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Case Report

## A case of hybrid medical management of advanced cornual ectopic pregnancy

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### ABSTRACT

Cornual ectopic pregnancy is perilous and treacherous entity which accounts for 2-4% of all ectopic pregnancies and has a maternal mortality of 2-2.5%. There is always a dilemma in diagnosis due to the area being in close proximity to the endometrial cavity. The precise localisation is difficult till the gestation is advanced, which poses problems in its subsequent management. Surgical approach in this highly vascular area leads to excessive bleeding is a daunting nightmare for a surgeon and also imposes a great threat to the future fertility of the patient. Here we present a case of 26 year old spontaneously conceived primigravida who presented for booking visit at 10 week period of gestation. On transvaginal sonography, there was a suspicion of right cornual ectopic pregnancy which was later confirmed on magnetic resonance imaging (MRI). Despite due to advanced viable gestation, with an evident cardiac activity and very high serum  $\beta$ -human chorionic gonadotropin ( $\beta$ hCG) (more than 1 lakh mIU/ml), we tried a pioneering technique of conservative hybrid approach with intracavitary instillation and systemic antimetabolite drug methotrexate, in view to safeguard her future fertility by diminishing the likelihood of hysterectomy. While on the treatment, patient developed hyper reaction to methotrexate, which was managed with a multidisciplinary approach. She responded very well to the therapy with complete resolution of the cornual ectopic pregnancy.

**Keywords:** Cornual ectopic pregnancy,  $\beta$ hCG, Methotrexate, Hybrid approach

### INTRODUCTION

Pregnancy implantation in the intrauterine portion of fallopian tube is known as cornual ectopic or interstitial ectopic pregnancy.<sup>1</sup> These cases may rupture with massive haemorrhage and present as medical emergency necessitating immediate surgical intervention. However, few patients may be asymptomatic and managed conservatively.

Here authors present a case of 26 year old spontaneously conceived primigravida who presented at 10 weeks period of gestation for routine antenatal check-up and was incidentally detected to have the pregnancy located in the right cornu. Keeping the prospects of her future fertility we tried a hybrid approach with methotrexate. The elaborated

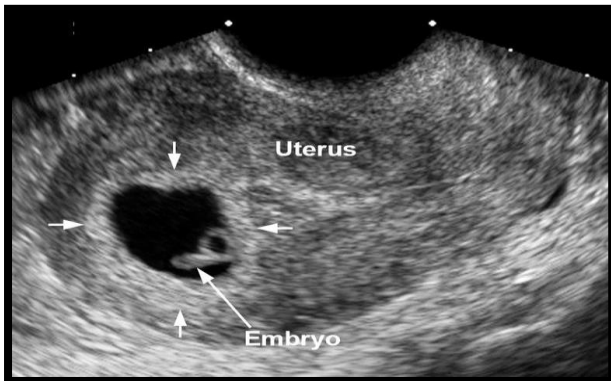
case report along with its review of literature is presented in subsequent paragraphs below.

### CASE REPORT

26 years old primigravida, spontaneously conceived, presented for routine antenatal checkup, with history of amenorrhea of 2 and a half months. There was no history of pain abdomen, bleeding per vaginum, any use of contraception or tubal surgery. No history of assisted reproductive technology (ART) procedures or no history of tuberculosis (TB) in past was elicited.

On examination at our centre, she had body mass index (BMI) of 19.5 kg/m<sup>2</sup>. Respiratory system, central nervous system and cardiovascular system examination were

essentially normal. Abdomen was soft and non-tender. On transvaginal sonography, a viable pregnancy of 10 weeks 6 days with fetal cardiac activity was seen near right cornu, as evident in Figure 1.

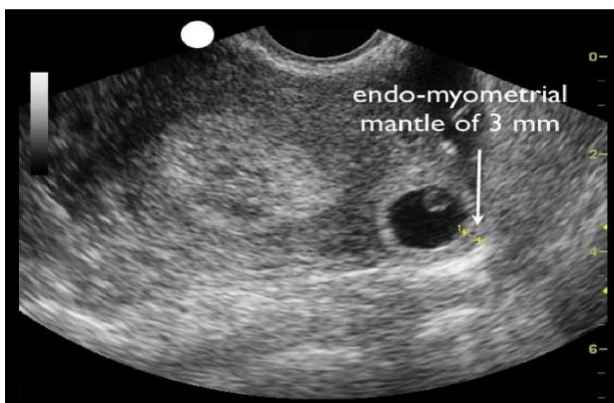


**Figure 1: On transvaginal sonography, a viable pregnancy 10wks 6days with fetal cardiac activity was seen near right cornu.**

In the Figure 2, ultrasonography revealed empty uterine cavity with an eccentrically located pregnancy in right cornu.

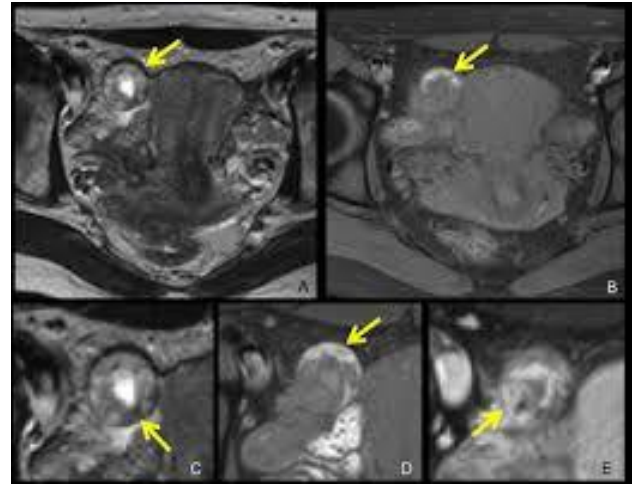


**Figure 2: Ultrasonography revealed empty uterine cavity with an eccentrically located pregnancy in right cornu.**



**Figure 3: A thin myometrial layer (<5 mm) around the gestation sac.**

For further confirmation, magnetic resonance imaging (MRI) was done which confirmed an eccentrically located heterogeneous mass, suggestive of gestational sac, along with abnormal thinning of myometrial mantle and a prominent interstitial line sign seen clearly in Figure 4 below.



**Figure 4: MRI showing an eccentrically located heterogenous mass, suggestive of gestational sac, alongwith abnormal thinning of myometrial mantle and a prominent interstitial line sign seen.**

The baseline serum  $\beta$ hCG was 1,41,480 mIU/ml. Her initial haematological and biochemical parameters were within normal limits. Despite her advanced viable gestation and high serum  $\beta$ hCG, decision was taken for hybrid management with intracavitary and systemic methotrexate therapy, keeping in mind about her future fertility preservation and after elaborated counseling and obtaining due consent from the patient. Further progress of the treatment and follow up was done with serial serum  $\beta$ hCG monitoring and transvaginal sonography.

On initial day of therapy, USG guided embryo reduction was done by instillation of 0.1 ml intracardiac injection of potassium chloride. The cessation of fetal cardiac activity was confirmed by ultrasound. In view of the fact that the levels of  $\beta$ hCG were lofty, injection methotrexate 50 mg was also injected into the gestational sac in the same sitting.

Owing to the increased levels of  $\beta$ hCG, accordance was taken to compliment the systemic methotrexate alternating with leucovorin as per multidose regime for management of ectopic pregnancy. Following the initial two doses of intravenous methotrexate (50 mg each) on day 1 and day 3, patient developed signs of hyper reaction to methotrexate in form of ulcerative stomatitis and macular rash. Decision to stop further doses of methotrexate was taken. The serum methotrexate levels after 72 hours of the last dose were 1.5  $\mu$ mol/l which was marginally raised from the normal value. Subsequently, patient developed pancytopenia and elevated levels of transaminases. Strict

barrier nursing protocol was initiated. The toxicity was managed with intravenous leucovorin under the antibiotic cover. Pancytopenia was corrected with granulocyte colony-stimulating factor (G-CSF).

By day 7, the serum  $\beta$ hCG was 83,337 mIU/ml and transvaginal sonography showed a reducing sac and patient improved symptomatically. Serum methotrexate levels done on day 9 were 0.215  $\mu$ mol/l. The serum  $\beta$ hCG on day 9 was 31,446 mIU/ml and subsequently on day 13, it was 8190 mIU/ml.

On day 17, patient was asymptomatic with all haematological and parameters within normal limits. The serum  $\beta$ hCG was 1732 mIU/ml and TVS suggested complete resorption of the cornual ectopic pregnancy. The patient was discharged with weekly follow up of serum  $\beta$ hCG till it came below the reference value.

## DISCUSSION

Cornual ectopic pregnancies are rare but pose difficulty in diagnosis till the gestation is advanced. Transvaginal sonography is the preferred modality in diagnosis. The diagnosis is difficult till the gestation is advanced as the area is very close to endometrial cavity. Hence MRI may be needed for confirmation.

With advent of assisted reproductive techniques, incidence of ectopic pregnancy is on the rise. Despite the widespread use of transvaginal sonography and serum  $\beta$ hCG assays, their diagnosis gets delayed, since this part of the tube has good muscular and vascular support which results in greater distensibility and thus causes less pain.<sup>2</sup> Due to abundant blood supply in cornual region from both uterine and ovarian vessels, rupture occurring after 12 weeks of gestation often leads to severe haemorrhage and eventually maternal death.<sup>11</sup>

Interstitial pregnancy is usually diagnosed by ultrasonography and many cases during laparotomy after rupture of ectopic pregnancy. The sonographic criteria for diagnosis include empty uterine cavity, chorionic sac separated <1 cm from most lateral edge of uterine cavity, and thin myometrial layer (<5 mm) surrounding the sac.<sup>1</sup> Sonographic findings in two dimensions can be further confirmed using three-dimensional ultrasound, where available, to avoid misdiagnosis with early intrauterine or angular pregnancy.<sup>12</sup>

Ackerman et al described the interstitial line sign, which refers to the visualization of an echogenic line that runs from the endometrial cavity to the interstitial region, abutting the interstitial mass or gestational sac.<sup>13</sup>

Conventionally, methotrexate is administered if the patient meets following criteria: when patient is haemodynamically stable, no embryonic cardiac activity, gestational sac diameter <3.5 cm<sup>2</sup>,  $\beta$ hCG levels <5000 IU/ml, and in a tertiary care centre where emergency

laparotomy can be undertaken.<sup>4</sup> An randomized controlled trials (RCT) comparing methotrexate with laparoscopic salpingostomy surgery for tubal ectopics showed that methotrexate is equally successful to salpingostomy in terms of requirement for further treatment.<sup>14</sup>

In the literature, successful treatment of cornual pregnancy with just a single dose of methotrexate has been reported.<sup>15,16</sup> Medical treatment with a single methotrexate injection has been recommended. However, it is associated with significantly increased risk of failure, subsequent uterine rupture and emergency surgery.<sup>16</sup> Kim et al.<sup>17</sup> mentions a patient with  $\beta$ hCG level of 1,02,970 mIU/ml who was successfully treated by systemic methotrexate (MTX). Another patient in the same study with a  $\beta$ hCG level of 59,090 mIU/ml was treated by local MTX with a successful outcome.

Early diagnosis allows a varied choice of treatment options with high possibility of preserving fertility.<sup>3</sup> In a haemodynamically stable patient, conservative management by local methotrexate or potassium chloride or systemic methotrexate is well established. Late first trimester or early second trimester rupture leading to catastrophic haemorrhage is common in interstitial pregnancies. They are managed surgically by cornual resection or hysterectomy.<sup>3</sup>

## CONCLUSION

Cornual ectopic pregnancy is an uncommon variant and is a diagnostic and therapeutic challenge to clinician. The choice of treatment is largely dictated by clinical situation. Due to advanced gestation at the time of diagnosis, increased vascularity and anatomical difficulties cornual resection or hysterectomy was traditional approach. But keeping in view the present case, conservative approach is successful. Advanced cornual ectopic pregnancy could be managed successfully with hybrid MTX therapy to preserve fertility of the patient.

This particular case was neither meeting the conventional criteria for a medical management nor posed an emergent situation to operate. This case is a solitary one in literature, with such towering levels of  $\beta$ hCG (1,41,480 mIU/ml), to be managed conservatively with MTX, resulting in a successful outcome. We could face the challenge sitting at a tertiary care centre with operational readiness round the clock.

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