

Methotrexate in Interstitial Pregnancy: A Miraculous Fertility Rescuer

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ABSTRACT

Introduction: Interstitial (cornual) gestation is the most hazardous type of ectopic, where pregnancy gets implanted in the proximal portion of tube that traverses myometrium. It constitutes 2-4% of all ectopic pregnancies. It poses a significant diagnostic and therapeutic challenge and carries a greater maternal mortality. It usually presents at a later gestation more than 7-12 weeks. The usual clinical presentation is profuse intraabdominal bleeding and shock. Transvaginal sonography can be helpful, but often is not conclusive.

Case report: 21 year old nulliparous lady post laparoscopic left salpingo-oophorectomy, diagnosed to have a live interstitial ectopic pregnancy in left lateral wall of uterus with very high levels of β hCG. She was treated with 2 cycles of folinic acid rescue regime and β hCG monitored accordingly. β hCG showed a decline of 15% initially (2365.9mIU/ml) and weekly β hCG monitored thereafter and reduced to 3.39mIU/ml within 4 months.

Conclusion: Cornual resection/hysterectomy used to be the traditional treatment for these cases. However conservative management has been increasingly practiced successfully including medical treatment with systemic methotrexate and laparoscopic conservative surgery.

Keywords: Ectopic, Interstitial ectopic Pregnancy, Methotrexate, Rescue Regime

supplied with blood vessels. Maternal mortality ranges between 2-25% in the event of rupture³

Interstitial pregnancy traditional has been treated by cornual resection or hysterectomy. This was due to delayed diagnosis. With advancement of trans vaginal sonography and sensitive β hcG assays, Currently it is possible to diagnose interstitial pregnancy at an early gestational age and before rupture occurs. This has opened new avenues for conservative treatment. Methotrexate has been advocated in the treatment of tubal ectopic however its use in interstitial pregnancy is less common.

This is a report of a rare case of unruptured viable interstitial ectopic pregnancy in a nulliparous lady with a history of previous left Salpingo oophorectomy. The case was diagnosed in the 1st trimester by ultrasonography and β hcG measurement. She was managed medically with systemic methotrexate and serial ultrasound monitoring.

CASE REPORT

21 year old G2A1, with a history of previous laparoscopic salpingo oophorectomy for a large benign left ovarian cyst 3 months back, reported to Obstetrics and Gynaecology out patient department for routine antenatal check up.

Her first pregnancy was a spontaneous complete abortion in the first trimester. Now she is 8 weeks amenorrhea with no specific complaints.

On examination she was haemodynamically stable and abdomen was soft and non tender. Trans vaginal ultrasonography was done to assess the viability of pregnancy as a routine which showed the following findings.

1. Uterine cavity was empty with an endometrial thickness of 13mm
2. A single ectopic gestational sac of 2.6x2.5 cm with a live fetal pole noted, outside the endometrial cavity in the interstitial portion of the left fallopian tube with thinning of surrounding myometrium CRL 13 mm
3. Interstitial line visible between endometrial cavity and

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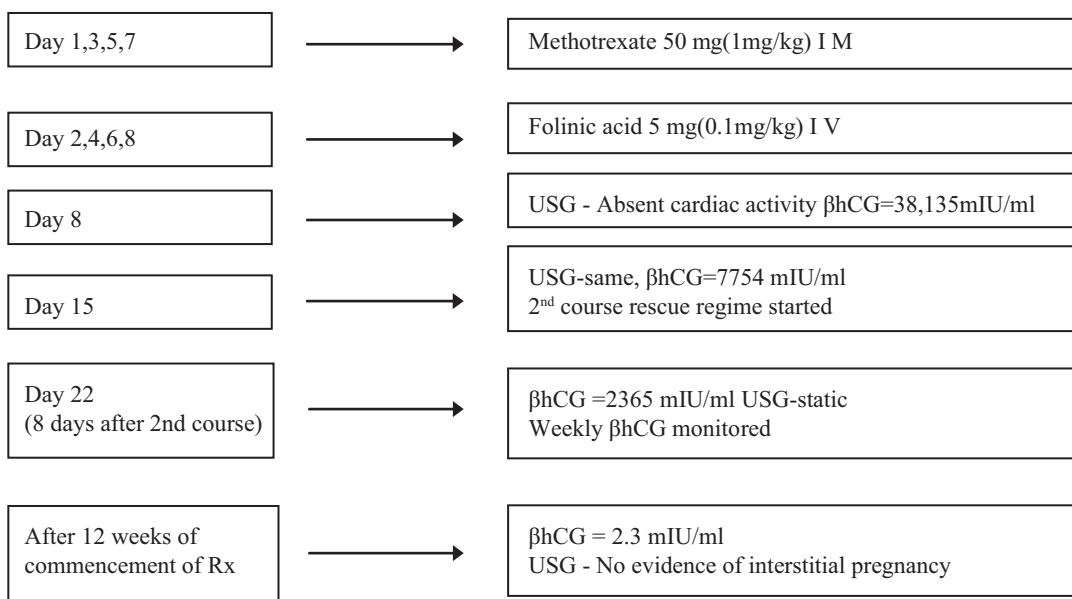
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INTRODUCTION

Ectopic pregnancy continues to be an important issue in the women health even in the new millennium. As women delay their child bearing, due to their professional aspiration, to the later years the need for the use of assisted reproductive technology (ART) is increasing. Unfortunately, ART is associated with higher rates of ectopic pregnancy including interstitial pregnancy. The unique anatomic location of interstitial pregnancy commonly leads to delay in diagnosis. Rupture of uterus occurs in 20% of cases that progress beyond 12 weeks of amenorrhea. Now better methods of early diagnosis of this condition has decreased the morbidity and mortality associated.

Interstitial part of the fallopian tube is the proximal portion embodied within the myometrium. It is approximately 1-2 cm long extending obliquely upwards and outwards from the uterine cavity¹. Pregnancy implanted in this site is called interstitial pregnancy. Here the gestational sac is lateral to the round ligament. The myometrium surrounding allows the gestation to continue and prevents its rupture until 12-16 weeks² The Incidence of interstitial pregnancy is about 2-4% of ectopic pregnancies. In case of rupture, that results in catastrophic haemorrhage because this area is richly



Regimen

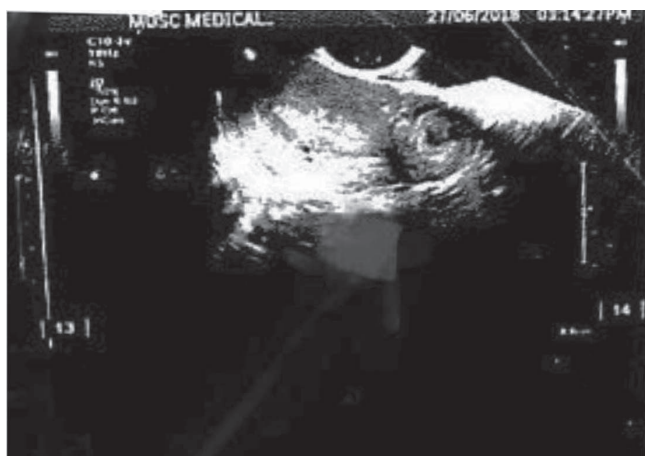


Figure-1:

- gestational sac.
- No free fluid in the abdomen
- So live interstitial pregnancy was diagnosed and she was admitted for further management.

Management

She was asymptomatic with stable vital signs. Her hemoglobin was 12.1 g / dl and β hCG level was 38482 mIU/ml.

In view of the viable interstitial pregnancy and high β hCG level the chance of a successful medical management was less. But she being a nulliparous lady fertility sparing is the determining factor for the treatment of choice. Surgical treatment can result in rupture of uterus in the next pregnancy. So optimum management strategy still remains uncertain and debated. Hence medical treatment with intramuscular methotrexate was discussed and she opted for that. She agreed to stay in the hospital for observation during medical treatment and have surgery only if she developed any signs rupture like pain, deterioration of vital signs or drop in haemoglobin. As it was a live ectopic with a high level of β hCG multiple dose of methotrexate with folinic acid rescue

was selected.

A complete blood count, liver function tests and renal function tests were done before starting methotrexate therapy.

DISCUSSION

The case presented was successfully managed with systemic methotrexate. Use of methotrexate in the treatment of interstitial pregnancy is less common. This case report and many others have confirmed the successful use of methotrexate in treating early interstitial ectopic pregnancy. It can be applied in a regimen of either systemic or local injection or a combination of both.

The most commonly used systemic dosing regimen includes one or two courses of 1 mg /kg/day of methotrexate administered intramuscular or intravenously on day 1,3,5,7 with folinic acid in between and 7 days free of therapy in between courses.

We also followed the same regimen in the management of this case-

The case presented here was successfully managed with systemic methotrexate. This case report and other s have confirmed the successful use of methotrexate in treating early interstitial ectopic pregnancies^{4,5,6,7}. The success in this case confirmed that medical treatment can be used successfully in early interstitial pregnancy even in the presence of detectable fetal heart beats with high serum β hCG levels (38,428 mIU/ml). This is in contrast to other papers suggesting that the presence of fetal heart beat is a contraindication to medical management⁸ The case reported declined surgical treatment and agreed to stay inpatient for the medical treatment until it was safe to discharge her for outpatient monitoring.

Therefore, early clinical diagnosis along with ultrasound may help to manage interstitial pregnancy medically avoiding unnecessary surgical morbidity, blood loss and the need for hysterectomy thereby reducing the maternal mortality and preserving fertility.

Risk factors of interstitial pregnancy⁹

- Previous ipsilateral salpingectomy
- Advanced maternal age
- ART
- Previous Ectopic
- Previous tubal surgeries
- PID, STD
- Others-smoking, intrauterine instrumentation, infertility, tubal sterilization

In this case there was a history of previous ipsilateral salpingectomy

Sonographic features of interstitial pregnancy may include⁹

1. An empty urine cavity
2. An eccentrically located gestational sac usually within the fundal region with laxity of surrounding myometrium.
3. The interstitial line sign is an echogenic line between the ectopic mass and the endometrial lining-highly suggestive.

Management options can range from expectant (rarely successful), conservative management and surgical. Traditionally treatment of interstitial pregnancy has been laparotomy, cornual wedge resection or hysterectomy, which is associated with high morbidity and detrimental effects on future fertility.

Conservative surgery using laparoscopy, hysteroscopy or medical management is appropriately indicated if the patient desires future fertility and the conditions for such management are appropriate in this case.

A diverse array of alternately treatments are introduced with the common goal of achieving a minimally invasive, standardized management strategy such as laparoscopically assisted transcervical suction evacuation, laparoscopy assisted hysteroscopic removal of the sac and intra arterial chemoembolization of uterine artery.

Medical management includes single dose regime, multiple dose regime, and direct intrasac injection of MTX. It is cost effective and avoids risk of morbidities associated with surgery and anaesthesia.

The inclusion criteria for medical treatment are hemodynamic stable patients, unruptured ectopic, β hCG <5000U/L and size of ectopic mass <3.5 cm with normal LFT,RFT and CBC. Complications of medical treatment are treatment failure, rupture, rescue surgery or mortality. Common predictors of treatment failure are gestational sac>3.5 cm, positive of cardiac activity, presence of blood in the peritoneum, high progesterone level, high initial β hCG level.

In this case multiple dose therapy was intended to reduce the time lag of treatment response, follow up, risk of treatment failure, risk of rupture and associated morbidity and mortality. β hCG level and size of ectopic mass can be predictive of failure and rupture. No adverse reaction /complications were noted throughout the course of treatment.

CONCLUSION

Early diagnosis has made the use of medical management possible in interstitial ectopic pregnancy. Prompt diagnosis

and treatment is important to prevent catastrophic haemorrhagic complications. Multiple dose MTX-folinic acid rescue could be successfully used even in patients who did not meet the criteria for medical management in interstitial ectopic pregnancy. More evidence is needed to determine the efficacy and safety of medical management in interstitial pregnancy. However preliminary data appears promising.

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