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Successfully Avoiding Surgery in an Ectopic Cervical Pregnancy

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Abstract

The uterine cervix is a rare implantation site for ectopic pregnancy, surgical management should be carefully considered due to the risk of severe hemorrhage associated with this treatment. Methotrexate (MTX) is well documented as an effective medical approach in early gestations and low human chorionic gonadotropin (ß-hCG) levels yielding good results. This is the case,of a 39 year old woman with a 6.5 week old cervical pregnancy. Diagnosis was suspected and later confirmed due to the presence of a late, vaginal hemorrhage and pelvic pain, blood quantitative ß-hCG quantification, clinical exploration and ultrasonographic evaluation. Since the patient was hemodinamically stable and had concerns with her fertility we opted for a medical treatment with MTX in a multiple dose regimen. Treatment was successful after 3 doses (62.5 mg. each, IV infusion), applied on days 1, 3 and 5, using leucovorin (1 g) on alternate days as rescue therapy. Initial ß-hCG levels were reported at 211 mIU/mL, by the time the patient was discharged she had a 77.5% decrease on the ß-hCG levels and diminished symptomatology, after two months follow-up, ß-hCG levels were 0 mIU/mL. Medical management successfully eliminated cervical pregnancy, thus avoiding the risks any invasive procedures may pose.

Keywords: Ectopic; Cervical; Methotrexate; MTX; Pregnancy; ß-hCG; Fertility

Introduction

Ectopic pregnancy constitutes a rare medical emergency (1 in 9000-10,000 pregnancies) due to rupture risk and subsequent hemorrhage [1,2]. In many cases, hysterectomy was one of the preferred treatment options for cervical pregnancies [1,2] with major drawbacks being: high morbidity associated with this procedure and ending a woman's reproductive capability. Currently, conservative (medical) management techniques are favored over surgical options, mainly due to the uncontrollable hemorrhage any invasive procedure may ensue and end in a hysterectomy, with all the complications associated with it. Medical treatments consist on the systemic or local use of methotrexate (MTX), with various dose regimens, alone or in combination with intracardiac-embryonic injection of potassium chloride [3,4]. Clinical parameters must be assessed in order to proceed with this conservative treatment.

Case Presentation

A 39, year old native mexican (Otomi origin) with no previous surgical or obstetric history, positive for alcohol consumption and smoking, arrives to our unit referring 4 days with pelvic pain and vaginal bleeding and a 6.5, week delay on her menses. Upon physical exploration we found a BMI of 23 kg/m^2, slightly increased heart rate (90 bpm) with normal blood pressure and normal Glasgow evaluation, a generalized pain was observed on lower abdomen and pelvis, increased upon palpation and leg flexion. Speculoscopy increased pelvic pain and revealed an active trans-cervical bleeding. Cervix was erythematous and swollen. Laboratory tests were performed, including complete blood count (CBC), coagulation tests, urinalysis, blood ß-hCG and a pelvic, transvaginal ultrasound. CBC reported normal hemoglobin (13.5 g/dL), hematocrit (40.5%), leukocytes (8.5 x 10^3 µL) and platelets (234,000). Urinalysis had no significant findings except for the presence of erythrocytes that were most probably present due to sample contamination. ß-hCG was 211 mIU/mL and pelvic sonogram confirmed the presence of a gestational sac below de interior cervical ostium, within the cervical main structure and positive vascular activity around the gestational sac (Doppler evaluation, (Figures 1 and 2). A 6.5 week old cervical pregnancy was diagnosed with a controlled vaginal bleeding, hence, medical treatment protocol was initiated due to patient's hemodynamic stability, low ß-hCG levels and patient's desire for fertility preservation.

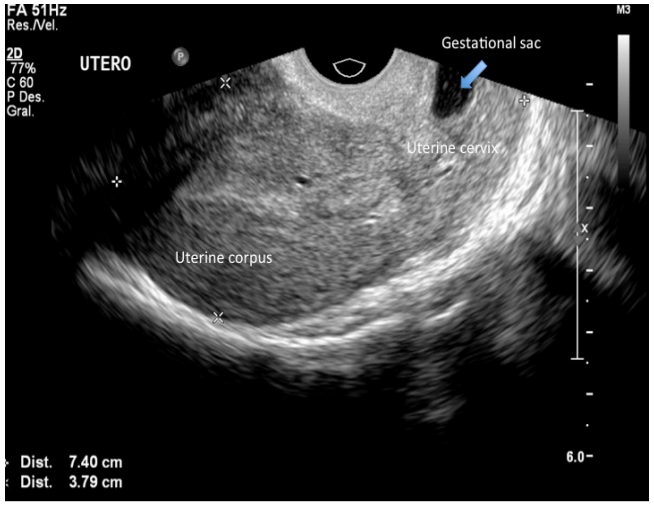

Figure 1: Vaginal sonogram showing uterine corpus and cervix, where a gestational sac is identified in the latter.

Once the patient was admitted basal further laboratory parameters were obtained (CBC, blood chemistry screen, liver enzymes (alanine aminotransferase (ALT), aspartate aminotransferase (AST)), bilirubin levels, total proteins, albumin, blood clotting tests, blood type and Rh identification. MTX dose was calculated at 1 mg per kilogram, body weight (62.5 mg), doses were given on days 1,3 and 5, alternating with

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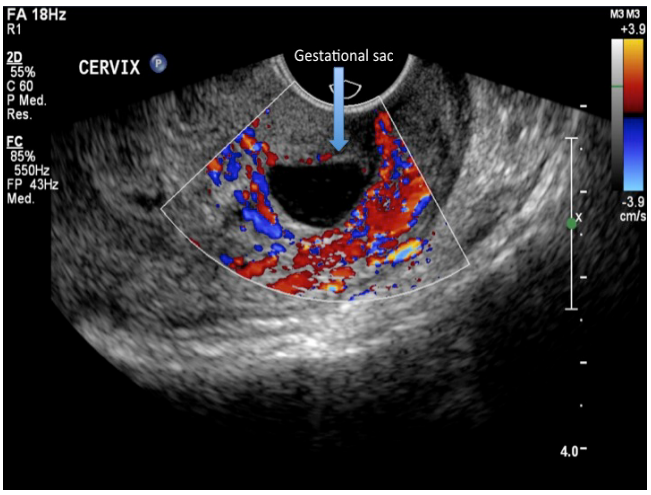

Figure 2: Doppler ultrasonography helps identify the intense vascular reaction surrounding the gestational sac in uterine cervix, revealing the active decidual reaction.

Day according to first MTX dose.	Seric ß- hGC levels (mUI/mL)
1 (62.5 mg of MTX was administered)	211
3 (62.5 mg of MTX was administered)	133
5 (62.5 mg of MTX was administered)	7
6	68
7	48
12	12
18	4
24	1

Serical ß-hCG level determinations were performed on the 3 days of MTX administration, afterwards determinations were performed to see a gradual decrease. Leucovorin was administered on days 2,4 and 6 (not shown).

Table 1: ß-hCG level determinations on specific day of treatment.

1 g of leucovorin on days 2,4 and 6 (rescue therapy). Laboratory follow up was performed with blood ß-hCG and methotrexate levels (Table 1).

MTX serical levels were always reported under 0.1 µmol/L, while ß-hCG dropped from 211 mIU/mL on day 1 to 7 mUI/mL on day 5, vaginal bleeding and pelvic pain were significantly reduced. By day 6, levels slightly increased to 68 mUI/mL, only after the last chemotherapy administration a significant decrease was observed, reaching 1 mIU/mL by day 24. The patient was discharged on day 7, after vaginal bleeding and pelvic pain had disappeared. The only complaints associated to chemotherapy were headache that was treated with ibuprofen (200 mg t.i.d.). By day 18, no ultrasonographic image of a gestational sac could be seen. Follow-up, through outpatient consultation revealed complete absence of ß-hCG by day 60 (not reported in Table 1) and totally asymptomatic, she opted for a barrier contraception method and is being followed (until 6 months after discharge) with MTX and ß-hCG level determinations. Patient provided written consent for the publication of this case.

Discussion

Cervical ectopic pregnancies have a low incidence (1 in 9,000 - 10,000 pregnancies), even when considering the most common extrauterine implantation sites, they roughly represent 1% overall ectopic pregnancies [2,3]. The anatomic site and complications associated to it, award special considerations due to significant hemorrhage risk.

Specific causes remain unknown though previous conditions like fibroids, curettage, cesarean sections, Asherman's syndrome and intrauterine devices, all may alter implantation surface conditions increasing risk for an ectopic implantation [4,5]. Assisted Reproduction Techniques (ART) is currently on the rise and associated to a 3.7% incidence of ectopic gestations, rendering higher possibilities for cervical pregnancies [6]. Histopathological diagnosis is based on the presence of cervical glands opposite an intimate placental attachment, the placenta must be below the entrance of the uterine vessels or below the peritoneal reflection of the anteroposterior surface of the uterus, and no fetal elements in the corpus uteri should be present [1]. Clinically, these patients may initiate with vaginal bleeding before knowing they are pregnant, pelvic discomfort and a gradual increase on bleeding volumes may follow. All these events were observed in our patient, although none of the risk factors, mentioned were identified except smoking, which is associated to ectopic pregnancies, though not specifically to cervical implantations [7].

Our patient desired to preserve her fertility, therefore inquired on non-surgical resolutions. Currently, surgical treatment options include intracervical balloon tamponade after cervical curettage, cervical cerclage, angio-embolization of uterine arteries, curettage and local prostaglandin injection, hysteroscopic resection, ultrasound guided MTX injection, intrauterine irrigation of hydrogen peroxide and bilateral uterine artery ligation [8-10]. As for medical treatment options, MTX is the most widely used systemic agent and was first described for cervical pregnancy in 1983 [11]. MTX is a folic acid antagonist, interfering with DNA synthesis, through dehydrofolate reductase inhibition, stopping cell proliferation [8]. This action is opposite to that generated by folic acid, therefore, folinic acid (leucovorin) is administered on alternate days to diminish side effects as nausea, abdominal pain, neutropenia, liver function and bone marrow effects [12,13]. Our case had optimal conditions for MTX treatment since there was no hemodynamic compromise, no evidence of yolk sac, no fetal cardiac activity and ß-hCG levels of 211 IU/mL (below 5000 mIU/mL). Krissi H et al. [12] found mean ß-hCG levels for 102 cases of ectopic pregnancies of 2350 ± 2955 mIU/mL, achieving 74.5% success with a single MTX dose and 76.2% on a second dose, overall success rate was 90.2%, similar to what has been reported by other authors [14,15], Based on a meta analysis where the multidose regimen had a 92.7% success rate vs 88.1% on the single dose rate, the decision was taken to start the prior [16,17].

Response to MTX treatment was adecuate, the only complaint the patient refered was a headache that was treated with ibuprofen. Initial MTX dose diminished ß-hCG levels by 37% (from day 1 to day 3); levels on the 5th day were 7 IU/mL and by the 6th day we saw them escalate to 68 IU/mL. Only after the last MTX dose we observed a constant descent, reaching 1 IU/mL by day 24. Vaginal bleeding and pelvic pain were minimum by day 7 (patient discharge), disappearing on the 12th day after the first MTX dose. A followup ß-hCG level determination was performed two months after treatment reporting 0 IU/mL, and ultrasonographic evaluation found no evidence of a gestational sac.

Folic acid deficiencies are associated with neural tube defects, skull, limb, digital, vertebral and cardiac malformations, these may be all potentially caused by MTX which may reach high concentrations in liver, kidney, gallbladder, spleen and skin, detectable 116 days after exposure. For this reason, 6 month followup with contraception was indicated to our patient [18].

We believe this is a case where all conditions were met for a successful medical treatment, avoiding the risks involved in a surgical proceedure

and retaining the patient's fertility. Follow-up on MTX levels should be done for at least 6 months. Patients with similar characteristics should be offered this treatment prior to invasive procedures.

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