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ABSTRACT

Background: Cornual ectopic or interstitial pregnancy refers to pregnancy implantation in the intrauterine portion of fallopian tube. Although it is an unusual type of ectopic pregnancy with an estimated rate of 2-4% of other types of ectopic gestation it carries a major risk of maternal morbidity and mortality rate of 2-5% which is the highest rate compared to other types of ectopic pregnancy. Due to its abnormal location there is an inherent difficulty and delay in the diagnosis and treatment. Majority of cases present as acute emergency with life threatening situations. Previously the traditional treatment of cornual pregnancy has been immediate surgical intervention in the form of hysterectomy or cornual resection at laparotomy or laparoscopy. Recently the current trend of treatment has been shifted to conservative medical treatment to minimize the unfavorable effect of surgery on maternal morbidity and future fertility. There are various reports of satisfactory results of conservative medical treatment for cornual pregnancy, but it is still controversial if it is the safest treatment option for the problem.

Materials & methods: This is a case report of a patient who has been diagnosed in Gulf medical hospital Ajman, UAE as a cornual ectopic pregnancy. She was managed conservatively with successful results. A single dose of methotrexate injection of 50 mg /m² was administrated. Patient follows up showing minimal side effects.

Results & conclusion: Cornual pregnancy can be treated successfully with methotrexate injection with minimal side effects. This indicates that methotrexate can be used as an alternative treatment to surgical management to prevent possible risk of surgical intervention.

Keywords: Cornual ectopic, pregnancy, methotrexate
INTRODUCTION

Cornual or interstitial pregnancy refers to a pregnancy that implants in the proximal tubal segment than lies within the muscular uterine wall. Although it is an unusual problem with an estimated rate of 2-4% of all ectopic pregnancies, it carries the major risk of maternal morbidity and mortality rate of 2-2.5% which is the highest compared to other types of ectopic pregnancies. This abnormal location of pregnancy usually occurs following the same risk factors of other types of ectopic gestation specifically in vitro fertilization (IVF) or previous salpingectomy. In the majority of cases, there are no specific risk factors.

According to the report of Confidential Enquiry into Maternal and Child Heath report for 2000-2002, it was concluded that cornual pregnancy is the most dangerous type of ectopic pregnancy. Four out of 11 deaths from ruptured ectopic pregnancy were due to ruptured cornual pregnancy. The diagnosis was late and made only after rupture in all cases.

There is a challenge in the diagnosis and treatment of the problem of cornual ectopic pregnancy. The majority of cases present as acute emergencies with a life-threatening situation. The abnormal location which can be misinterpreted with intrauterine pregnancy leads to delay and difficulty in the diagnosis. Therefore, it is associated with high morbidity and mortality rate. The other hazard of the problem is the risk of uterine rupture due to weakened myometrium wall. And because of the abundant blood supply in cornual area from uterine and ovarian vessels, uterine rupture may lead to massive hemorrhage and even death despite great development in the diagnostic procedures and treatment modalities.

The basic diagnosis in this condition depends on serial quantitative assessment of serum Beta-Human chorionic gonadotrophin (Beta-HCG) and Transvaginal ultrasonography (TVS). The routine use of ultrasound is imperative for rapid and accurate diagnosis to prevent serious complications or death and to enhance the use of more conservative medical management.

1. An empty uterus
2. A gestational sac seen separately and <1 cm from the most lateral edge of the uterine cavity
3. A thin myometrium layer surrounding the sac <5 mm.

Treatment

Previously in the traditional treatment of cornual pregnancy, surgery has been the main option due to avoid uterine rupture and massive bleeding. The main surgical procedures include hysterectomy or cornual resection at laparotomy, laparoscopy or the use of hysteroscopy. Radical surgery was used as a life saving measures in cases of massive bleeding or rupture uterus. Laparoscopic procedure is considered before laparotomy in unruptured cases with the availability of skilled surgeon. Recently there is a change in the clinical practice of management toward the higher use of conservative treatment due to the immediate detrimental effect of surgical intervention with anesthesia in addition to the future effects on fertility.

Medical treatment

A recent development in the management of ectopic pregnancy has been the introduction of medical management which was started on mid 80-ties. The medical methods have focused on the use of methotrexate. The earlier protocol for medical treatment was based on multiple dose regimens of methotrexate and prolonged hospitalization which were associated with significant side effects. Currently these
protocols have been modified to the use of a single –dose regimen with outpatient management11.

**Systemic methotrexate**

Methotrexate, a folic acid antagonist, inhibits DNA synthesis in actively dividing cells including trophoblast. It has a success rate up to 95% if it is used in appropriately selected cases12. The criteria to recommend for methotrexate treatment of ectopic pregnancy are as follows13:

- Hemodynamic stability
- Ability and willingness of the patient to comply with post treatment follow up:
- Initial serum Beta- HCG concentration less than 5000IU/L
- Absence of fetal cardiac activity by ultrasound scanning.

There is evidence for the increased use of methotrexate in the treatment of cornual ectopic pregnancy14. This may be due to the early assessment and accuracy in the diagnosis with the development and availability of high resolution ultrasound and serum B-HCG measurement. In addition to that, there is an extensive increase in the experience of the use of methotrexate in the management of ectopic pregnancy.

Regarding the route of administration of methotrexate, the systemic route of administration was reported to be preferable over the local injection of ectopic gestational sac as it is less invasive and not operator dependent10.

**Methotrexate versus surgical therapy**

Previously the management of ectopic pregnancy was limited to surgery. With growing experience with methotrexate the treatment of selected cases of ectopic pregnancies has been revolutionized. Medical treatment of ectopic pregnancy in selected cases may be considered as the first line therapy over surgical treatment for many reasons mainly related to the prevention of surgical and anesthetic implications with less damage to the tubes and a better chance of preserving fertility after treatment in addition to less cost and hospitalization11.

This presentation is a case report of Cornual ectopic pregnancy with a serum Beta-HCG titer of 8318.5IU/ mL which was successfully treated with a single dose of intramuscular injection of methotrexate injection (50 mg/m²).

**CASE REPORT**

A 37 year – old Jordanian lady, para 3 presented to the outpatient department of Gulf medical Hospital Ajman on 23rdDecember 2014. She attended because of vaginal spotting for the last month. She was on natural contraception and denied a history of missed period. Serum B-HCG level was 8318.5IU/mL. Transvaginal ultrasound showed an empty uterine cavity, polycystic ovaries, and anterior uterine fibroid with cystic lesion in the cornua of a size of 3.5cm (figure 1&2). There was no free fluid in the pelvic cavity. Full blood count showed hemoglobin level of 12.4 and Hematocrit of 35.60%. The clinical examination showed normal vital signs. Abdomino-pelvic examination showed normal size uterus with no palpable adnexal mass or tenderness. There was no guarding or tenderness. The patient was diagnosed as case of cornual ectopic pregnancy. After counseling about the method of treatment the patient was willing for methotrexate injection and refused any surgical intervention. The patient was admitted to the gynecological ward for full monitoring. Full blood count with liver and renal function test were normal. A verbal and written consent were obtained from the patient for methotrexate injection with continuous follow up and surgical intervention if
required after that. As there was no contraindication to methotrexate injection a single injection with dose of (50mg/m²) was administered intramuscularly after complete evaluation. She was advised not to take folic acid until complete resolution of the ectopic pregnancy with avoidance of sexual activities. On the fourth day after methotrexate therapy the patient returned with mild abdominal pain with increasing level of serum Beta-HCG titer to 12320 IU/ml. Clinical examination revealed a stable condition. Repeated transvaginal sonogram did not show free fluid in the pelvic cavity with no change in the size of the ectopic gestational sac. Full blood count showed normal hematological findings. On the seventh day of methotrexate administration serum Beta-HCG titer was dropped to 7000IU/ml. Continuous follow up was done with weekly measurement of the concentration of serum Beta-HCG and transvaginal ultrasound scanning. The level of Beta-HCG titer was decreasing gradually and continuously in each week to be 250IU/ml on 17th February 2015. The patient did not attend for follow up until the last visit on 26th April 2015. She had no complaint with a stable condition and serum concentration of BetaHCG titer was< 5.00IU/ml. The findings of transvaginal ultrasound revealed degenerated and reduced diameter of the mass to 0.7cm on the left cornua.

![Image 1](image1.png)  ![Image 2](image2.png)

**FIGURE 1**  **FIGURE 2**

**DISCUSSION**

While all ectopic pregnancies are associated with a risk of hemorrhage, interstitial pregnancies are associated with highest risk of massive uncontrollable bleeding with a mortality rate of 2%.\(^{15}\) This high mortality rate is partially due to the difficulty and delay in the diagnosis as well as the speed of hemorrhage. The condition may be misinterpreted with normal intrauterine pregnancy and associated with delay in diagnosis. Previously most cases were diagnosed at the time of laparotomy with rupture. Because of the late diagnosis surgery was the most common management option. In spite of the higher rate of maternal morbidity and future implications on fertility there was no role for expectant management due to the high risk of rupture and massive hemorrhage.\(^{16}\)

In the present case, there were no specific symptoms apart from minimal vaginal bleeding. This may be usual in early cases of ectopic pregnancy. There is an increasing evidence of asymptomatic cases with ectopic pregnancies without the usual presentation of lower abdominal pain and vaginal bleeding.\(^{16}\)

For our patient, the diagnosis was mainly based on the results of transvaginal ultrasound scanning and serial quantitative assessment of serum B HCG concentration. Transvaginal ultrasound scanning is considered as basic diagnostic
facility to the early diagnosis of cornual pregnancy. The ultrasonography diagnosis is challenging and needs expert hands. The diagnosis may be helped by the eccentric position of the gestational sac with an empty uterine cavity and the presence of a thin (less than 5mm) or even absent myometrium surrounding the sac are highly suggestive of cornual ectopic pregnancy. The accuracy of diagnosis may be improved with the use of Doppler studies showing increase vasculature around the gestational sac. The gestational sac is usually visualized away from the thickened endometrium of pregnancy. In experienced hands, the diagnosis of cornual pregnancy can be established in 71% of the cases with use of tranvaginal ultrasound. The sensitivity of the diagnosis has been improved with the use of 3-D and 4 –D ultrasound scanning.

In addition to sonographic assessment serial serum monitoring was useful in establishing the diagnosis and monitoring in this patient although there are reports of doubling serum Beta-HCG in cornual ectopic pregnancy. It is contrary to the other types of ectopic pregnancies which is known to be associated with inconsistent and suboptimal increase or plateau of serum Beta-HCG. Therefore, caution is highly recommended with interpretation of the results in addition to the extended and prolonged follow up as the hormone concentration will take a longer time to return to the normal level with cornual pregnancy.

In the management of this patient the medical management was considered as the option of choice as the criteria were suitable to select this method in addition to the strong patient refusal for surgical management. The only controversy in the selection of the patient may be related to the high level of serum Beta HCG titer (8318.5IU/ml) at the time of presentation. The Royal college guideline has recommended that patient is suitable for medical treatment. If the serum Beta-HCG titer is < 3000 IU. However, there are previous reports of cases being treated successfully with methotrexate in spite of the higher level of serum B-HCG. Jermy K et al suggested that when the initial serum Beta HCG is greater than 5000 IU second systemic dose of methotrexate is more likely to be required for a successful outcome conversely the initial serum Beta HCG titer in our patient was higher and treated with single injection without the need for surgical intervention or repeated doses. In our case the level of serum BHCG concentration was near to the level of (8096IU/ml) reported by Goruk et al on 2012 for a patient who was also treated successfully with a single dose of methotrexate. However, there are previous reports stating that the best predicton of success of medical therapy is the initial Beta-HCG level. Based on Lipscomb et al efficacy studies it was reported that the success rate was 94% for a single injection of methotrexate when the initial level of serum B-HG level is less than 10,000 mIU/ml, and 93% when the level is less than 15000 mIU/ml. There is no clear data regarding the effects of ectopic size, but the larger the ectopic it is more likely that the treatment fails.

In spite of the reported increase in the percentage of patients treated with single dose of methotrexate, failure rate is high and has been reported in 15% of cases who required additional doses or surgical therapy. So careful counseling of the patient is required with close monitoring as rupture is possible even after the treatment. The patient should be informed for strict and extended follow up.

With regard to the future fertility, the patient with cornual pregnancy should be informed that likelihood of recurrence in subsequent pregnancies is higher compared with other types of ectopic pregnancy. If the uterus is conserved, there is an increasing incidence of uterine rupture in future pregnancies. However, the data about the absolute increase in such risks is still conflicting.

In consideration to the optimum mode of delivery in subsequent pregnancy, cesarean section is advised by many clinicians. However it is still controversial about the safety of cesarean section versus vaginal delivery after cornual ectopic treatment.
In conclusion cornual pregnancy is associated with significant diagnostic challenge and carries a higher rate of maternal morbidity and mortality than tubal pregnancy. With the availability of high resolution ultrasound with rapid accurate estimation of serum BHCG early diagnosis can be established. Strict follow up of the specific diagnostic criteria of transvaginal ultrasound can improve the accuracy of diagnosis. With early diagnosis, for properly selected patients conservative management should be considered as an initial treatment. Single dose of methotrexate with close monitoring and follow up is effective and safe option. It can be utilized as an alternative to surgical intervention with its associated complications.

REFERENCES


