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## Case Report

# Medical treatment of ectopic pregnancy: case report

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### ABSTRACT

Ectopic pregnancy occurs when the embryo implants outside the uterine cavity. It is a leading source of morbidity and mortality within pregnancy. Methotrexate, a folic acid antagonist, has been widely used to treat appropriately selected ectopic pregnancies. We report the case of a 20-year-old woman, married, G2P0, having as antecedent a right tubal ectopic pregnancy benefiting from a right salpingectomy two years ago, who presents actually a paucisymptomatic ectopic pregnancy. Medical treatment with methotrexate was chosen with monitoring of the patient's hemodynamic status and hCG level.

**Keywords:** Ectopic pregnancy, Methotrexate,  $\beta$ -hCG, Medical treatment of ectopic pregnancy

### INTRODUCTION

Ectopic pregnancy is a significant cause of morbidity and mortality in the first trimester of pregnancy.<sup>1</sup> Early diagnosis and appropriate treatment can reduce the risk of maternal mortality and morbidity related to ectopic pregnancy. Generally, the treatment is surgical, but recently, a medical management can be proposed. A treatment with methotrexate (MTX), a folic acid antagonist highly toxic to rapidly replicating tissues, achieves comparable results to surgery for the treatment of appropriately selected ectopic pregnancies and is now used commonly.<sup>2</sup> An unruptured ectopic pregnancy can be managed with either surgery or methotrexate. Surgery is specifically indicated in cases of suspected tubal rupture and when MTX is contraindicated.

#### Risk factors

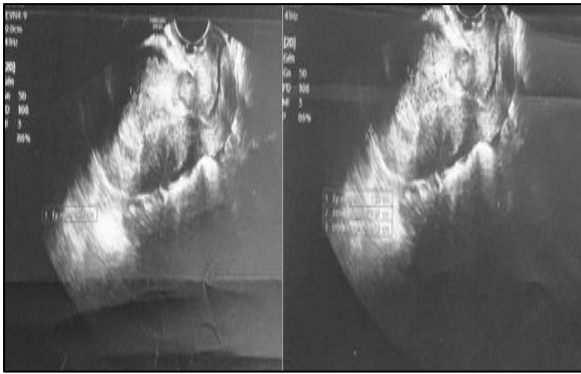
Any pregnant woman can potentially have an ectopic pregnancy. But any damage to the fallopian tubes predisposes a woman to ectopic pregnancy. Knowledge of risk factors can help identify women who may benefit from close monitoring and early treatment.

High-risk conditions include: previous ectopic pregnancy, history of tubal surgery (including a previous tubal sterilization), history of sexually transmitted infection, tubal infection, pelvic adhesions, and current use of an intrauterine device, conception resulting from assisted reproduction, cigarette smoking and in utero exposure to diethylstilbestrol.<sup>3,4</sup>

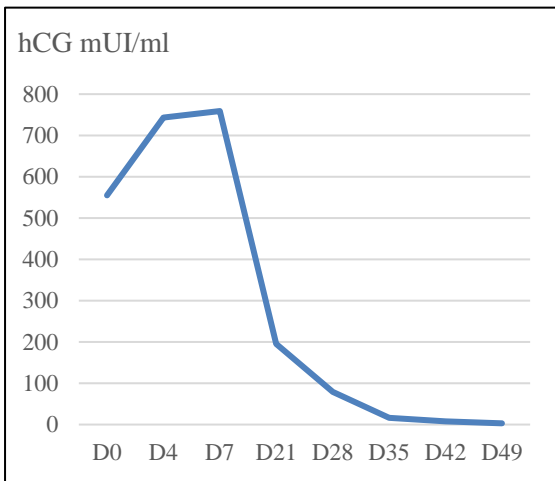
### CASE REPORT

Mrs. A.B, a young woman of 20-years-old, married, G2P0, with a story of right salpingectomy two years ago for a right tubal ectopic pregnancy, and the notion of recurrent genital infections. She consulted in Al Farabi Hospital's emergency department for recurrent first trimester pregnancy losses with amenorrhea of 6 weeks + 4 days. Upon clinical examination, her vital signs were stable. The abdominal examination found a sensitivity of the left iliac fossa. The digital vaginal examination found a posterior closed cervix, a minimal bleeding with a cul-de-sac of Douglas pain. Quantitative  $\beta$ -human chorionic gonadotrophin ( $\beta$ HCG) concentration was 555 mUI/ml and her hemoglobin count measured 9,7 g/dL. A bedside pelvic ultrasound showed an empty uterine cavity measuring 78/41 mm with regular and homogeneous

contours, 13.4 mm thickened endometrium hyperechoic decidualized with a left latero-uterine image of 45mm and an effusion of 13mm in the pouch of Douglas. (Figure 1).



**Figure 1: Empty uterus with a decidual endometrium on the pelvic ultrasound.**



**Figure 2: Evolution of our patient’s β-human chorionic gonadotrophin level after medical treatment.**

Colour flow Doppler ultrasound demonstrated a ‘ring of fire’ sign, showing the intense peritrophoblastic vascular activity around the sac.

In our case, we had a paucisymptomatic ectopic pregnancy with a Fernandez score less than 13. Therefore, we choosed medical treatment. A pre-methotrexate assessment was normal (blood count and liver enzymes), so we prescribed an intra-muscular methotrexate injection dosed at 1 mg/kg and analgesic treatment at demand with strict rest. The patient was informed of the possibility of the onset of pain during the 3 days after the injection of methotrexate and of the possibility of surgical treatment if medical treatment failed. Since the patient lived in a rural zone, she was cooperant to be hospitalized during the methotrexate cure for close surveillance. Her hemodynamic state and the quantitative β-human chorionic gonadotrophin (βHCG) concentration level were monitored on D4 and D7. An increase in the quantitative

β-human chorionic gonadotrophin (βHCG) concentration level was noted on D7 at 759 mIU/ml compared to 743 mIU/ml on D4. Hence, a 2nd methotrexate dose was given (1 mg/kg IM). (Figure 2)

**Table 1: Contra-indication of MTX.**

Contra-indications to MTX therapy <sup>5-9</sup>	
<b>Absolute contra-indications</b>	
Intrauterine pregnancy	
Evidence of immunodeficiency	
Moderate to severe anemia, leukopenia or thrombocytopenia	
Sensitivity to MTX	
Active pulmonary disease	
Active peptic ulcer disease	
Clinically important hepatic dysfunction	
Clinically important renal dysfunction	
Breast feeding	
<b>Relative contra-indications</b>	
Embryonic cardiac activity detected by transvaginal ultrasonography	
High initial hCG concentration (>5.000 mIU/mL)	
Ectopic pregnancy > 4 cm in size in transvaginal ultrasonography	
Refusal to accept blood transfusion	
Inability to participate in follow-up	

**Table 2: Fernandez score for the medical treatment of ectopic pregnancy.**

	1 point	2 points	3 points
<b>Gestational age (days)</b>	>49 d	Between 42 and 49 d	<42d
<b>hCG level (mIU/ml)</b>	<1000	1500 - 5000	>5000
<b>Progesterone level (ng/ml)</b>	<5	5 - 10	>10 or not known
<b>Abdominal pain</b>	Absent	Provoked	Spontaneous
<b>Hematosalpinx (cm)</b>	<1	1 - 3	>3
<b>Hemoperitoneum</b>	0	1 - 100	>100

The clinical evolution of the patient was good since the pain and the bleeding disappeared. She was stable and remained asymptomatic throughout the treatment period. She didn’t need any blood transfusion. She was discharged with weekly quantitative β-human chorionic gonadotrophin (βHCG) test control advice. The quantitative β-human chorionic gonadotrophin (βHCG) concentration level became negative on day 35 after the first dose of methotrexate and the pelvic ultrasound showed a minimal intra-abdominal fluid (<3 mm).

**DISCUSSION**

Medical treatment protocols for methotrexate (MTX) were established in the late 1980s and have become a widely

accepted primary treatment for non-complicated ectopic pregnancy.<sup>5,6</sup>

Ideally, the perfect case for medical management of an ectopic pregnancy with MTX should have the following criteria: hemodynamic stability, commitment to follow-up, no severe or persistent abdominal pain and normal liver and renal function tests.

As with all medical interventions, the first line of evaluation is the clinical presentation. An immediate surgical management is indicated if the patient is unstable or present an acute abdomen.

Infertility patients are usually good candidates for conservative management because they are closely monitored as part of their treatment. In addition, in these patients, it is preferable to preserve fertility because of the increased risk of ectopic pregnancy due to previous surgery and/or history of tubal abnormalities.

However, sometimes, the use of MTX is impossible due to some contra-indications (Table 1).

Before to the first dose of MTX, the patient should be screened with a complete blood count, liver enzymes, serum creatinine and blood type and Rhesus. Women having a history of pulmonary disease should have a chest x-ray to avoid the risk of interstitial pneumonitis.

There are two commonly used MTX treatment regimens, either the multiple dose regimen or the single dose one. The multiple-dose protocol is a regimen was the first one used to treat ectopic pregnancy.<sup>6,10</sup> It alternates MTX treatment with folic acid (leucovorin) therapy. It is continued until  $\beta$ -human chorionic gonadotrophin falls by 15% from its peak concentration. Approximately half of patients treated with this regimen will not require a full 8-day regimen.<sup>10,11</sup>

Following administration of treatment, the surveillance includes an interview for clinical symptoms and weekly surveillance of plasma  $\beta$ -human chorionic gonadotrophin levels. A clinical examination and an ultrasound can be performed at any time of the onset of functional signs suggesting a hemorrhagic complication of ectopic pregnancy. A second MTX injection should be considered if the decrease in the plasma  $\beta$ -human chorionic gonadotrophin level on D7 is not satisfactory compared to the initial one (in practice the  $\beta$ -hCG level on D7 should be strictly lower than the level on D0 or strictly lower at 85% of the  $\beta$ -hCG level on D4 if it is available). As soon as  $\beta$ -hCG levels start to decline, they are weekly checked to ensure that their level is declining to become undetectable.

Complete resolution of an ectopic pregnancy usually takes between 2 and 3 weeks but can take 6 to 8 weeks when initial  $\beta$ -hCG levels are very high.<sup>12,13</sup> When declining  $\beta$ -hCG levels again rise, the diagnosis of a persistent ectopic

pregnancy is made and the medical treatment is highly suspected. Therefore, a surgical treatment should surely be undertaken.

In order to facilitate the choice of patients who are candidates for medical or surgical treatment, a score had been proposed: Fernandez's score (Table 2).<sup>14,15</sup> It is calculated based on gestational age, pre-therapeutic hCG levels, progesterone levels, presence of abdominal pain, size of hematosalpinx and extent of hemoperitoneum. Each item is next to 1 to 3 points.

With the one-injection regimen of methotrexate, if the Fernandez score is strictly less than 13, the success rate is 82% to 95%. Surgical treatment is indicated if the score is  $\geq 13$ .

The dosage of progesterone is a limiting parameter for the Fernandez score because this dosage is only very rarely possible in routine and especially in emergency. In practice, we will note 3 the progesterone level when it is not known.

When these criteria are fulfilled, there is no difference in the success rates between medical treatment with MTX and conservative surgery.<sup>2,11,12</sup>

## CONCLUSION

Ectopic pregnancies must be diagnosed at early stages, to improve their outcomes. Medical management with Methotrexate is effective for ectopic pregnancies to preserve the fertility. The medical management by MTX seems to offer more benefits than the surgical treatment: it is less invasive, less expensive and is independent of expertise like laparoscopy. However, the risk of tubal rupture after medical treatment associated with a prolonged follow-up makes the compliance important in patient selection.

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