Takeuchi et al., J Clin Case Rep 2013, 3:1
DOI: 10.4172/2165-7920.1000240

Journal of Clinical Case Reports

Case Report Open Access

Verrucous Squamous Carcinoma of the Esophagus Successfully Diagnosed by Endoscopic Mucosal Resecion: A Case Report

Nobuhiro Takeuchi[1]*, Shuho Semba[2], Kazuyoshi Naba[3], Tetsuo Maeda[1], Hidetoshi Tada[1], Ryota Aoki[1], Yu Nishida[1] and Yusuke Nomura[1]

[1]*Department of Gastroenterology, Kawasaki Hospital, Kobe, Japan*
[2]*Division of Pathology, Department of Pathology, Kobe University Graduate School of Medicine, Kobe, Japan*
[3]*Department of Laboratory Medicine, Kawasaki Hospital, Kobe, Japan*

Abstract

A 62-year-old male with a history of type 2 diabetes mellitus and alcoholic liver disease presented with dysphagia, heartburn, and appetite loss. He had lost 10 kg weight within 1 month. The patient gave a history of excessive alcohol intake and a smoking habit of 60 cigarettes per day for 40 years. Upper gastroenteroscopy revealed a wart-like, whitish, protruding mass with circumferential stricture at a point 35 cm from the incisor down to the cardia. Although esophageal cancer was suspected, repeated biopsies of the mass revealed no malignant findings. Concurrent esophageal candidiasis was treated with an antifungal drug. Increased esophageal stricture made food intake impossible; therefore, total parenteral nutrition was initiated. Endoscopic mucosal resection revealed highly keratinized, well-differentiated squamous cell carcinoma with invasion into the submucosa. A diagnosis of verrucous squamous carcinoma was confirmed. Subtotal esophageal resection and esophagostomy was performed with video assistance. Postoperative pathological findings were compatible with the diagnosis of verrucous squamous carcinoma, which is known to be a slow-growing tumor that rarely metastasizes to lymph nodes or distant organs. However, verrucous squamous carcinoma is rarely diagnosed by endoscopic biopsy. Moreover, endoscopic mucosal resection or surgery should be considered in cases when endoscopic examination fails to confirm the diagnosis of carcinoma and if the lesion presents some characteristics of verrucous squamous carcinoma.

Introduction

Verrucous squamous carcinoma (VSC) of the esophagus is an extremely rare variant of squamous cell carcinoma and was first reported by Minielly et al. [1] in 1967. It is a low-grade, slow-growing, locally invasive tumor with a cauliflower-like appearance. Metastasis to lymph nodes or distant organs is rare. Here we present a case of VSC of the esophagus in which diagnosis could not be confirmed by endoscopy and several repeated endoscopic biopsies. The final diagnosis was confirmed by endoscopic mucosal resection (EMR).

Case Report

A 62-year-old male with a history of type 2 diabetes mellitus and alcoholic liver disease was admitted to our institution with complaints of dysphagia, heartburn, and appetite loss. He reported weight loss of 10 kg within 1 month along with recurrent vomiting and minimal oral intake. The patient had a history of excessive alcohol intake and a smoking habit of 60 cigarettes per day for 40 years. Initial clinical examination revealed a weight of 49.0 kg and height of 174.0 cm. With a body mass index was 16.2; the patient appeared to be emaciated.

Physical examination revealed mild anemia and a soft, flat abdomen with no palpable mass and normal bowel sounds. Blood chemistry analysis revealed mild anemia (red blood cell count: 337 × 104/μl; haemoglobin: 10.6 mg/dl), mild renal dysfunction (serum creatinine: 1.17 mg/dl; serum urea nitrogen: 21.1 mg/dl), elevated gamma-glutamyl transpeptidase (117 IU/l), elevated C-reactive protein levels (3.3 mg/dl), and abnormal glucose tolerance (glucose: 206 mg/dl; hemoglobin A1c: 7.2%). In tumor marker analysis, carcinoembryonic antigen levels were within normal limits (3.3 ng/ml) and squamous cell carcinoma antigen levels were slightly elevated (4.8 ng/ml). Plain chest and abdominal radiography revealed no abnormalities. Contrast-enhanced abdominal computed tomography revealed a mass in the lower esophagus with no swollen lymph nodes or local invasion, and a marginally enhanced mass at the fundus of the stomach (Figures 1a and 1b). Upper gastroenteroscopy revealed a wart-like, whitish, protruding mass with a circumferential stricture at a point 35 cm from the incisor; the mass extended into the cardia of the stomach (Figures 1c and 1d). Although esophageal cancer was suspected, repeated biopsies of the mass revealed only chronic inflammation with no malignancy. Upper gastroenteroscopy performed 9 days after admission revealed a more severe stricture with a whitish mass in the lower esophagus (Figure 2a). Several biopsies taken from the mass at that time revealed no features

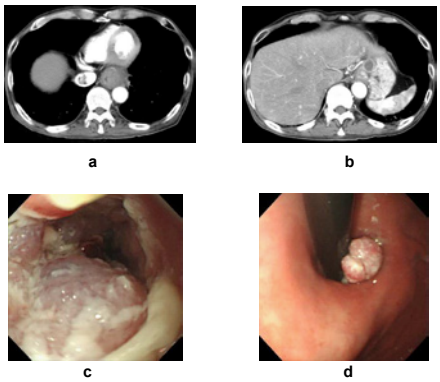


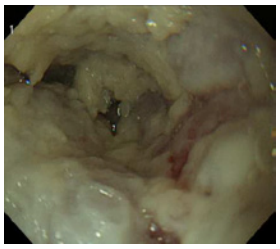
Figure 1: (a,b) Contrast-enhanced abdominal computed tomography revealed a mass in the lower esophagus with no swollen lymph nodes or local invasion, and a marginally enhanced mass at the fundus of the stomach. **(c,d):** Upper gastroenteroscopy revealed a wart-like, whitish, protruding mass with a circumferential stricture at a point 35 cm from the incisor; the mass extended into the cardia of the stomach.

***Corresponding author:** Nobuhiro Takeuchi, Department of Gastroenterology, Kawasaki Hospital, 3-3-1 Higashiyama-cho, Kobe, Hyogo 652-0042, Japan, Tel: +81-78-511-3131; Fax: +81-78-511-3138; E-mail: takeuchi_nobuhiro@kawasaki-hospital-kobe.or.jp

Received November 29, 2012; **Accepted** December 22, 2012; **Published** December 24, 2012

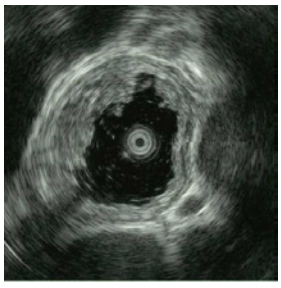
Citation: Takeuchi N, Semba S, Naba K, Maeda T, Tada H, et al. (2013) Verrucous Squamous Carcinoma of the Esophagus Successfully Diagnosed by Endoscopic Mucosal Resecion: A Case Report. J Clin Case Rep 3:240. doi:10.4172/2165-7920.1000240

of malignancy. However, esophageal candidiasis was suggested, and an anti-fungal drug, dose of 300mg amphotericin B per day, was initiated. Moreover, total parenteral nutrition was initiated due to lack of oral intake and low nutritional status. Endoscopic ultrasonography performed on day 40 after admission revealed a thickened esophagus wall with no tumor invasion into the submucosal layer (Figure 2b). Esophageal fluoroscopy performed on day 42 revealed an irregular, circumferential tumor with a longitudinal diameter of 8 cm, in the lower esophagus (Figure 2c). EMR performed on day 54 revealed a highly keratinized, well-differentiated squamous carcinoma with local invasion to the lamina propria (Figure 2d). A diagnosis of Verrucous Squamous Carcinoma (VSC) of the esophagus was confirmed. Subtotal esophageal resection using video-assisted surgery and esophagostomy was performed on day 102 after admission. Gross morphology of the resected specimen revealed a wart-like, whitish, circumferential tumor, 14.0 × 5.0 cm in size (Figure 3a). Microscopic examination revealed mild atypical cells with slightly irregular nuclei, obvious nuclei, and irregular arrangement on the basal membrane; moreover, partial invasion to the muscularis propria was observed (Figure 3b). These observations were compatible with the diagnosis of VSC of the esophagus. Histological analysis staged the lesion as pT3, pN0, M0, ly0, v0, pM0, pDM0, pEM0, and stage II. The patient was asymptomatic with no evidence of recurrence at the 12-month follow-up.



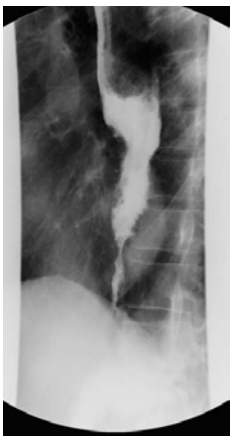
a

Figure 2a: Upper gastroenteroscopy performed 9 days after admission revealed a more severe structure with a whitish mass in the lower esophagus.



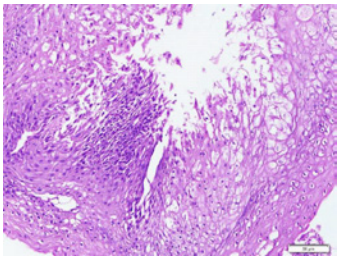
b

Figure 2b: Endoscopic ultrasonography performed on day 40 after admission revealed a thickened esophagus wall with no tumor invasion into the submucosal layer.



c

Figure 2c: Esophageal fluoroscopy performed on day 42 revealed an irregular, circumferential tumor with a longitudinal diameter of 8 cm, in the lower esophagus.

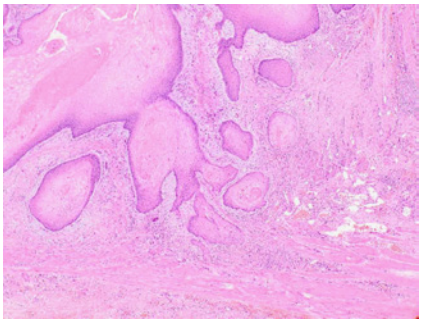


d

Figure 2d: EMR performed on day 54 revealed a highly keratinized, well-differentiated squamous carcinoma with local invasion to the lamina propria.

a

Figure 3a: Grossmorphology of the resected specimen revealed a wart-like, whitish, circumferential tumor, 14.0×5.0 cm in size.



b

Figure 3b: partial invasion to the muscularis propria was observed.

Discussion

VSC was first reported by Ackermann [2] in 1948. Usually, VSC develops in the oral cavity, larynx, nasal cavity, penis, vagina, and scrotum. VSC of the esophagus was first reported by Minielly et

al. [1] in 1967. In total, no more than 30 cases have been reported worldwide. VSC of the esophagus is a high-grade tumor forming an irregular warty mass that develops slowly and invades locally to adjacent organs. It tends to develop in heavy drinkers or heavy smokers [3]. Endoscopy reveals a warty mass proliferating laterally with a cauliflower-like appearance and papillary growth. VSC of the esophagus is sometimes misdiagnosed as papilloma, leiomyoma, inflammatory tumor associated with reflux esophagitis, or squamous epithelial hyperplasia. Pathological analyses reveal squamous carcinoma cells with hyperkeratosis and marked papillary growth. VSC and other squamous carcinomas differ histologically; VSC proliferates externally and internally into the muscularis propria, while papilloma proliferates only internally. Irritation and inflammation in the esophageal mucosa have been associated with VSC of the esophagus [4]. Retained esophageal contents resulting from achalasia along with esophageal hernia, esophageal diverticulum, reflux esophagitis, and chronic inflammation may be involved in the pathogenesis of VSC. Moreover, some authors have reported an association between VSC and the human papilloma virus [5]. Although VSC of the esophagus is a high-grade tumor, it has a tendency towards severe local invasion, forming fistulae to adjacent organs such as the lungs, pleura, and trachea. However, it rarely metastasizes to lymph nodes or distant organs. In some cases, pneumonia develops as a result of the fistula formation and patients die because of respiratory failure; therefore, VSC of the esophagus requires surgical therapy. Microscopic specimens obtained from biopsies from the mucosal surface of VSC tumors usually present features of acute or chronic inflammation; therefore, diagnosis of VSC of the esophagus from microscopic specimens or endoscopy could be challenging. Kojima et al. [6] reported that in some cases of VSC, few atypical tumor cells make alveolar formations; in addition, severe hyperkeratosis of the mucosal surface may prevent malignant cell collection in the deeper sections of the mucosa. Hence, endoscopic biopsy must be carefully performed for accurate diagnosis. If VSC of the esophagus is suspected due to clinical presentation despite a lack of evidence of malignancy on endoscopic biopsy, surgical resection should be planned. VSC has been reported to respond poorly to radiation therapy and chemotherapy [7]. Radiation therapy may induce malignant transformation of high-grade tumors into low-grade or anaplastic tumors, resulting in rapid metastasis [8]. Very few reports support the effectiveness of chemotherapy in treatment of VSC. Although one case has been reported documenting the effectiveness of bleomycin [9], the effect of chemotherapy on VSC of the esophagus generally remains controversial. About 30 cases of VSC of the esophagus have been reported in the literature (Table 1). The male–female ratio is

Author	Year	Age	Sex	Complaint	Past History	Location	Size	Treatment	Prognosis
Minielly 1)	1967	58	M	Dysphagia	Achalasia	U	8.5cm	Surgery	Death after 1 month
Minielly 1)	1967	70	F	Dysphagia	Diverticulum	U	Giant	Radiation	NA
Minielly 1)	1967	70	F	Dysphagia	Achalasia	U	Giant	Radiation	Death after 2 months
Minielly 1)	1967	36	M	Dysphagia	Diverticulum	L	9*8cm	Surgery	Death after 2 months
Minielly 1)	1967	57	M	Dysphagia	-	L	NA	Supportive	Death after 5 months
Parkinson 10)	1970	76	M	Melena	Stricture	M	7.5cm	Supportive	Death after 1 month
Meyerowitz 11)	1971	45	M	Melena	-	L	8.0*5.5cm	Surgry+Radiation	Death after 9 months
Sridhar 12)	1980	54	M	Dysphagia	Hiatus hernia	L	2cm	Surgery	NA
Sakurai 9)	1983	78	F	Dysphagia	-	U	10*5cm	Chemotherapy	NA
Agha 13)	1984	66	M	Dysphagia	Diverticulum	U	Giant	Supportive	Death after 2 months
Barbier 14)	1987	50	F	Dysphagia	Hiatus hernia	L	NA	Surgery	Death after 10 months
Koerfgen 15)	1988	75	M	Dysphagia	Stricture	L	NA	Surgery	Alive 3 years follow up
Koerfgen 15)	1988	54	NA	Dysphagia	-	L	6.5*6.5cm	Surgery	Alive 18 months follow up
Kojima 6)	1988	70	M	Dysphagia	Achalasia	U	6.0*5.5cm	Surgery	Alive 30 months follow up
Jasim 16)	1990	79	M	Dysphagia	Hiatus hernia	L	9*6*2cm	Supportive	Death
Biemond 17)	1991	76	F	Dysphagia	Reflux esophagitis	M	15cm	Supportive	Death after 1 month
Roach 18)	1993	67	NA	Dysphagia	Hernia Achalasia	U	7cm	Supportive	Death after 2 months
Garrard 4)	1994	51	F	Dysphagia	-	M	10cm	Surgery	Alive 9 months follow up
Kavin 19)	1996	76	NA	Odynophagia	-	L	NA	Supportive	Death after 1 month
Malik 20)	1996	66	M	Dysphagia	Reflux esophagitis	L	5cm	Surgery	Alive 3 years follow up
Tajiri 21)	2000	40	Na	No symptom	-	L	8*6cm	EMR	Alive 4 years follow up
Ereno 22)	2001	65	F	Dysphagia	-	L	11	Surgery	NA
Osborn 3)	2003	67	M	Dysphagia	Achalasia	L	8*8cm	Surgery	Alive 9 months follow up
Mizutani 23)	2004	72	M	Hematomenesis, melana	-	L	8*7cm	Surgery	Alive 2 years follow up
Devlin 24)	2004	56	F	Heart burn	-	L	2.7cm	Surgery	Alive 14 months follow
Wong 25)	2005	59	M	Heart burn	-	M	4.8*2.5cm	Surgery	Alive 18 months follow up
Oh 26)	2009	73	F	Heart burn	Reflux esophagitis	U	3.5cm	Supportive	Alive 23 months follow up
Na 27)	2009	50	M	Dysphagia	Reflux esophagitis	L	7.5*4.8*0.7cm	Surgery+Radiaton	Alive 6 months follow
Macias-Garcia 28)	2009	71	F	Dysphagia, Heart burn, Hematoemesis	Reflux esophagitis	M	3.9*2.5cm	Surgery	NA
Tonna 5)	2010	61	M	Dysphagia, Odynophagia	Candidasis	NA	10cm	Surgery	Alive 1 year follow
Chu 29)	2011	45	M	Dysphagia , Odynophagia	-	M	5cm	Surgery	NA
Lagos 30)	2012	74	M	Anorexia	-	L	9cm	Surgery	Death after 4 days
This study	2012	62	M	Dysphagia , Heart burn	-	M	14*5cm	Surgery	Alive 1 year follow up

NA: not available, EMR: endoscopic mucosal resection

Table 1: Verrucous squamous carcinoma of the esophagus reported in the literature.

about 2:1, and age at which diagnosis is generally made ranges 36-76 years. Characteristic signs and symptoms include dysphagia (76%), heartburn (12%), odynophagia (9%), and melena (9%). Patients with VSC may have past histories of reflux esophagitis (15%), hiatus hernia (9%), achalasia (9%), and diverticulum (9%). About half of esophageal VSC lesions (52%) are located in the lower portion of the esophagus. Tumor size at the time of diagnosis is relatively large. Most cases (64%) reported in the literature were treated surgically. The prognosis of VSC of the esophagus was poor in the past, but has improved in recent years probably because of the technical improvement of surgical treatment. The etiology of VSC of the esophagus is unknown, but an association with tobacco use and alcohol has been demonstrated [3,10-30].

Conclusion

We presented a rare case of VSC of the esophagus. In cases of whitish, wart-like tumors with no evidence of malignancy on repeated biopsy, the possibility of VSC of the esophagus should be considered, although it is an extremely rare tumor. Moreover, EMR or surgery should be considered to confirm this diagnosis if no evidence of malignancy can be obtained from repeated biopsy.

References

1. Minielly JA, Harrison EG Jr, Fontana RS, Payne WS (1967) Verrucous squamous cell carcinoma of the esophagus. Cancer 20: 2078-2087.
2. Ackermann LV (1948) Verrucous carcinoma of the oral cavity. Surgery 23: 670–678.
3. Osborn NK, Keate RF, Trastek VF, Nguyen CC (2003) Verrucous carcinoma of the esophagus: clinicopathophysiologic features and treatment of a rare entity. Dig Dis Sci 48: 465-474.
4. Garrard CL, Sheih WJ, Cohn RA, Sawyers JL (1994) Verrucous carcinoma of the esophagus: surgical treatment for an often fatal disease. Am Surg 60: 613-616.
5. Tonna J, Palefsky JM, Rabban J, Campos GM, Theodore P, et al. (2010) Esophageal verrucous carcinoma arising from hyperkeratotic plaques associated with human papilloma virus type 51. Dis Esophagus 23: E17-E20.
6. Kojima T, Minami K, Kouyama K, Kawaguchi M, Saitou T, et al. (1988) A case of verrucous squamous cell carcinoma of the esophagus. Gastroenterological Endoscopy 30: 582–587.
7. Rotmensch J, Herbst A (1993) Neoplasms of vulva and vagina: Neoplasms of the cervix. (3rdedn). Piver MS, Hempling RE, Craig K (Eds.), Cancer medicine.
8. Perez CA, Kraus FT, Evans JC, Powers WE (1966) Anaplastic transformation in verrucous carcinoma of the oral cavity after radiation therapy. Radiology 86: 108-115.
9. Sakurai T, Fuchigami T, Omae T, Iwashita A, Kume K, et al. (1983) Bleomycin in verrucous squamous cell carcinoma of the oesophagus. Postgrad Med J 59: 578-580.
10. Parkinson AT, Haidak GL, McInerney RP (1970) Verrucous squamous cell carcinoma of the esophagus following lye stricture 57: 489-492.
11. Meyerowitz BR, Shea LT (1971) The natural history of squamous verrucose carcinoma of the esophagus. J Thorac Cardiovasc Surg 61: 646-649.
12. Sridhar C, Zeskind HJ, Rising JA (1980) Verrucous squamous-cell carcinoma: an unusual tumor of the esophagus. Radiology 136: 614.
13. Agha FP, Weatherbee L, Sams JS (1984) Verrucous carcinoma of the esophagus. Am J Gastroenterol 79: 844-849.
14. Barbier PA, Luder PJ, Wagner HE, Becker CD, Scheurer U, et al. (1987) Verrucous acanthosis--so-called verrucous carcinoma-of the esophagus. Z Gastroenterol 25: 93-97.
15. Koerfgen HP, Husemann B, Giedl J, Hohenberger W (1988) Verrucous carcinoma of the esophagus. Endoscopy 20: 326-329.
16. Jasim KA, Bateson MC (1990) Verrucous carcinoma of the oesophagus-a diagnostic problem. Histopathology 17: 473-475.
17. Biemond P, ten Kate FJ, van Blankenstein M (1991) Esophageal verrucous carcinoma: histologically a low-grade malignancy but clinically a fatal disease. J Clin Gastroenterol 13: 102-107.
18. Roach E, Barr G (1993) Verrucous carcinoma of the oesophagus and achalasia. J Gastroenterol Hepatol 8: 107-109.
19. Kavin H, Yaremko L, Valaitis J, Chowdhury L (1996) Chronic esophagitis evolving to verrucous squamous cell carcinoma: possible role of exogenous chemical carcinogens. Gastroenterology 110: 904-914.
20. Malik AB, Bidani JA, Rich HG, McCully KS (1996) Long-term survival in a patient with verrucous carcinoma of the esophagus. Am J Gastroenterol 91: 1031-1033.
21. Tajiri H, Muto M, Boku N, Ohtsu A, Yoshida S, et al. (2000) Verrucous carcinoma of the esophagus completely resected by endoscopy. Am J Gastroenterol 95: 1076-1077.
22. Ereno C, Lopez JI, Loizate A, Bilbao FJ (2001) Verrucous carcinoma of the esophagus. Endoscopy 33: 297.
23. Mizutani S, Oyama T, Uchikoshi F, Nakahara M, Tsujimoto M, et al. (2005) A case of verrcous carcinoma of the esophagus with successful resection. Journal of Japan Surgical Association 66: 2146-2150.
24. Devlin S, Falck V, Urbanski SJ, Mitchell P, Romagnuolo J (2004) Verrucous carcinoma of the esophagus eluding multiple sets of endoscopic biopsies and endoscopic ultrasound: a case report and review of the literature. Can J Gastroenterol 18: 459-462.
25. Wong LM, Moulton CA, Hosking P, Cade R (2005) Warts in the oesophagus: a potentially fatal but curable carcinoma. ANZ J Surg 75: 616-617.
26. Oh K, Nishigami T, Takubo K, Shimada Y, Fujimoto J (2009) A case of verrucous squamous cell carcinoma of the esophagus. Esophagus 6: 263-267.
27. Na S, Choi KD, Yoo C, Chang Y, Song HJ, et al. (2009) Verrucous carcinoma of the esophagus. Gastrointest Endosc 70: 803-806.
28. Macias-Garcia F, Martinez-Lesquereux L, Fernandez B, Parada P, Larino-Noia J, et al. (2010) Verrucous carcinoma of the esophagus: a complex diagnosis. Endoscopy 42: E137-E138.
29. Chu Q, Jaganmohan S, Kelly B, Hobley J (2011) Verrucous carcinoma of the esophagus: a rare variant of squamous cell carcinoma for which a preoperative diagnosis can be a difficult one to make. J La State Med Soc 163: 251-253.
30. Lagos AC, Marques IN, Reis JD, Neves BC (2012) Verrucous carcinoma of the esophagus. Rev Esp Enferm Dig 104: 443-445.