Case Report

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Failed Treatment of an Ectopic Pregnancy Despite Beta-HCG of < 2

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Abstract

Missing an ectopic pregnancy in a female with abdominal pain of child bearing status can be detrimental to the patient as well as the career of the physician. Being the third leading cause of maternal mortality at 6%, and encompassing approximately 2% of all pregnancies, this is a diagnosis that physicians cannot afford to miss. The following is an unusual presentation of an ectopic pregnancy with a negative beta-HCG (BHCG) and a discussion of the literature on medical treatment of entopic pregnancies with methotrexate.

Keywords: Ectopic Pregnancy; Failed out-patient Treatment

Introduction

Being the third leading cause of maternal mortality at 6% percent, and encompassing approximately 2% of all pregnancies [1], ectopic pregnancy is a diagnosis that the emergency physician cannot afford to miss. In most emergency departments the most efficient way to rule out ectopic is a urine pregnancy test. The following is a unique case presentation of a female with abdominal pain that turned out to be an ectopic pregnancy.

Case Report

A 39-year-old, Gravid 2 Para 1, Caucasian female with a past medical history of ovarian torsion, cholecystectomy and hernia repair presented to the emergency department complaining of abdominal pain and vaginal bleeding for one day. Sixty days prior to this visit, the patient had been diagnosed with an ectopic pregnancy with an initial beta-HCG of 5362

Table 1. Lab Reults From Ed Visit

Test	Result
Urinalysis	
Color	Straw
Clarity	Clear
Glucose	Negative
Bilirubin	Negative
Ketones	Negative
Specific Gravity	1.025
Blood	Large
Urine Protein	Negative
Urobilinogen	0.2
Nitrite	Negative
Leukocyte Esterase	Negative
pH	7.0
Urinalysis, Micro	
RBC	2 to 10 HPF
WBC	0 HPF
Bacteria	None seen
Urine Pregnancy	Negative
ABO/RH and AB Screen	
ABO/RH(D)	O Positive
Antibody Screen	Negative

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Table 2. Lab Reults From Ed Visit

Test	Result	Lab Standard (where applicable)
Electrolytes		
Sodium	140 mmol/L	135 - 145 mmol/L
Potassium	3.9 mmol/L	3.5 - 5.0 mmol/L
Chloride	104 mmol/L	95 - 108 mmol/L
Carbon Dioxide	25 mmol/L	24 - 32 mmol/L
Calcium, Serum	8.4 mg/dL	8.5 - 10.5 mg/dL
Glucose,Random,Bld	136 mg/dL	50 - 140 mg/dL
Magnesium, Serum	1.8 mg/dL	1.8 - 2.3 mg/dL
BUN	12 mg/dL	10 - 25 mg/dL
Albumin, Serum	3.7 g/dL	3.7 - 4.8 g/dL
Creatinine	1.0 mg/dL	0.6 - 1.1 mg/dL
CBC		
WBC Count	6.0 K/uL	3.8 - 10.6 K/uL
RBC Count	4.48 M/uL	4.15 - 5.55 M/uL
Hemoglobin	12.5 g/dL	12.0 - 15.0 g/dL
Hematocrit	38.0	36 - 4 6%
MCV	84.8 fl	80 - 100 fl
MCH	27.9 pg	26 - 34 pg
MCHC	32.9 g/dL	31 - 37 g/dL
RDW	13.8 %	< 14.5%
Platelet Count	207 K/uL	140 - 400 K/uL
Differential		
Neutrophil	65%	
Lymphocyte	24%	
Monocyte	9%	
Eosinophil	2%	
Basophil	0%	

and was treated one day later with methotrexate. When obstetrics followed up on the beta-HCG seventeen days prior to this visit, at which point the beta-HCG was recorded as 164 with a subsequent dose of methotrexate the next day. On her follow-up appointment 10 days prior to our visit, the patient's beta-HCG recorded as < 2.

On the day the patient was seen in our emergency department, she described the pain as intermittent pressure with sudden onset, similar to her prior ovarian torsion. Unlike that episode, however, this pain was also associated with dysuria. She denied any lightheadedness, syncope, weakness, or dizziness. Her vital signs were stable with a blood pressure of 115/65, pulse 68, RR 18 and remained so throughout her stay. Her physical exam was normal, including a soft abdomen with no tenderness to palpation and no peritoneal signs. At this point, 6 mg of morphine and 4 mg of ondansetron were ordered for the patient's comfort. The patient was taken to radiology for a pelvic ultrasound and then moved to the OBGYN room for a pelvic exam.

CBC, electrolytes, GFR, serum beta-HCG and type and screen were ordered in addition to the urine pregnancy and urinalysis that had been ordered from triage. Her lab results were discordant with a negative urine pregnancy but positive serum B-HGC of 105 (Table 1, Table 2).

The patient's ultrasound showed a complex mass in the right adnexa with free pelvic fluid. OBGYN evaluated the

Table 3. Serum B-HCG Trend From Date of Initial Diagnosis of Ectopic Pregnancy to Date of ED Visit

Timeline	B-HCG
Day of visit	105
11 days prior	< 2
14 days prior	153
18 days prior	164
19 days prior	174
24 days prior	207
26 days prior	218
34 days prior	314
39 days prior	554
42 days prior	955
47 days prior	2907
49 days prior	3910
52 days prior	6001
55 days prior	7912
60 days prior	5362

patient and decided to admit her to the OR. The patient had an exploratory laparotomy with right partial salpingectomy. During the operation an approximate 6 cm ectopic pregnancy was visualized in the right tube. The pathology report confirmed ectopic tissue. Patient continued to be stable and was discharged from the hospital.

Discussion

This patient presentation was very unusual for an ectopic, having been treated twice by methotrexate and having a negative beta-HCG ten days prior to arrival to the ED. A review of the literature was performed on Pubmed using "ectopic pregnancy methotrexate failure" for the search. The guidelines for Medical Management of Ectopic Pregnancy from The American College of Obstetricians and Gynecologists (ACOG) were also reviewed.

Approximately 97% of ectopic pregnancies are implanted in the fallopian tube, as was the case in our patient. Risk factors for ectopic pregnancy included infections such as pelvic inflammatory disease, in utero exposure to diethylstilbestrol, and a history of previous ectopic, previous abdominal or pelvic surgery, smoking, infertility and the use of assisted reproductive technologies. Of these factors, our patient had only one risk factor: her previous abdominal surgery. According to ACOG, the use of methotrexate in the treatment of ectopic pregnancy has a 71.2% to 94.2% success rate. These success rates vary depending on treatment regimen used (single dose, two-dose, or fixed multidose), gestational age, and beta HCG level [2]. Unfortunately our patient had no records of earlier imaging for determining gestation age; however records of the patients serial B-HCG were obtained (Table 3).

Many studies have been performed using B-HCG as a predictor of failure of methotrexate treatment; however, the conclusions of these studies vary from an initial B-HCG level >1790 mIU/ml, > 2000 mIU/ml, to > 5000 mIU/ml as a predictor of failure of the therapy [3-5]. With B-HCG > 2000 mIU/ml the failure rate can be as high as 26% [5]. The ACOG recommendation does not suggest any parameters for the different regiments, nor does it suggest which B-HCG is appropriate for which regiment. The recommendation does mention, however, that the two-dose regimen through recent studies showed an 87% success rate, with the single dose being as effective. The most recent data though shows the fixed regimen to be more effective, especially if cardiac activity is present. The absolute contraindications to any of this medical therapy include breastfeeding, immunodeficiency, alcoholism, preexisting blood dyscrasias, active pulmonary

disease, PUD, and any dysfunction in the hepatic, renal, or hematological systems of the patient [1].

Our patient initially underwent the single dose regimen and after the plateau of the BHCG, the dose was repeated. Per the ACOG guidelines, after the methotrexate is given a post treatment B-HCG should be taken at 4 - 7 days with an expectant decrease of about 15%. The B-HCG should then be measured weekly until the levels return to non-pregnant status. The methotrexate can be repeated at the same dose if the aforementioned criteria were not met or if during follow up the B-HCG levels plateau or increase [2]. An early rising of B-HCG can be observed in 50 - 70% of cases treatment with methotrexate and thought to be due to long half-life of B-HCG (36 hours), release of B-HCG into circulation from trophoblastic cells due to methotrexate exposure, or a difference in folic acid levels in patient causes different B-HCG curves [6]. This rise however, if associated with a decrease at day 3, is associated with an 80% success rate of treatment [7]. Our patient was treated with a single dose of methotrexate 59 days prior to our visit after her initial B-HCG was 5362 a day earlier. The patient saw the initial rise in the B-HCG post treatment day 4 with her B-HCG at 7912 and did not fall until post treatment day 7 when her B-HCG was 6001 and post treatment day 10 when it was at 3910. Per the literature she had increased risk of failure due to not only B-HCG > 5000 but also the patient's B-HCG did not decrease > 15% until day 10 post treatment. A second dose of methotrexate was given on Aug 27. A second dose most likely was given due to plateau of the B-HCG levels.

No reports were found in searching Pubmed for cases of methotrexate causing a dilution effect on B-HCG. Only one other case involving failed treatment of a cervical ectopic pregnancy had a similar occurrence of B-HCG returning to normal levels, then rising again. No explanation in the report was given for this occurrence [8].

The possibility of this being a different ectopic than the first was discussed, however, with the size of the ectopic at 6cm, this was doubtful. Our patient presented to the ER 11 days after her B-HCG was < 2. According to the literature the size of a fetus at 2 weeks is only about 100 - 150 cells or 1 cm. During surgery, our patient was found to have a 6 cm ectopic with the pathology report confirming ectopic tissue.

Ectopic pregnancies are sometimes difficult to diagnosis. They do not behave as a normal IUP would. This case above describes one of these cases. Extra caution and attentiveness should be given to patient recently treated with methotrexate, even with B-HCG at pre-pregnancy levels. Relying on serum B-HCG instead of urine B-HCG may prevent potential missed ectopic pregnancies.

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