

C. Panayotidis · A Alhuwalia

## Conservative treatment of ectopic pregnancy with methotrexate in a nonoperable patient with Crohn's disease

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**Abstract** We present a case of conservative management using methotrexate for ectopic pregnancy in a nonoperable patient with complicated severe Crohn's disease. This case demonstrates the successful use of methotrexate in an unusual situation in which laparoscopy or laparotomy could have further jeopardised the patient's medical status.

**Keywords** Ectopic pregnancy · Methotrexate · Crohn's disease

### Case study

A 21-year-old nulliparous woman was referred to the emergency department for lower abdominal pain with suspected early pregnancy. She was not taking oral contraceptives, and her menstrual period was delayed by 10 days. She had a positive urine pregnancy test and was referred to the gynaecological department to exclude an ectopic pregnancy. The patient was stable with no vaginal bleeding. She had mild abdominal discomfort but no rebound or tenderness. She reported that she usually had regular heavy periods with primary dysmenorrhoea, and she was known to have a large left dermoid ovarian cyst that was being managed conservatively because of her history of complicated Crohn's disease. Her history of Crohn's disease was longstanding, and she had had four laparotomies (one midline, three transverse incisions). She had an ileocolonic resection with creation of a defunctioning ileostomy and colonic mucus fistula with a future reanastomosis plan. During the previous year her condition had improved, but she continued to complain of persistent chronic abdominal pain.

The woman was admitted to the gynaecological ward for further observation and complementary examinations with ultrasound scanning and beta human chorionic gonadotrophin (bHCG) levels. The transvaginal scan demonstrated a normal-sized uterus and endometrial thickness of 7 mm but no evidence of intrauterine pregnancy. The left ovary was enlarged to 8×9×6 cm, compatible with a dermoid complex cyst. The right adnexa measured 3×2 cm with an additional round image of 1–1.5 cm. Moderate free fluid in the pouch of Douglas was seen. An ectopic pregnancy could not be excluded with these findings, especially when the admission bHCG level was found to be 2,450 IU.

Conservative medical treatment was discussed because laparoscopy or laparotomy could be very difficult and dangerous due to multiple abdominal adhesions caused by the patient's previous surgery. A single intramuscular dose of methotrexate was administered, 50 mg/m<sup>2</sup> body surface. Close monitoring was achieved with serial measures of bHCG levels and clinical examination. Transvaginal ultrasound scanning was attempted 1 week after the methotrexate administration in order to visualise any possible site of the ectopic pregnancy but was unsuccessful. The bHCG levels progressively decreased (day 1: 2,477; day 2: 2,649; day 3: 2,838; day 4: 2,100; day 7: 1,810; day 11: 892; day 14: 396). Negative bHCG levels were achieved on day 27 postinjection. Light per vagina spotting was observed during the 5th day postinjection and mild abdominal discomfort during the first week. The patient started oral contraception and will be reviewed in the gynaecological clinic regularly. In the near future she will be operated on for the intestinal reanastomosis, and ovarian cystectomy will be attempted in order to conserve her left ovary.

C. Panayotidis (✉) · A Alhuwalia  
Department of Gynaecology and Obstetrics,  
South Manchester University Hospitals NHS Trust,  
Wythenshawe, Manchester, UK  
E-mail: costapan@hotmail.com

### Discussion

Ectopic pregnancy is a major emergency in gynaecology. In the United Kingdom, 32,000 ectopic pregnancies are

diagnosed each year, with an incidence in recent years of 11.1/1,000 pregnancies. The use of laparoscopy for diagnosing and treating ectopic pregnancy is the gold standard in current practice according to the guidelines of the Royal College of Obstetricians and Gynaecologists (RCOG) [1]. For this patient, the classical approach with diagnostic laparoscopy was impossible due to the risks of bowel or bladder trauma. Major surgery such as laparotomy could cause deterioration in this woman who had just recently improved her bowel condition and started to gain weight. Examination had to be interpreted carefully in light of her previous surgery, which made ultrasound scanning particularly difficult. Her symptoms were sporadic, with abdominal pain related to her previous surgery or to menstruation. For these reasons, medical treatment using methotrexate was the best initial treatment for this patient.

The use of methotrexate, which is an antimetabolite, antimitotic agent, is well reported, especially for cases of corneal/cervical or isthmic ectopic pregnancies. Cases of nonoperable patients in the very early stages of pregnancy who were treated with methotrexate have not been reported yet. This patient satisfied all the criteria for medical treatment using methotrexate: low initial bHCG level (<2,500 UI), early pregnancy (<6 weeks), no foetal heart seen, clinically stable with no acute abdomen [1].

Prior to injection of methotrexate, the patient must be counselled extensively on the risks, benefits, adverse effects, and possibility of failure of medical therapy, including tubal rupture necessitating surgery. The success rate of the single-dose regimen varies between 71% and 92%. The single-dose regimen is recommended by RCOG guidelines [1]. Failure of medical treatment is defined as occurring when bHCG levels increase, plateau, or fail to decrease by 15% from days 4–7 postinjection. It seems that more symptoms, such as abdominal discomfort or moderate vaginal bleeding, are more likely related to a higher percent-

age of successful treatment. Gastrointestinal side effects of methotrexate may mimic acute abdomen, and clinical examination is mandatory to evaluate treatment failure. The patient may have increased abdominal pain in the first week after methotrexate treatment as well as a transient increase in bHCG titres 1–4 days after treatment, leading to unnecessary anxiety and additional treatment. Multiple-dose regimens may have slightly better results [2] but may have more side effects. The use of oral methotrexate has had promising results, but its efficacy remains to be established [3]. If there is no significant fall in bHCG after 7 days, clinicians should consider and discuss with the patient either repeat methotrexate or surgical treatment. bHCG levels may fall slowly; the median time to resolution is about 1 month. Clinicians should also discuss contraception with the patient and warn about the risk of future ectopic pregnancy.

Single-dose methotrexate therapy is an effective and cost-saving therapy that preserves the fallopian tubes in small, unruptured ectopic pregnancies. Medical treatment is an option for women who do not want to undergo operation, and it is very useful when the surgical approach would potentially be very dangerous for the patient.

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