Successful treatment using Actinomycin D in a case of methotrexate-resistant ectopic pregnancy: A case report

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Received: 3 Jan 2019 Published: 23 Sep 2019

Abstract
Ectopic pregnancy is an urgent clinical condition that represents a serious hazard to reproductive power, and thus threatens woman's health. Commonly, methotrexate is considered for early resolution of placental tissue. Despite its potential advantages such as minimizing hospitalization and quick recovery, its high skin and gastrointestinal side-effects and requiring time monitoring may limit its application. Recently, high effectiveness of the single-agent chemotherapy agents, such as Actinomycin D, has been suggested. Herein, a case of methotrexate-resistant EP that was successfully treated with Actinomycin D was described.

Keywords: Ectopic pregnancy, Actinomycin-D, Beta HCG

Conflicts of Interest: None declared
Funding: None

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Cite this article as: Aminimoghaddam S, Omranipoor A. Successful treatment using Actinomycin D in a case of methotrexate-resistant ectopic pregnancy: A case report. Med J Islam Repub Iran. 2019 (23 Sep);33:100. https://doi.org/10.34171/mjiri.33.100

Introduction
Ectopic pregnancy (EP) is an urgent clinical condition that represents a serious hazard to reproductive power, and thus threatens woman's health. Because of its related adverse clinical consequences, early and prompt diagnosis followed by early aggressive intervention is the choice treatment approach to manage this condition (1). Both congenital factors (tubal hypoplasia, elongation, stenosis, accessory ostia, diverticula, polyps, and tortuosity) and acquired factors (pelvic inflammatory disorders, contraceptive failure, sterilization failure, and reproductive inducing interventions) affect the incidence of EP (2). Due to serious complications of EP, including tubal rupture, massive hemorrhage, severe hemodynamic instability and death, early management of EP, which is done by both medical and invasive interventional approaches, is recommended to reduce fatality rate. Two medical and surgical approaches are now used to manage EP (3). In medical approach, both local and systemic medications, such as methotrexate, potassium chloride, prostaglandins, hyperosmolar glucose, and mifepristone, are used (4). Methotrexate is commonly considered for early resolution of placental tissue. However, despite its potential advantages, such as minimizing hospitalization and quick recovery, its high skin and gastrointestinal side-effects and requiring time monitoring may limit its application (5, 6). Moreover, some cases of complete failure of this medical ap-

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→ What this article adds:
Other scholars used MTX or Actinomycin-D for treating low-risk GTN. Also, some studies addressed using MTX for treating EP, while a few studies investigated the applicability of using Actinomycin-D for treating EP. Evaluating this approach was the main aim of this study. For this purpose, the level of toxicity and the BHCG level were measured. The results of this study showed that the level of toxicity was low and the level of BHCG was reduced fast. The results and the approach have made this study unique.
Successful treatment using Actinomycin D in an ectopic pregnancy

proach have also been reported. Recently, high effectiveness of the single-agent chemotherapy agents, such as Actinomycin D, has been suggested (7, 8). Some studies have even indicated that Actinomycin D could induce remission more than methotrexate (9-14). Herein, a case of methotrexate-resistant EP that was successfully treated with Actinomycin D was described. The new message of this paper is about Actinomycin D for medical treatment of EP. Other scholars used MTX or Actinomycin-D for treating low-risk GTN. Also, some studies addressed using MTX for treating EP, while a few studies investigated the applicability of using Actinomycin-D for treating EP. Evaluating this approach was the main aim of this study, and for this purpose, the level of toxicity and BHCG level were measured.

The results of this study showed that the level of toxicity was low and the level of BHCG was reduced fast. The obtained results and the used approach have made this study unique.

Case report

The case described in this report was a 30-year-old woman (G6AB3EP2) with a history of curettage (2 times) due to invisibility of FHR, one spontaneous abortion and 2 left tubal EP, which were successfully managed by methotrexate administration. The patient was submitted having a delayed menstruation and a BHCG level of 1720 IU/L. Transvaginal sonography revealed an eccentrically located

in the gestational sac at the superior fundal level of the uterus surrounded by 4 mm myometrial tissue and separate empty uterine cavity. EP was finally confirmed. Hence, the patient received a multidose treatment regimen of methotrexate (60mg) and leucovorin (6mg). However, the detection of raising BHCG level to 2210 IU/L and 6800 IU/L 2 and 4 days after initial treatment, respectively, convinced the patient to refer to the hospital due to the failure of drug therapy. Based on the sonography reports on admission, GS was not found in imaging, but an echogenic mass with the dimensions of $26 \times 28$ mm$^2$ was found in the superior fundal level of the right uterine cornea (transitional zone), with a 4.5 mm echo free region suspecting right interstitial EP. At the first day of admission, the patient had a BHCG level of 6800IU/L, which was also revealed by TVS an EL with the diameter of 12 mm and an echogenic lesion sized 26 mm, indicating a right interstitial EP. Due to the lack of response to the standard treatment, pulse treatment regimen was performed again. Methotrexate was started with the dosage of 85 mg one day after admission, and BHCG level was rechecked 4 and 7 days later, which reached to 6946IU/L and 6500IU/L, respectively. One day after methotrexate injection, assessing intrauterine cavity by TVS and MRI (Fig. 1) revealed an intramural heterogenic zone consisting small cystic regions sized $39 \times 38 \times 35$ mm$^3$ at right interstitial region, suggesting interstitial EP surrounded by a narrow band of the myometrium (Fig. 2). A second dose

![Fig. 1. Sagital view of pelvic MRI](image1)

![Fig. 2. Coronal view of pelvic MRI](image2)
was administered on day 7. A partially decreasing trend of βHCG level was noticed a few days after treating with methotrexate (6400IU/L in the 11th day and 6300 IU/L in the 14th day). Finally, considering the inappropriate response to methotrexate and lack of change in the condition of the mass, the patient was treated with intravenous Actinomycin D (2 g). On the day of injection, bleeding and disposing the tissues sized 3 to 4 cm were observed, confirming decidual reaction in pathological assessment. A week after administrating Actinomycin D, the level of βHCG reached to 910 (IU/L). The downward trend of βHCG continued which was less than 4 (IU/L) after 2 weeks. The sonography performed on discharge showed a mass sized 43 ×40 mm with a good general condition, stable hemodynamics, and lack of clinical manifestations such as abdominal pain. βHCG was rechecked 6 months later and was negative.

Conflict of Interests
The authors declare that they have no competing interests.

References