedere vârsta pacientei și potențialul malign al tumorii, se practică chistectomie asociată în bloc cu histerectomie și anexectomie controlaterală. Evoluția postoperatorie este fără incidente sau complicații postoperatorii și bolnava se externează în ziua a 6 postoperator. Examenul histopatologic confirmă un chistadenom mucinos, fără atipii.

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Figura 1: Abdomen destins de prezența unui proces înlocuitor de spațiu.



Figura 2: Formațiune tumorală ocupând întreaga cavitate peritoneală – aspect computer tomografic, secțiune transversală.



Figura 3: Aspectul formațiunii tumorale la deschiderea cavității peritoneale.



Figura 4: Formațiune chistică gigantă, mobilizată din cavitatea abdominală.

Discuții

Tumorile abdominale gigante, chiar și cele benigne, datorită dimensiunilor și efectului de compresie asupra organelor din jur pot determina apariția unor complicații severe (hemoragie intratumorală, ocluzie intestinală, compresie ureterală cu disfuncție renală) care impun intervenții chirurgicale de urgență [1]. În cazul prezentat, asocierea hipertensiunii intraabdominale cu disfuncția renală a determinat apariția sindromului de compartiment abdominal, care, dacă nu ar fi fost tratat la timp, ar fi atras dezvoltarea altor disfuncții cu evoluția spre deces a bolnavei. Datorită dimensiunilor mari tumorale, stabilirea diagnosticului preoperator este o adevărată provocare. În Tabelul I, sunt prezentate principalele afecțiuni care fac obiectul diagnosticului diferențial al tumorilor gigante abdominale [5-11]. În literatura de specialitate sunt citate cazuri în care eliberarea tumorii din cavitatea abdominală poate conduce la complicații pulmonare severe [12,13]. Howard et colab. recomandă monitorizarea intraoperatorie a presiunii venoase centrale datorită creșterii brutale a presarcinii rezultate în urma decompresiei bruște a venei cave inferioare, putând duce la edem pulmonar acut [13]. Tumorile epiteliale ale ovarului reprezintă aproximativ 70% din totalitatea tumorilor ovariene. Chistadenomale seroase reprezintă majoritatea cazurilor de tumori epiteliale (80%), celelalte fiind chistadenomale mucinoase [1,14]. Ambele pot ajunge la dimensiuni considerabile, fiind citate în literatura de specialitate, chiste de 50 cm diametru și cântărind peste 50 de kg [15]. Din punct de vedere al agresivității, aceste tumori pot fi: benigne, borderline și maligne. Cele benigne sunt cele care ajung la dimensiuni mari, dar care, odată cu îndepărtarea chirurgicală pacienta este considerată vindecată. Tumorile borderline pot produce în 10 % din cazuri diseminări la



Figura 5: Aspect intraoperator al formațiune tumorale gigante cu punct de plecare din ovarul stâng; uter și anexe drepte de aspect normal.

Tabelul I: Diagnosticul diferențial al principalelor formațiuni abdominale gigante [5-11].

Tip Tumoral	Maliginitate
Ascită	±
Diverticuli ai vezicii urinare	-
Tumori stromale gastrointestinale	±
Hidronefroze	-
Tumori suprarenaliene	±
Splenomegalie	±
Tumori retroperitoneale	±
Chisturi pancreatice	±
Pseudochisturi pancreatice	-
Chiste omentale sau peritoneale	-
Abcese după perforații de organe cavitare	±
Anevriasm aortic	-
Tumori uterine	±
Chisturi tubare	±

distanță, având o rată de supraviețuire la 10 ani de 60%. Cele maligne, chiar și la mici dimensiuni produc diseminări intraperitoneale, având o agresivitate crescută și o rată de supraviețuire la 10 ani de 30% [16]. În ceea ce privește abordul chirurgical, nu există un consens unanim acceptat pentru indicația laparoscopică a chistelor de dimensiuni foarte mari. Dacă diagnosticul histopatologic preoperator nu poate fi precizat prin puncție ghidată ecografic, laparoscopia nu reprezintă o opțiune pentru chiste mai mari de 20 de cm [3,17]. În schimb, dacă se certifica preoperator benignitatea chistului, se poate efectua puncția evacuatorie a acestuia permițând intervenția chirurgicală laparoscopică la orice dimensiuni [4,18].

Concluzii

Tumorile abdominale gigante, chiar în condiții de benignitate pot determina complicații extrem de severe care necesită chirurgie de urgență. Diagnosticul preoperator este dificil de stabilit, existând multiple afecțiuni care pot evolua spre mase intraabdominale gigante. Sindromul de compartiment este o complicație redutabilă care trebuie rezolvată imediat. Alegerea tipului de chirurgie (deschis sau laparoscopic) depinde de dimensiunea tumorii și de posibilitatea stabilirii diagnosticului histopatologic preoperator.

Conflict de interese

Autorii nu declară niciun conflict de interese.

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References

1. Crum CP, Lester SC, Cotran RS (1981) Pathology of female genital system and breast. In: Kumar V, Jones HW, Jones GS (eds) Text Book of Gynecology (10th edn), Williams & Wilkins, Baltimore, USA.
2. Young TH, Lee HS (2008) Giant ovarian cyst. N Engl J Med 358: e22.
3. Alobaid A, Memon A, Alobaid S, Aldakhil L (2013) Laparoscopic management of huge ovarian cysts. Obstet Gynecol Int.
4. Jeong EH, Kim HS, Ahn CS, Roh JS (1997) Successful laparoscopic removal of huge ovarian cysts. J Am Assoc Gynecol Laparosc 4: 609-614.
5. Jolles H, Coulam CM (1980) CT of ascites: differential diagnosis. AJR Am J Roentgenol 135: 315-322.
6. Zanini P, Cavalca A, Benatti E, Drei B (1996) Benign giant ovarian cystadenoma. Description of a clinical case. Minerva Ginecologica 48: 215-219.
7. Rattan KN, Budhiraja S, Pandit SK, Yadav RK (1996) Huge omental cyst mimicking ascites. Indian J Pediatr 63: 707-708.
8. Zamir D, Yuchtman M, Amar M, Shoemo U, Weiner P (1996) Giant mesenteric cyst mimicking ascites. Harefuah 130: 683-684.
9. Chen SS (1979) A large retroperitoneal cyst mimicking ascites. A case report. J Reprod Med 22: 261-263.
10. Grobe JL, Kozarek RA, Sanowski RA, Earnest DL (1983) "Pseudo-ascites" associated with giant ovarian cysts and elevated cystic fluid amylase. Am J Gastroenterol 78: 421-424.
11. Kinkel K, Hricak H, Lu Y, Tsuda K, Filly RA (2000) US characterization of ovarian masses: a meta-analysis. Radiology 217: 803-811.
12. Pandya SH, Divekar R, Tuteja L (1992) Anaesthetic management in removal of a huge ovarian cyst. J Postgrad Med 38: 88-90.
13. Howard BK, Goodson JH, Mengert WF (1953) Supine hypotensive syndrome in late pregnancy. Obstet Gynecol 1: 371-377.
14. Petros M, Koliba P, Sevcík L, Curík R (2005) Giant benign mucinous cystadenoma of both ovaries in early puerperium: case report and review of literature. Ceska Gynekologie 70: 156-158.
15. Ioffe OB, Simsir A, Silverberg SG (2004) Practical gynecologic oncology. Williams & Wilkins, Maryland, USA.
16. Posabella A, Galetti K, Engelberger S, Giovannacci L, Gyr T, et al. (2014) A huge mucinous cystadenoma of ovarian: a rare case report and review of the literature. Rare Tumors 6: 5225.
17. Eltabbakh GH, Charboneau AM, Eltabbakh NG (2008) Laparoscopic surgery for large benign ovarian cysts. Gynecol Oncol 108: 72-76.
18. Ateş O, Karakaya E, Hakguder G, Olguner M, Secil M, et al. (2006) Laparoscopic excision of a giant ovarian cyst after ultrasound-guided drainage. J Pediatr Surg 41: E9-E11.

Breast Contralateral Metachronous Cancer: Metastases or Second Primary Breast Tumor?

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Abstract

Breast contralateral metachronous cancer is relatively rare. Familial history, BRCA 1 and BRCA 2 mutations, histopathologic type, stage of primary neoplasia and hormone status, is considered risk factors for breast metachronous cancer. The differential diagnosis between a breast contralateral metachronous cancer and a distant metastasis from the primary tumor is difficult and a subject of debate in the literature. We present herein two cases with breast metachronous contralateral tumors; the first is considered as distant metachronous metastasis and the second case, as a second primary tumor. A literature review was also performed.

Keywords: Breast cancer; Breast contralateral metachronous cancer; Metachronous metastases; Mastectomy

Introducere

Cancerul mamar ocupă o poziție primordială în patologia tumorală la femeie și, cu toate că a fost îndelung studiat, este și în prezent, în atenția cercetătorilor din medicina contemporană, datorită patogeniei sale complexe, a diversității structurale și evolutive și a răspunsului său variat la terapia multimodală.

Deși cancerul mamar este frecvent, neoplazia mamară metacronă contralaterală este rară, riscul anual estimat la o pacientă tratată de o tumoră primară unilaterală fiind de 0,5-1% [1], iar după unele opinii, 10% din pacientele cu o tumoră malignă mamară inițială, fac al doilea cancer [2], dar procentul poate fi semnificativ mai mare la cele cu istoric familial de cancer și cu o neoplazie multicentrică inițială.

Bilateralitatea reprezintă o particularitate importantă a cancerului mamar, cu posibilități evolutive diferite și prognostic dificil de apreciat, în funcție de vârsta, statusul hormonal, tipul histopatologic și intervalul de timp după care se depistează a două tumoră. Astfel, în funcție de acesta, tumorile ce apar până la 6 luni de la o neoplazie mamară unilaterală tratată, sunt considerate sincrone, iar cele ce apar după 6 luni, sunt considerate a fi metacrone [3,4]. Dar, cancerul mamar contralateral metacron este o metastază de la prima tumoră primară sau este o a doua tumoră primară? Este important de stabilit acest aspect, deoarece are implicații terapeutice și prognostice diferite. În acest sens, lucrarea de față este un studiu clinic comparativ și retroactiv a două paciente de vârstă apropiată, cu tumori metacrone mamare contralaterale, demonstrând două posibilități evolutive diferite.

Prezentarea cazurilor clinice

1) Pacienta GG de 48 de ani, se internează în Clinica de chirurgie generală și de transplant hepatic a Institutului Clinic Fundeni din București în aprilie 2009, pentru tumoră mamară dreaptă de 3 x 2 cm, în cadranul supero-extern, ulcerată, invadând pielea, fixă, infiltrativă, cu adenopatie axilară dreaptă tumorală în grupul toracic lateral drept și la baza axilei (Figura 1). Tumora este cunoscută și evoluează de 4 ani dar a fost neglijată de pacientă; coșorbiditățile includ. ciroză hepatică VHC, decompensată vascular și parenchimatous (ascită, varice esofagiene gradul II) și pleurezie dreaptă, diagnosticată și tratată simptomatic și sporadic de 6 ani, cu evoluție trenantă. Sânul stâng și axila stângă clinic

normale. Pacienta nu prezintă istoric familial de cancer mamar. Testele serologice și biochimice au evidențiat citoloză și colestază severă, probele de coagulare sunt alterate, iar markerii tumorali (AFP, CA 15.3, CA125) în limite normale. Examinarea computer-tomografică toraco-abdominală a evidențiat hepatosplenomegalie importantă, cu hipertrofie de lob stâng și caudat, ascită, dar fără metastaze intrahepatice sau intraperitoneale (Figura 2), pleurezie dreaptă recidivantă cu disfuncție respiratorie mecanică, fără metastaze intratoracice.

Datorită cirozei agravate, cu alterarea severă a funcționalității hepatice și a disfuncției respiratorii prin hidrotorax drept cu etiologie incertă (neoplazică sau cirotică), se recurge la tratament de reechilibrare și de susținere hepatică și la toracoscopie exploratorie pentru a realiza o pleurodeză cu talc; intraoperator, se constată micrometastaze pleurale drepte (M₁). Se realizează biopsii pleurale talcaj și biopsie tumorală mamară. Dreaptă (Figura 3 and 4).

Examenul histopatologic evidențiază un carcinomul ductal invaziv de grad G2, cu receptori de estrogen și progesteron pozitiv, metastatic. Tumora este clasată cT4bN1M1. Pacienta urmează terapie antihormonală neoadjuvantă cu Tamoxifen, conform protocolului oncologic stabilit, chimioterapia și radioterapia fiind contraindicate de afecțiunea hepatică agravată. Evoluție a fost mulțumitoare cu stabilizarea cirozei hepatice și cicatrizării tumorii ulcerate după 18 luni de hormonoterapie, fără recidivarea pleureziei neoplazice sau apariția altor metastaze, motiv pentru care, s-a practicat mastectomie radicală dreaptă tip Madden cu limfadenectomie axilară (Figura 5). Postoperator, evoluția a fost favorabilă. Histopatologic, a fost confirmat carcinomul

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Figura 1: Aspect clinic: tumoră mamară dreaptă ulcerată, malignă (pacienta GG, 48 de ani).



Figura 2: Tomografie computerizată abdominală: ficat cirotic dar fără metastaze.

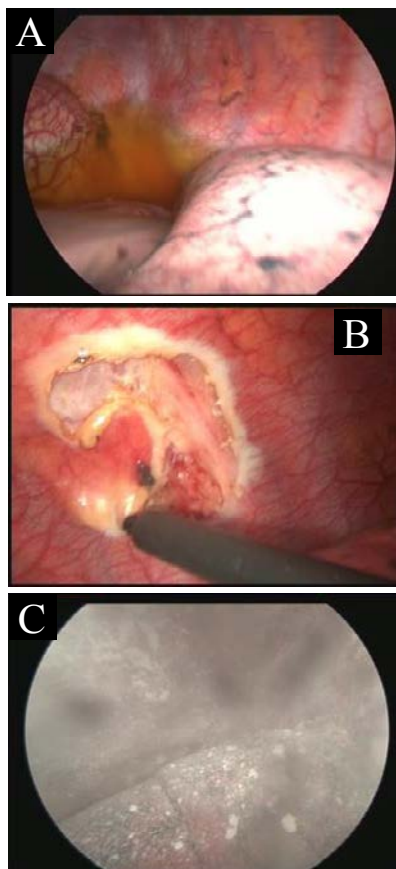


Figura 3: A: Hidrotorax drept neoplazic prin micrometastaze pleurale, toracoscopie exploratorie; B: biopsie pleurală toracoscopică; C: Talcaj pleural toracoscopic.

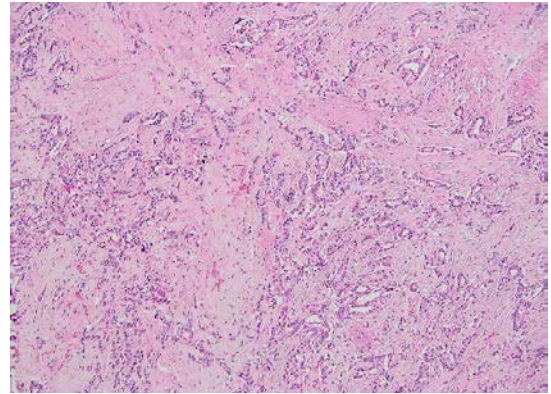


Figura 4: Carcinom ductal invaziv sân drept (aspect histopatologic la parafină, HE x 100).

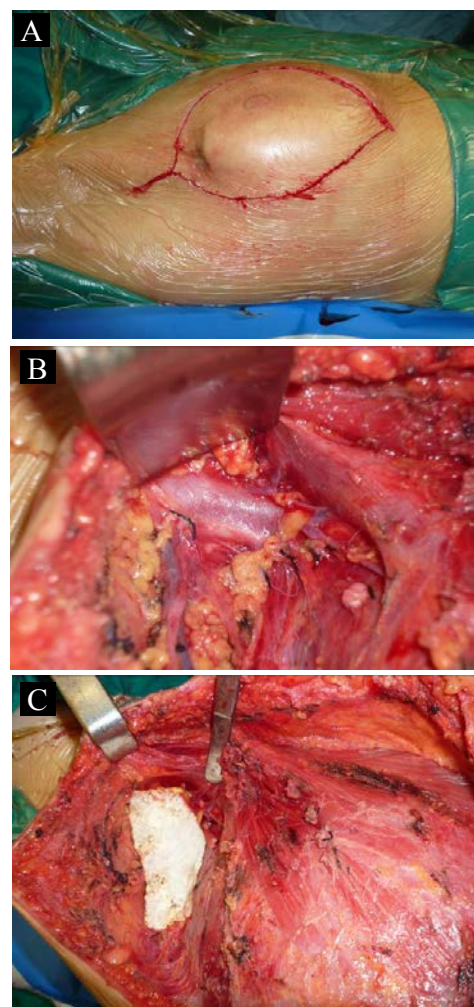


Figura 5: A: Mastectomie radicală modificată dreaptă tip Madden; B: Limfadenectomie axilară dreaptă; C: Aplicație de Tachosil® după limfadenectomie axilară, ca agent limfostatic, sigilant.

ductal invaziv G₂, cu metastaze carcinomatoase în 6 ganglioni, iar imunohistochimic, s-au evidențiat receptorii estrogenici (ER) pozitivi în 70% și progesteronici (PGR) în 25% din celulele tumorale (Figura 6). Tumora este deci clasată pT4bN2aM1 și se continuă hormonoterapia. După 14 luni de tratament, în 2011, pacienta se prezintă cu tumoră mamară stângă, contralaterală, de 1 x 1 cm în cadranul supero-intern, dură, cu adenopatie axilară stângă tumorală, aspect clinic și

mamografic sugestiv pentru malignitate. Întrucât ciroza hepatică a fost stabilizată, fără alte pusee de evolutivitate și nu au mai fost depistate alte metastaze la distanță, cu excepția micrometastazelor pleurale drepte staționare sub hormonoterapie, s-a practicat mastectomie radicală stângă modificată tip Madden cu examen extemporaneu intraoperator, care a confirmat un carcinom ductal invaziv G2-3 (Figura 7 and 8) iar imunohistochimic, receptori de estrogeni și progesteron pozitivi (60 și respectiv 10%) (Figura 9). După alte 5 luni postoperator, se depistează 2 formațiuni tumorale subcutanate în regiunea pectorală dreaptă, în zona cicatriceală corespunzătoare primei mastectomii radicale, care au fost excizate, confirmându-se a fi metastaze subcutanate de carcinom ductal invaziv. Evoluție este nefavorabilă cu apariția metastazelor osoase și pleuro-pulmonare bilaterale și agravarea ireversibilă a cirozei hepatice, urmată de deces, după 4 ani de la diagnosticarea primului cancer.

2) Pacienta GI de 43 de ani, s-a internat în ianuarie 1996 cu tumoră mamară dreaptă de 2,5 cm localizată în cadrul supero-extern, fără adenopatii axilare sau supraclaviculare palpabile, clinic și mamografic cu caractere incerte; sânul stâng și axila stângă sunt clinic și imagistic normale. Bilanțul imagistic (computer-tomografia toraco-abdomino-pelvică) nu decelează metastaze, iar markerii tumorali sunt în limite normale. Pacienta nu are istoric familial de cancer mamar. S-a practicat mastectomie radicală dreaptă modificată tip Madden, cu examen extemporaneu intraoperator, diagnosticul histopatologic fiind carcinom ductal invaziv, cu zone de schir, G2, fără metastaze în ganglionii axilari; imunohistochimic receptori de estrogen și progesteron sunt în 80 și respectiv 20% (Figura 10). Tumora este clasată pT2N0M0. Postoperator, pacienta urmează tratașent adjuvant: chimioterapie, radioterapie și hormonoterapie (Tamoxifen 20 mg pe zi, timp de 5 ani). Evoluție favorabilă timp de 20 de ani, fără recidive sau metastaze la distanță, serologic cu markerii tumorali în limite normale. În februarie 2016, la vârsta de 65 de ani, cu diabet de tip II stabilizat terapeutic (insulinemie și glicemie în limite normale sub tratament antidiabetic oral), se prezintă cu o formațiune tumorală mamară

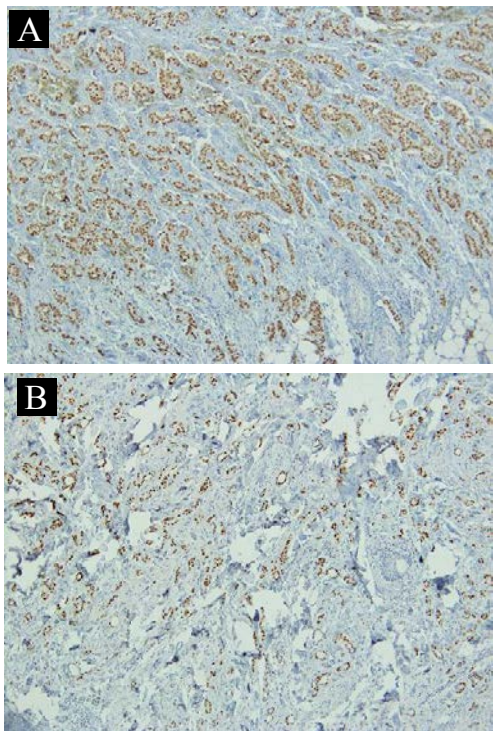


Figura 6: Studiu imunohistochimic: A: receptori de estrogeni în celulele tumorale – 70% (x 100); B: receptori de progesteron în celulele tumorale – 25 % (x 100).

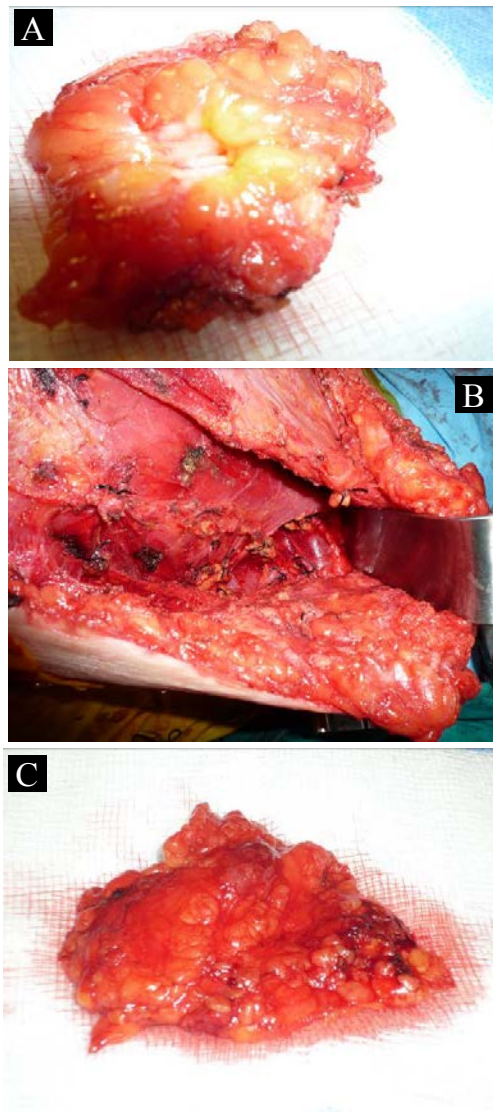


Figura 7: Tumoră mamară stângă contralaterală malignă, metacronă, la pacienta GG, 50 ani. cu tumoră mamară dreaptă malignă operată, de 14 luni. Aspect macroscopic intraoperator A: Piesă de sectorectomie stângă pentru examen extemporaneu B: Mastectomie radicală stângă contralaterală tip Madden C: Metastaze ganglionare axilare Aspect macroscopic pe piesa de limfadenectomie axilara stângă contralaterală.

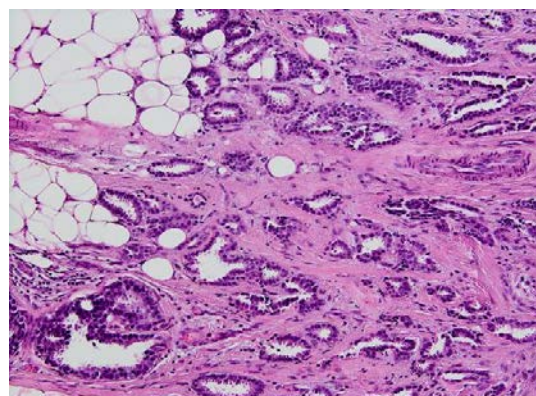


Figura 8: Aspect de microscopic: carcinom ductal invaziv G2 stâng contralateral la pacienta GG, 50 ani, (HE x200).

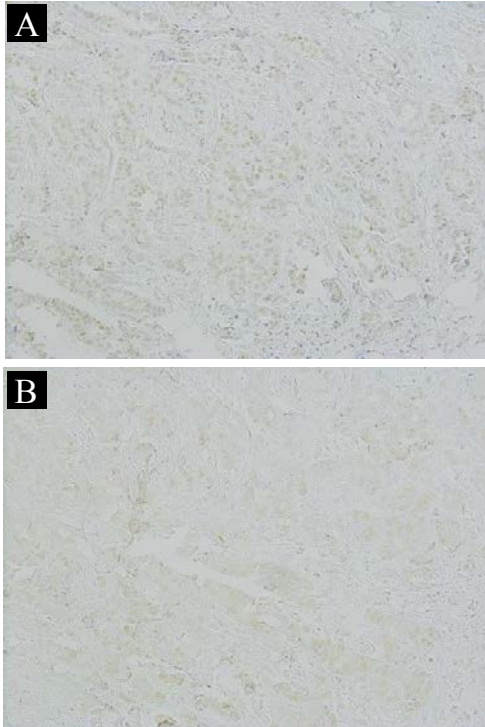


Figura 9: Studiu imunohistochimic al tumorii contralaterale mamare. **A:** receptori de estrogeni în celulele tumorale – 60% (x 100); **B:** receptori de progesteron în celulele tumorale - 10 % (x 100).

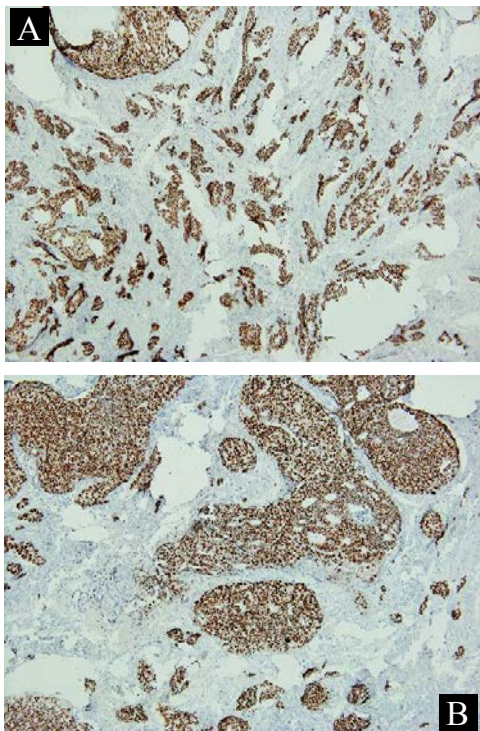


Figura 10: Carcinom ductal invaziv G₂ mamar drept. **A:** receptori de estrogeni în celulele tumorale – 80% (x 100); **B:** receptori de progesteron în celulele tumorale - 20 % (x 100).

stângă, deci contralaterală, în cadranul supero-intern, de 3 cm, dură, fără adenopatii axilare sau supraclaviculare palpabile, diagnosticată clinic și mamografic cu aspect sugestiv de malignitate (Figura 11). Nu se evidențiază recidive tumorale sau metastaze ganglionare axilare

în regiunea mamară dreaptă, iar cicatricea postmastectomie radicală dreaptă este suplă, cu mobilitate normală a brațului.

S-a practicat mastectomie radicală stângă tip Madden cu limfadenectomie; examenul extemporanu intraoperator dar și cel la parafină evidențiază un carcinom lobular invaziv bine diferențiat G3 (Figura 12 and 13), fără metastaze ganglionare axilare, estrogen-receptor și progesteron-receptor pozitiv (60 și respectiv 15% din celulele tumorale) (Figura 14). Tumora a fost clasată pT2N0M0. Evoluție a

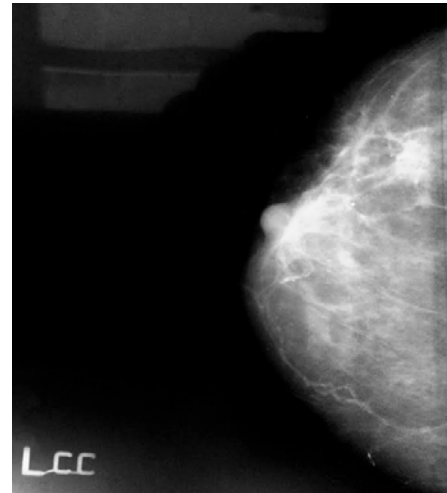


Figura 11: Tumoră mamară stângă supero-internă contralaterală metacronă. G.I. 65 de ani. Aspect mamografic.



Figura 12: Tumoră mamară stângă contralaterală metacronă. Aspect intraoperator. G.I. 65 de ani.

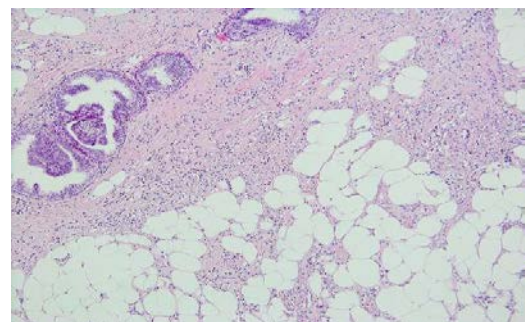


Figura 13: Carcinom lobular invaziv metacron contralateral, G.I. 65 de ani (HE x 100).

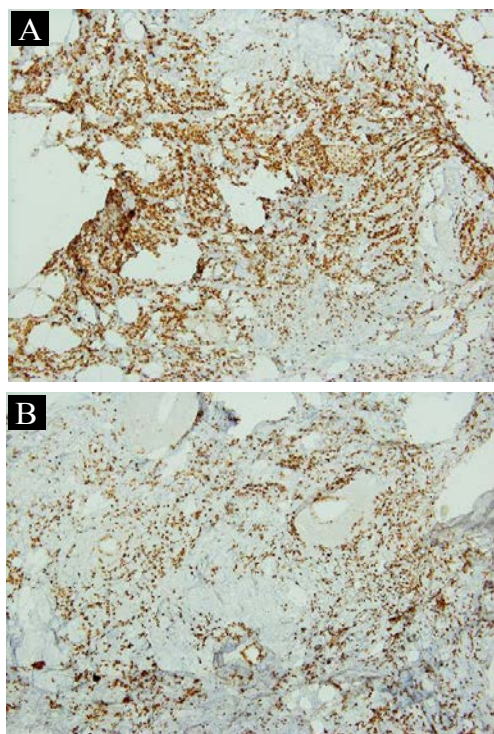


Figura 14: Studiul imunohistochimic al tumorii mamare controlaterale metacronă **A:** receptori de estrogeni în celulele tumorale – 60% (x 100); **B:** receptori de progesteron în celulele tumorale – 15 % (x 100).

fost favorabilă cu vindecare per primam. A urmat hormonoterapie (Tamoxifen) postoperator, iar în prezent nu prezintă semne clinice, imagistice și biologice de recidivă neoplazică.

Discuții

Conform opiniei majoritare din literatură, cancerul mamar metacron contralateral, apare la peste 6 luni după o tumoră primară unilaterală tratată multimodal și, în principiu este de tip histopatologic diferit [3-7].

Neoplaziile diagnosticate în intervalul de 3-6 luni de la o tumoră primară tratată, sunt considerate sincrone și provin din focare de oncogenă multicentrică, cu origine monoclonală, latente, subclinice la momentul decelării primului cancer, și care se dezvoltă ulterior simultan sau succesiv. Nu există diferențe atestate prin studii imunohistochemice între cancerelor sincrone simultane sau succesive de sân și, întrucât au același tip histopatologic, tumorile sincrone sunt considerate, după unii autori, metastaze ale aceleiași neoplazii [7,8].

Se apreciază că incidența cancerului contralateral la pacientele operate de o tumoră primară unilaterală este de 4-20% [9] și poate fi semnificativ modificată de o serie de factori de risc ca: istoricul familial de cancer mamar sau ereditatea (modificările genomice), vârsta pacientei la diagnosticarea primului cancer, statusul receptorilor hormonal, tipul histopatologic, gradul celular, stadiul avansat și terapia sistemică a neoplaziei inițiale [7]. Astfel, după unii autori [8] există un risc de 44% de cancer contralateral la pacientele cu istoric familial neoplazic mamar și cu mutații ale genelor BRCA 1 și BRCA 2, comparativ cu populația generală, de numai 4%, după 10 ani de la o tumoră unilaterală. Procente asemănătoare au fost raportate și de Easton D și colab. [9], care identifică un risc de cancer contralateral de 46-87% la populația cu mutații BRCA 1 și de 26-84% la cea cu mutații BRCA 2, comparativ cu 10% la populația generală. Mutațiile genei BRCA 1 au fost asociate cu cancerul mamar metacron contralateral, în special la pacientele tinere, sub 45 de ani și cu istoric familial, ceea ce

sugerează o predispoziție genetică la aceste cazuri, cu o evoluție mai gravă și prognostic rezervat [4], iar BRCA 2 a fost asociat cu tumorile sincrone contralaterale [4,9], cu toate că Steinmann [10] nu identifică mutații genice semnificative la un lot de 70 de paciente cu cancer bilateral, comparativ cu cele cu tumoră unilaterală. Un alt factor de risc important pentru cancerul mamar contralateral, este tipul histopatologic al tumorii primare inițiale unilaterale; astfel, carcinomul ductal invaziv este asociat cu un risc crescut pentru cancer contralateral metacron, după un interval mediu de 4,6 ani [5,11], iar carcinomul lobular este mai sugestiv pentru cancerelor contralaterale sincrone, fiind de regulă multicentric [12], cu toate că Bernstein și colab [13,14]. îl consideră ca având, în aceeași măsură, risc crescut de cancer metacron contralateral. Opinii asemănătoare au Carsten R. și colab. [15], care au semnalat un risc crescut de cancer metacron la pacientele sub 50 ani, cu carcinom ductal invaziv și lobular inițial și cu tumori cu receptori de estrogen negativi, cu fenotip mult mai agresiv. Astfel, se atribuie un rol important în evoluția ulterioară și în aceeași măsură, cu valoare prognostică, statusului receptorilor estrogenici și progesteronici al tumorii primare inițiale, din studiul imunohistochimic, considerându-se că, profilul receptorial pentru cancerul contralateral ca parametru predictibil pentru prognostic și risc de apariție, este influențat de terapia, în principiu multimodală, a tumorii unilaterale. În acest sens, o tumoră cu receptori estrogenici și progesteronici în procent mai mare la tumoră unilaterală, este mai receptivă la terapia antihormonală cu Tamoxifen sau alți inhibitori de aromatază, reducându-se semnificativ riscul de cancer metacron contralateral cu 30-47%, dar crește procentul de tumori estrogen-receptor negative contralaterale, cu fenotip mai agresiv și cu prognostic rezervat [8,15-17]. Același aspect este raportat și de Sandra Swain și colab. [18], care susțin că Tamoxifenul în doză de 20 mg pe zi, scade riscul de cancer metacron contralateral cu 30%, dar îi agravează prognosticul, prin reducerea celulelor receptor-estrogen pozitive. Mecanismul s-ar putea explica prin faptul că, acționând ca un antiestrogen la nivelul receptorilor membranari din țesutul glandular mamar, Tamoxifenul inhibă proliferarea celulelor tumorale estrogen-receptor pozitive, dar, cum cancerul are structură heterogenă, cu celule receptor-pozitive și negative, în consecință, cele pozitive răspund cu reducerea proliferării lor, iar cele negative continuă să crească selectiv [19]. Nu este cunoscut încă, pe deplin, rolul Tamoxifenului pe celulele estrogen-receptor negative din tumoră inițială unilaterală și nici asupra receptorilor progesteronici [20]. Deoarece unii autori nu au semnalat o influență semnificativă a hormonoterapiei asupra tumorii unilaterale în reducerea riscului cancerului metacron contralateral [12], „disputa continuă”, Tamoxifenul fiind considerat un antiestrogenic pentru sân, dar „progestogenic”, cu efecte proliferative, carcinogenice pentru endometru, oase și ficat, dar, în același timp, scade mortalitatea cu 30% prin patologia ischemică cardio-vasculară și prin fracturi patologice pe fond osteoporotic [21]. În cazul pacientelor noastre, deși vârsta lor a fost apropiată, sub 50 ani, fără istoric familial de cancer, ambele cu carcinom ductal invaziv identificat în tumoră primară inițială, cu același grad celular, același nivel de imunitate antitumorală (markeri tumorali cu titru normal) și cu status hormonal asemănător, evoluția clinică și prognosticul la distanță au fost diferite, prima având o evoluție agravată, cu o supraviețuire de circa 4 ani, cu toate că și ciroza hepatică în stadiu avansat ca patologie asociată, a influențat nefavorabil prognosticul. Dar, în contextul celor menționate mai sus, deși carcinomul ductal invaziv unilateral, a fost la ambele paciente cu status receptorial estrogenic favorabil (peste 70%) totuși, la tumoră contralaterală metacronă, s-a identificat un procent mare de receptori hormonal, de 60-70% receptori de estrogen, deși ambele au urmat hormonoterapie cu Tamoxifen, ceea ce ar putea explica evoluția favorabilă în cazul celei de a doua paciente și mulțumitoare în cazul primei paciente, cu o supraviețuire de 4 ani, și aceasta avea o patologie asociată semnificativ agravată. Ipoteză, după unii autori, explicația ar fi existența unui „mecanism alternativ de salvare”, ce poate fi relevant, prin care celulele tumorale estrogen-receptor (ER) negative se

„pozitivează”, la pacientele care au primit Tamoxifen adjuvant, deoarece 80% din cele cu cancer contralateral au un procent crescut de ER, dar pot avea loc și alterări proteice în structura receptorială, cu alterarea funcționalității lor, evidențiabile în expresia c-erbB2, consecința fiind rezistența la hormonoterapie [18,22]. Acest aspect este sugestiv, mai ales în cazul primei paciente, care a urmat numai hormonoterapie cu Tamoxifen, 20 mg pe zi, deoarece chimioterapia și radioterapia au fost contraindicate de „afecțiunea hepatică în stadiu avansat. Receptorii progesteronici au avut procent redus atât în localizarea unilaterală, cât și în cea contralaterală, la ambele paciente, ceea ce concordă cu opinia din literatură, conform căreia, nu s-a raportat o creștere a receptorilor progesteronici la cancerele metacrone, după hormonoterapie pentru cancerul unilateral, decât sporadic maxim 30%, ceea ce denotă un fenotip mai agresiv al acestora [4]. De asemenea, chimioterapia și radioterapia pentru tumora inițială unilaterală, reduc riscul de cancer metacron contralateral [3]; chimioterapia fiind considerată a avea dublu efect: scade riscul de cancer contralateral metacron, dar crește rezistența la tratament a acestuia, comparativ cu primul, deci îi agravează prognosticul [23]. Evoluția favorabilă în al doilea caz, cu remisie completă a primei neoplazii, diagnosticată într-un stadiu curabil, un interval liber de boală de 20 de ani și un cancer metacron contralateral operabil, (mastectomie radicală contralaterală cu viză curativă din punct de vedere oncologic și fără metastaze ganglionare axilare identificabile histopatologic sau la distanță), poate fi explicabilă prin efectul benefic al terapiei multimodale aplicată la prima tumoră receptor-pozitivă, dar care rămâne în continuare cu prognostic la distanță rezervat, datorită carcinomului lobular metacron, comparativ cu prima pacientă, care a urmat numai hormonoterapie pentru prima tumoră diagnosticată în stadiu avansat și care a avut un prognostic rezervat. În cazul cancerului mamar metacron contralateral, este important de precizat dacă este o metastază tardivă a primei tumori sau este a doua tumoră primară, distincție ce nu este ușor de realizat, dar este necesară deoarece are implicații terapeutice și prognostice diferite. Astfel, Chaudary și colab. (citată de 24) în 1984, au propus criterii semnificative pentru diagnosticul diferențial al acestor două entități, ca: tipul histopatologic, grading-ul celular și stadiul TNM al primei tumori (în special prezența sau absența metastazelor ganglionare) și statusul hormonal al celulelor tumorale. Conform acestor considerente, o a doua tumoră primară, se caracterizează printr-un tip histopatologic diferit de prima, cu grading celular mai înalt, în contextul absenței metastazelor ganglionare sau la distanță la momentul diagnosticului primei tumori și status hormonal redus, comparativ cu prima neoplazie, în special pentru receptorii progesteronici (Chaudary și colab.), deși, după unii autori, pattern-ul biologic al cancerelor metacrone este controversat [24]. Având în vedere criteriile Chaudary de diagnostic diferențial, în cazul celei de a doua paciente, tumora contralaterală mamară este considerată a doua tumoră primară, metacronă, deoarece a fost diagnosticată după un interval de 20 de ani liber de boală oncologică activă de la tumora unilaterală, histopatologic și imunohistochimic diferită (carcinom lobular G3 metacron și carcinom ductal invaziv unilateral G2, cu receptori de progesteron de numai 15%, comparativ cu 30% inițial), în contextul absenței metastazelor ganglionare sau la distanță de la tumora inițială, remisă complet sub tratament chirurgical radical adaptat stadiului bolii și a celui oncologic adjuvant, după un protocol terapeutic complet. Dar, în cazul primei paciente, fără istoric familial de cancer, a doua tumoră contralaterală metacronă a fost diagnosticată ca fiind carcinom ductal invaziv cu același pattern celular G2 și semnificativ estrogen-receptor pozitivă ca și cea mamară unilaterală, dar care la momentul diagnosticului inițial, prezenta metastaze ganglionare axilare homolaterale și carcinomatoză pleurală, evidențiabile histopatologic, deci pT4bN2aM1. Deși neoplazia a fost stabilizată din punct de vedere clinic, serologic și imagistic pe o

anumită perioadă, ceea ce a permis mastectomia radicală unilaterală, numai cu intenție citoreductivă, în imposibilitatea unei terapii adjuvante complete, datorită tarei hepatice asociate, totuși a doua tumoră contralaterală, poate fi considerată metastază metacronă, în contextul extinderii bolii neoplazice la nivel loco-regional și sistemic (metastaze axilare ganglionare și pleurale existente la momentul diagnosticului), urmată fiind apoi de apariția celor două metastaze subcutanate parietale în regiunea mamară unilaterală inițial. Metastazarea contralaterală mamară ar fi posibilă prin „căi anatomice de drenaj limfatic existente sau create postterapeutic între cele două regiuni mamare, care ar facilita migrarea și grefarea celulelor neoplazice contralateral [25]. Conform datelor din literatură, metastazele contralaterale mamare metacrone sunt foarte rare, dar posibile în special la paciente sub 50 ani, cu cancer unilateral multicentric lobular sau ductal invaziv, fenotipic agresive (mutații BCRA 1, 2, status receptorial negativ) și cu metastaze ganglionare axilare, cu invazie extracapsulară unilaterală [12,25]. La această categorie de paciente, se recomandă hormonoterapia, chimioterapia și iradierea profilactică contralaterală, mastectomia radicală contralaterală profilactică și histerectomia totală cu anexectomie bilaterală [12,26,27].

Pentru depistarea precoce a cancerului metacron, se recomandă monitorizare clinică, serologică (markeri tumorali) și imagistică (ecografie mamară, mamografie), imagistică prin rezonanță magnetică (IRM) mamară bilaterală, în special la pacientele cu risc crescut, cu eficiență considerată superioară, mai ales dacă se ia în discuție mastectomia profilactică contralaterală [28,29]. Astfel, s-a raportat o sensibilitate a IRM pentru tumora metacronă contralaterală, de 86-100% și specificitate de 93% [30], identificându-se în 3,1% din cazuri, cancer metacron contralateral infraclinik, la paciente cu examen clinic și mamografic negativ, respectiv la 30 din 969 bolnave examinate IRM [2]. Tratamentul cancerului metacron contralateral este multimodal, cu viză de radicalitate oncologică, adjuvant sau neoadjuvant, în cazul metastazelor metacrone și individualizat, după stadiul evolutiv și tipul histopatologic, în cazul tumorilor primare „secundare”, ce pot fi diferite: carcinoame lobulare, ductal invazive sau sarcoame contralaterale postiradiere [6]. Prognosticul cancerului metacron contralateral este diferit: pentru metastaze este rezervat, având în vedere contextul evolutiv al bolii, similar cu cel al cancerelor sincrone, considerate de origine monoclonală, iar pentru cancerul metacron primar, prognosticul și mortalitatea la peste 10 ani, sunt similare cu cele ale neoplaziei unilaterale [23].

Concluzii

Cancerul metacron mamar contralateral este o entitate distinctă, cu potențial clinic și evolutiv diferit. Varsta sub 50 de ani, predispoziția genetică (istoricul familial, mutațiile genice BCRA 1,2), tipul histopatologic lobular și ductal invaziv, stadiul avansat, grading-ul celular și statusul hormonal al tumorii unilaterale, sunt considerați factori de risc pentru cancerul bilateral mamar. Tratamentul multimodal al tumorii unilaterale, poate influența riscul apariției cancerului contralateral. Diagnosticul diferențial între metastază și a doua tumoră primară metacronă contralaterală este important, deoarece are implicații terapeutice și prognostice distincte. Cazurile celor două paciente prezentate, ilustrează două posibilități de evoluție diferită a cancerului mamar contralateral, metastaza metacronă mamară contralaterală fiind o entitate foarte rară.

Conflict de interese

Autorii nu declară niciun conflict de interese

References

1. Beckmann KR, Buckingham J, Craft P, Zhang Y, Roder D, et al. (2011) Clinical characteristics and outcomes of bilateral breast cancer in an Australian cohort. *The Breast* 20: 158-164.

2. Lehman CD, Gatsonis C, Kuhl CK, Hendrick RE, Pisano ED, et al. (2007) MRI Evaluation of the Contralateral Breast in Women with Recently Diagnosed Breast Cancer. *N Engl J Med* 356: 1295-1303.
3. Broët P, Rochefordière A, Scholl SM, Fourquet A, Mosseri V, et al. (1996) Contralateral breast cancer: metastasis or second primary cancer? *Bulletin du Cancer* 83: 870-876.
4. Elzbieta S, Jolanta S, Beata P, Anna Z, Joanna P, et al. (2014) Are synchronous and metachronous bilateral breast cancers different? An immunohistochemical analysis aimed at intrinsic tumor phenotype. *Int J Clin. Exp Pathol* 7: 353-363.
5. Xavier SGMJ, Bernard A, Vincent S, Phillippe B, Thierry D, et al. (1996) Infiltrating Lobular Carcinoma of the Breast. Clinicopathologic Analysis of 975 Cases with Reference Data on Conservative therapy and Metastatic Patterns. *Cancer* 77: 113-120.
6. Bhawna BJ, Chandan RC, Tshering DB, Madhumita M (2013) Metachronous presentation of breast sarcoma following carcinoma. A rare occurrence. *Clin cancer Investig J* 2: 359-361.
7. Alkner S, Bendahl P, Ferno M, Manjer J, Ryden L (2011) Prediction of outcome after diagnosis of metachronous contralateral breast cancer. *BMC Cancer* 11: 114.
8. Tomi F, Akinyemiju (2013) Risk of asynchronous contralateral breast cancer: multiple approaches for a complex issue. *Glands Surgery*.
9. Easton DF, Narod SA, Ford D, Steel M (1994) The genetic epidemiology of BRCA1. *Breast Cancer Linkage Consortium* 344: 761.
10. Steinmann D, Bremer M, Rades D, Skawran B, Siebrands C, et al. (2001) Mutations of the BRCA1 and BRCA2 genes in patients with bilateral breast cancer. *Br J Cancer* 85: 850-858.
11. Bassarova AV, Torlakovic E, Sedloev T, Hristova SL, Trifonov DV, et al. (2005) Simultaneous bilateral breast carcinoma: Histopathological characteristics and CD44 and catenin-cadherin profile. *Histol Histopathol* 20: 791-799.
12. Vichapat V, Gillet C, Fentiman AS, Tutt A, Holmberg L, et al. (2011) Risk factors for metachronous contralateral breast cancer suggests two aetiological pathways. *European Journal of Cancer* 47: 1919-1927.
13. Bernstein JL, Lapinski RH, Thakore SS, Doucette JT, Thompson WD (2003) The descriptive epidemiology of second primary breast cancer. *Epidemiology* 14: 552-558.
14. Bernstein JL, Thompson WD, Risch N, Holford TR (1992) Risk factors predicting the incidence of second primary breast cancer among women diagnosed with a first primary breast cancer. *Am J Epidemiol* 136: 925-936.
15. Carsten R, Katharina W, Ulrike BG, Engel J, Stegmeier C, et al. (2014) Risk of Contralateral Second Primary Breast Cancer According to Hormone Receptor Status in Germany. *Breast Cancer Research* 16: 452.
16. Alkner S, Bendahl PO, Fernö M, Nordenskjöld B, Rydén L, et al. (2009) Tamoxifen reduces the risk of contralateral breast cancer in premenopausal women: Results from a controlled randomised trial. *Eur J Cancer* 45: 2496-2502.
17. Gronwald J, Tung N, Foulkes WD, Offit K, Gershoni R, et al. (2006) Tamoxifen and contralateral breast cancer in BRCA1 and BRCA2 carriers: an update. *Int J Cancer* 118: 2281-2284.
18. Sandra MS, Wilson JW, Bryant J, Wickerham L, Ficher B, et al. Estrogen Receptor Status of Primary Breast Cancer. Is Predictive of Estrogen Receptor Status of Contralateral Breast Cancer.
19. Hofmann TB, Gebhard BP, Rudas M, Gnatt M, Taucher S, et al. (2002) Pattern of Hormone Receptor Status of Secondary Contralateral Breast Cancer in Patients Receiving Adjuvant Tamoxifen. *Clinical Cancer Research* 8: 3432-3438.
20. Christopher IL, Kathleen EM, Weiss NS, Daling JR (2001) Tamoxifen Therapy for Primary Breast Cancer and Risk of Contralateral Breast Cancer 93:1008-1013.
21. Grilli S (2006) Tamoxifen the dispute goes on. *Ann Ist Super Sanita* 42: 170-173.
22. Kuukasjärvi T, Kononen J, Helin H, Holli K, Isola J (1996) Loss of estrogen receptor in recurrent breast cancer is associated with poor response to endocrine therapy. *J Clin Oncol* 14: 2584-2589.
23. Hartman M, Czene K, Reilly M, Adolfsson J, Bergh J, et al. (2007) Incidence and prognosis of synchronous and metachronous bilateral breast cancer. *J Clin Oncol* 25: 4210-4215.
24. Gong SJ, Rha SY, Jeung HC, Roh JK, Yang WI, et al. (2007) Bilateral Breast Cancer: Differential Diagnosis Using Histological and Biological Parameters. *Jpn J Clin Oncol* 37: 487-492.
25. van der Ploeg IMC, Oldenburg HSA, Rutgers EJT, Peeters MJTFDBV, Kroon BBR, et al. (2010) Lymphatic drainage patterns from the treated breast. *Ann Surg Oncol* 17: 1069-1075.
26. Szczepka JR, Hutka BU, Grzybowska E, Maka B, Nowicka E, et al. (2004) BRCA1 and BRCA2 mutations as prognostic factors in bilateral breast cancer patients. *Ann Oncol* 15: 1373-1376.
27. Haffty BG, Harrold E, Khan AJ, Patnare P, Smith TC, et al. Outcome of conservatively managed early-onset breast cancer by BRCA1/2 status. *The Lancet* 359: 1471-1477.
28. Herrinton LJ, Barlow WE, Yu O, Geiger AM, Elmore JG, et al. (2005) Efficacy of prophylactic mastectomy in women with unilateral breast cancer. *Cancer Research Network project. J Clin Oncol* 23: 4275-4286.
29. Polednak AP (2001) Frequency of prophylactic contralateral mastectomy among breast cancer patients. *J Am Coll Surg* 192: 804-805.
30. Robertson C, Kumar S, Ragupathy A, Boachie C, Fraser C, et al. (2011) Surveillance mammography for detecting ipsilateral breast tumour recurrence and metachronous contralateral breast cancer: a systematic review. *Eur Radiol* 21: 2484-2491.

