

Case Report

Successful Management of Live Ectopic Pregnancy with High B-Hcg Titres by Systemic Methotrexate Injection: A Case Report

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Abstract

Background: Use of methotrexate (MTX) as a nonsurgical management of unruptured ectopic pregnancies has been well accepted. However, use of it in high serum chorionic gonadotropin concentration and in live fetus has been considered as relative contraindication for medical therapy. The aim of this report is to emphasize that these contraindications can be revisable in some situations and discuss about this fact that the success rate can be affected by the type of protocols used for medical treatment.

Case presentation: A 31 years old primigravid woman was admitted to our hospital due to a sonogram's report of ectopic pregnancy with a high initial serum B-hCG concentration (26900) and presence of fetal cardiac activity. Her vital signs were stable and she did not agree with operative intervention. Two-dose protocol was scheduled but appropriate response to treatment was obtained after receiving the third dose of methotrexate. Negative serum B-hCG (< 1 mIu/ml) was achieved on day 80 without any related treatment complication on follow up.

Conclusions: Use of double- dose protocols of MTX in medical treatment of ectopic pregnancy increase the chance of successful and nonsurgical treatment even in live fetus with high B-hCG titers.

Keyword: Systemic methotrexate; Ectopic pregnancy; Medical management; Protocol; Case report

Abbreviations: MTX: methotrexate; B-hCG: Beta human chorionic gonadotropin

1. Background

Ectopic pregnancy is referred to any pregnancy that occurs outside of the uterine cavity .The three approaches in the management of ectopic pregnancy are surgery, methotrexate therapy, or expectant management. Treatment with methotrexate (MTX), a folic acid antagonist, currently has comparable results with surgery for the treatment of appropriately selected ectopic pregnancies and is commonly used [1]. But there are some factors that affect the effectiveness of this method. A high serum chorionic gonadotropin concentration (above 5,000 mIU/mL) is the most important factor associated with increase in failure rate of treatment with methotrexate [2, 3]. Another factor that affects the efficacy of MTX therapy is the presence of fetal cardiac activity. Previous studies state that the presence of fetal cardiac activity on TVUS is another relative contraindication to medical treatment [1, 3, 4] We reported here a case of ectopic pregnancy with a high initial serum B-hCG concentration (26900) and with existence of fetal cardiac activity which has responded well to treatment with 3 dose of methotrexate.

2. Case Presentation

A 31-year –old primigravida woman, was admitted to Omolbanin university teaching Hospital (Mashhad, Iran) due to a sonogram's report of ectopic pregnancy. She had 7 weeks delay of menstruation and her Beta- human chorionic gonadotropin titer was 26900. Trans vaginal sonogram evaluation revealed an empty uterus with an ectopic gestational sac Clinging to the right ovary with embryonal pole of 6 weeks' size, according to Crown-rump Length, with live fetus inside.On general examination, her condition was good, her vital signs were stable, and she was just suffering from mild pain and tenderness in the right lower abdomen. She had no significant past medical, surgical or gynecological problems. The patient was counseled about the risk and benefits of both medical and surgical treatment. The patient refused operative intervention and she signed the Consent form in which all benefits, disadvantages, and complications of medical management were mentioned.

Due to the high titer of B-hCG and presence of fetal cardiac activity, the two-dose protocol was scheduled. Complete Blood count and liver and renal function tests were normal. Two doses of methotrexate (50 mg/m^2) on days 0 and 4 were administered and after the second dose, the heartbeat of the fetus was stopped. Serum hCG values were measured and compared on days 4 and 7 after treatment; that were 47200 and 49000, respectively. Because there was no reduction in the level of the hCG and the patient was absolutely stable, the third dose was administered on day 7. After that, the evaluation of hCG level showed that it was adequate. She was discharged and followed up on an outpatient basis with weekly values of B-hCG. Negative titer was achieved on day 80. The patient remained

asymptomatic throughout the following period.

3. Discussion

Use of methotrexate (MTX) as a nonsurgical management of unruptured ectopic pregnancies has been well accepted and used from 1982 [3, 5]. There are some absolute contraindications to the methotrexate therapy, including intrauterine pregnancy and breastfeeding, bone marrow dysfunction indicated by significant anemia, leukopenia, or thrombocytopenia, Sensitivity to methotrexate, Active pulmonary disease, Active peptic ulcer disease, Clinically important hepatic and renal dysfunction and Inability to participate in follow-up [1]. Although some conditions such as presence of fetal cardiac activity, a high initial hCG concentration (greater than 5000 mIU/mL), Ectopic pregnancy greater than 4 cm in size in transvaginal ultrasonography and refusal to accept blood transfusion are mentioned as relative contraindications, reduction in treatment effectiveness is the main reason for offering these cut-offs [1, 5]. Considering different rate of success in different articles, actually these cut-off are only a suggestion regarding a value below which methotrexate therapy will be more successful [3]. As in one systematic review a higher failure rate of 14.3% in HCG levels higher than 5000 mIU/mL compared with 3.7% failure rate for HCG levels less than 5000 mIU/mL is reported [2]. Presence of fetal cardiac activity has also been considered as a relative contraindication for methotrexate therapy due to the increased rate of treatment failure [1, 5]. But in a large analysis of three hundred fifteen ectopic pregnancies, in the presences of fetal cardiac activity the success rate as high as 88 percent is also reported and do not accept this factor as a contraindication for methotrexate therapy [4]. Although the authors didn't mention that how much percent of these patients required two doses of methotrexate. On the other hand, the type of methotrexate protocols used is another factor that can be effective in overall treatment success. In a recent systematic review that compare three types of methotrexate protocols (single-dose, two-dose, or multi-dose), the 2-dose methotrexate protocol was superior to the single-dose protocol and was more successful in woman with higher initial hCG level (>5000) and large adnexal mass. Reduction in treatment failure was not significant in multiple dose but there was a higher chance of side effects [6] ectopic pregnancy sac greater than 4 cm in size is the other relative contraindication for medical therapy. Of course most ectopic gestational sacs do not reach sizes greater than 4 cm due to the restriction on tube extension. We were unable to find a study on the use of medical treatment in ectopic pregnancy over 4 cm, but it seems that serum chorionic gonadotropin concentration is the only factor significantly linked to the failure of the treatment [4].

Medical treatment reports in patient with very high level of initial beta-hCG is rare [5, 7, 8]. In one of these reports with a high level of initial B-hCG (89200), ultrasound-guided potassium chloride (KCL) intra sac injection, was used beside three doses of MTX. In this study negative titer was achieved on day 71 [7]. Use of ultrasound-guided injection of KCL in order to cause fetus cardiac asystole in live ectopic fetus has been reported since 1990 [7] and has been able to improve treatment success rate. But in some situation like our case due to lack of specialist, it is not available. In our case, we achieved on negative titer without potassium chloride (KCL) injection and just by methotrexate administration. There is another report with initial B-hCG level of 21130 that just use local injection of KCL without using MTX [8]. This is a remarkable success, but this approach need more research and clinical

studies for generalize recommendation. Our purpose in reporting this case is to emphasize that the contraindications proposed for medical treatment of ectopic pregnancies are relative and revisable in many situations. Although high initial serum chorionic gonadotropin concentration seems to be the only factor that contributed to increasing failure rate, the lower success rate in the high BHCG concentration, beside presence of cardiac activity must be balanced against the complications of surgery in each patient. Conservative management of ectopic pregnancy in specific circumstances and well selected patient can make the patient needless to undergo surgery. It should be noted that the patient must be counseled well and willing to accept potential risks, including tubal rupture, hemorrhage, and emergency surgery [1].

4. Conclusion

Although high initial titration in ectopic pregnancy may decrease the success of medical treatment, the use of a double-dose protocol may increase the chance of successful medical treatment and non-surgical management in fully selected patients.

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