

Heterotopic pregnancy after a spontaneous conception A case report with a review of clinical, laboratory, and imaging findings

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Abstract

Heterotopic pregnancy (HP) describes the simultaneous presence of two pregnancies at different implantation sites. One is intrauterine and the other is ectopic. It is challenging to diagnose HP. We present a very rare case of HP diagnosed in the first trimester by US and MRI and managed successfully.

Introduction

Heterotopic (also called heterotrophic) pregnancy is the simultaneous occurrence of two pregnancies in two different implantation sites. Most of the time one of the pregnancies is intrauterine and the other is an ectopic pregnancy. HP is estimated to occur in 1 every 3900 pregnancies after assisted reproductive technologies (ART) and reaching up to 1.5 in every 1000 pregnancies¹. In some studies, their reported incidence is as high as 1 in every 100 pregnancies after ART^{2,3,4}. Although the true incidence after ART is difficult to confirm, it is postulated that such an increased incidence in these patients after ART, is related to previous tubal pathology, multiple ovulations or multiple embryo transfers².

Following a spontaneous pregnancy, however, the incidence of HP is rare. In a large review of the world's literature on combined intrauterine and extrauterine pregnancies, the reported incidence was 1 every 30,000 pregnancies⁴. Spontaneous HP - in particular - poses a real challenge for healthcare professionals not only in treatment but in diagnosis. This is due to multiple factors, partly due to their rarity and unexpected occurrence. Ectopic pregnancies per se pose a diagnostic challenge on their own accord. HP will pose an even more diagnostic uncertainty; as seeing an intrauterine gestational sac may give false reassurance and B-human Chorionic gonadotrophins (β -hCG) serial measurements may not be useful due to the presence of two pregnancies in different locations⁵.

In our article, we present a case of spontaneous conception resulting in a HP. We review the diagnostic features, imaging, and management.

Case presentation

A 38-year-old gravida 5 para 4 woman presented with an increasing lower abdominal pain for 5 days, brownish vaginal discharge, nausea, and episodes of vomiting. This was a spontaneous conception. Apart from some tenderness in both adnexa, the abdominal and vaginal examination was unremarkable. Laboratory investigations revealed a serum β -hCG of 169,863 mIU/mL. Transvaginal ultrasound was performed using an endocavitary 5–9 MHz transducer. Grayscale ultrasound confirmed by color dopplers revealed a viable intrauterine pregnancy of 9 weeks and 5 days and a heterogeneous complex left adnexal mass suggestive of being a HP. The ovaries were unremarkable, and a small pelvic fluid collection was also seen. Doppler ultrasound of the described mass revealed a 'ring of fire' sign (Figure 1).

MRI imaging was done using a 1.5 T device (Siemens, Germany). A phased-array surface coil was centered over the abdomen to the symphysis pubis. Images were acquired from the level of the hepatic hilum to the symphysis pubis. The sequences included the turbo spin-echo (TSE) technique, gradient-echo (FLASH), and T1 and T2 weighting to obtain axial and coronal images. No contrast was given.

MRI study revealed a left adnexal rounded mass lesion (56 x 35 x 46 mm) intimately anterior to the normal left ovary, displaying a mixed hyper- and hypo-intense signal at T1 and T2 WI. It had a thick wall showing a high T2 signal (Figures 2-4).

The patient was taken to the operating theatre after careful counseling and informed consent. Under general anesthesia, a laparoscopy was performed which revealed a distended left fallopian tube. The other (right) tube and both ovaries were unremarkable. A left salpingectomy was performed, and this was sent for histopathological assessment. The postoperative course was uneventful, and the patient was discharged home after confirming the viability of the intrauterine pregnancy.

Histopathological examination of the specimen showed a dilated congested segment of the left fallopian tube while microscopic examination revealed fragments of a blood clot, decidual tissue, and chorionic villi with trophoblasts noted within the dilated fallopian tube consistent with a tubal ectopic pregnancy.

Discussion

Ectopic pregnancy can be a life-threatening condition and still remains a cause of up to 4.9 % of all maternal deaths in developed countries with almost 80% of all maternal deaths occurring during the first trimester of pregnancy ^{6,7,8}.

Ectopic pregnancies pose an increased diagnostic challenge and to an even greater extent. It is possible that due to the low index of suspicion in spontaneous HP with the false reassurance of the presence of an intrauterine pregnancy, the diagnosis can be delayed and a good number of women will thus present with serious clinical presentations as tubal rupture, acute abdomen, shock and hemoperitoneum ⁵.

In HP, the clinical picture may not be significant in asymptomatic patients, and seeing an intrauterine pregnancy by ultrasound may lower the vigilance of looking into the adnexa for another gestational sac or 'thinking ectopic'. A presentation of vaginal spotting or lower abdominal or adnexal pain and tenderness may be attributed erroneously to a threatened miscarriage especially with a low index of suspicion after seeing an intrauterine pregnancy ⁹.

In a review of the world literature on 589 combined intrauterine and extrauterine pregnancies, a combination of signs and symptoms including abdominal pain, peritoneal irritation and enlarged uterus were the most significant findings, with the pelvic inflammatory disease a significant risk factor ⁴. The early diagnosis of an ectopic pregnancy is possible due to a combination of ultrasound and serum measurements β -hCG. A doubling time of serum β -hCG of 66% was initially used in the early 80s ¹⁰. Following that a doubling time of 53% ¹¹ and more recently 35% or more, over a 2 day period, was suggested ¹². A doubling time of more than 35% over a period of 2 days suggests the diagnosis of a viable intrauterine pregnancy, thus excluding an ectopic pregnancy in many (not all) cases. Another concept in the early diagnosis of ectopic pregnancies is the discriminatory zone. Seeing an intrauterine pregnancy by transvaginal ultrasound should be possible with a serum β -hCG level of 1500-2000 iu/ml ¹³, or more recently a conservative level 3500 iu/ml was suggested ¹⁴. Above that level, nearly all viable intrauterine pregnancies should be visualized using transvaginal ultrasound. Failing to see an intrauterine pregnancy at such a level would raise the probability of an ectopic pregnancy.

Unfortunately, in HP pregnancies, both concepts; the doubling time and discriminatory zones, commonly used in early diagnosis of ectopic pregnancy, are unlikely to be helpful, thus posing an increased risk of misdiagnosis, with a third to half of HP cases thus presenting late and already ruptured before a diagnosis was made ^{5,15}. The level of serum β -hCG in HP represents the combined contribution of both the intrauterine (mainly) and extrauterine pregnancy. These confusing levels are unlikely to be of clinical use for the diagnosis of a HP.

Visualizing both an intrauterine and extrauterine gestational sac, yolk sac, fetal pole, or fetal heart activity is understandably diagnostic of a HP. Unfortunately visualizing both intrauterine and extrauterine fetal heart activity is rare ⁹.

To add to the diagnostic challenge, an HP can be misdiagnosed as a corpus luteum cyst with the low vigilance of having already confirmed an intrauterine pregnancy. When seeing what could be a corpus luteum in the adnexa using greyscale ultrasound, a Doppler ultrasound can be very useful in such cases, and determining the location of blood flow and ‘ring of fire’ sign, can improve the sensitivity of diagnosing an ectopic pregnancy over a corpus luteum cyst ¹⁶. This is what we performed in our case and seeing a ‘ring of fire’ sign on Doppler ultrasound, raised our suspicion towards the presence of a HP.

Although ultrasound remains the main imaging modality in ectopic and HP pregnancies, a subset of patients may need further imaging to provide additional information. These patients are a minority who for example need a precise diagnosis where the required information could not be obtained by ultrasound. This further imaging can be undertaken using MRI, which can provide images with high soft-tissue contrast without the use of intravenous contrast agents.

In a review of 1737 patients exposed to first trimester MRI exposure, as compared with non-exposure, was not associated with increased risk of harm to the fetus or in early childhood of up to 4 years of age, this includes the risk of stillbirth or neonatal death within 28 days of birth and any congenital anomaly, neoplasm, and hearing or vision loss from birth to age 4 years. In contrast, Gadolinium MRI at any time during pregnancy was associated with an increased risk of a broad set of rheumatological, inflammatory, or infiltrative skin conditions and for stillbirth or neonatal death ¹⁷.

Ultrasound remains the imaging modality of choice in pregnancy. MRI – in selected patients where a diagnosis cannot be made by ultrasound – has another advantage due to its excellent soft-tissue contrast without the use of ionizing radiation. We found it useful to review the findings suggestive of ectopic pregnancy on MRI and we feel it is important we are familiar with them. Findings on MRI include tubal dilation and wall enhancement, tubal hematoma, adnexal hematoma, and a gestational sac-like structure¹⁸. In our patient, an MRI revealed an adnexal rounded mass lesion with a thick wall showing a high T2 signal.

It should be emphasized that despite the evidence of reported safety of MRI, and the ability to gain valuable information without the resort to intravenous contrast agents as Gadolinium, a conservative approach should still be adopted, and MRI should only be used in very selected cases and ultrasound remains the main imaging modality in pregnant women with suspected HP or ectopic pregnancy.

Any treatment for HP should aim to target the ectopic pregnancy, selectively, without harmful effects on the ongoing intrauterine pregnancy.

With this in mind, systemic methotrexate is contraindicated with a viable intrauterine pregnancy ¹⁹ and local treatment modalities have thus been suggested to avoid the use of systemic agents in HP, as local injection of potassium chloride ²⁰ or hyperosmolar glucose in the ectopic pregnancy in the tube. Local injection of 50% glucose after aspiration of the tubal gestational sac fluid under transvaginal ultrasonographic guidance seemed effective in resolving the ectopic pregnancy without adversely affecting the concurrent intrauterine pregnancy ²¹.

Although local injections of these agents avoid surgery – at least initially – the risk of failure of such treatments and subsequent surgery and salpingectomy is high, reaching 55%, making them not an attractive or advisable modality in the context of HP with the other pregnancy in the tube ²². These modalities, however, may have a place in ectopic pregnancies with no concomitant intrauterine pregnancy, scar pregnancies, or in HP where the extrauterine sac is in an unusual location for example cervical or cornual²³.

Realistic and practical approaches in HP with one of the pregnancies in the tube are performing a laparoscopy (preferred option) or laparotomy (depending on the clinical condition and expertise) and undertaking a salpingectomy (usually if the other tube is normal) or salpingotomy¹⁹. Another advantage of the surgical

approach is that laparoscopy (or laparotomy) can confirm the diagnosis in addition to providing a definitive treatment.

We do however feel that although salpingotomy for a ‘sole’ ectopic pregnancy (without concurrent intrauterine pregnancy) is an established modality in selected cases especially with a damaged contralateral tube, a salpingotomy in cases of HP is not similar for two reasons.

Firstly, there is a risk of around 21% of a repeat operation via salpingectomy due to persistent tubal bleeding²⁴ and this risk should not be taken lightly in a woman with HP and ongoing remaining intrauterine pregnancy already subjected to a salpingotomy.

A second reason is that, as opposed to a radical surgery as a salpingectomy, a salpingotomy carries the additional risk of persistent trophoblasts of around 7%²⁵ which cannot be followed up by β -hCG due to the concurrent intrauterine pregnancy nor treated with systemic methotrexate for the same reason.

We thus feel it is thus appropriate to perform a salpingectomy rather than a salpingotomy in most HP cases when dealing with the tubal element of pregnancy as it minimizes the risks at, and after the procedure, that is inherently associated with salpingotomy.

Conclusions

Heterotopic pregnancy is a very rare condition that requires a high index of clinical suspicion that may occasionally face health care professionals in obstetrics, gynecology and emergency departments. It is even less common after a spontaneous conception. Although a high index of suspicion for ectopic pregnancy is part and parcel of the clinical practice, yet the guard can at times lower when seeing an intrauterine pregnancy with many cases of heterotopic pregnancy misdiagnosed and a good number only discovered at later stages after rupture of the ectopic arm of heterotopic pregnancy. We believe that cases like this one can play a small part to help keep that vigilance. Ultrasound remains the imaging modality of choice in diagnosing a heterotopic pregnancy, however, in carefully selected cases, an MRI with a reported safety in the first trimester can be utilized and may provide added information over ultrasound. Salpingectomy rather than salpingotomy via laparoscopy should be the treatment of choice in most heterotopic pregnancies with the extrauterine pregnancy in the tube.

Abbreviations

HP; Heterotopic pregnancy

US; Ultrasound

MRI ; Magnetic resonance imaging

ART; Assisted reproductive technologies

β - η [^]T**** ; Beta Human chorionic gonadotropin

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Conflict of interest

None declared.

Authors Contributions

Dr. Ahmed H. Abdelmonem and Dr. Gamal Sayed wrote and edited the manuscript. Dr. Reda Youssef wrote and edited the radiological part of the manuscript. Dr Abd Elwahid Abugazia and Dr. Samah Kohla reviewed and edited the manuscript.

Ethics approval

The case report was approved by the Medical Research Centre at Hamad Medical Corporation, Qatar, and the Clinical Imaging Research Committee (CIRC).

Declaration

This manuscript is original work and has not been submitted or is not under consideration for publication elsewhere. All the authors have reviewed the manuscript and approved it before submission. Name of Department and Institution where work was done: Department of Radiology, Women’s Wellness and Research Center, Hamad Medical Corporation, Doha, Qatar.

Consent for Publication

written informed consent of patient information, images and publication was signed by the patient before the submission of the manuscript.

Data availability statement

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Figure Legends

Fig. 1: TVU: Intrauterine and ectopic pregnancy with an intraperitoneal fluid collection.

Fig. 2: T2 Haste, axial and coronal, revealed left tubal ectopic pregnancy seen as a sac-like lesion with thick wall measures 56 x 35 x 46 mm contains fetus with crown-rump length 27 mm and intrauterine pregnancy with same crown-rump length.

Fig. 3: Axial T1 WI, Subchorionic hematoma as high signals.

Fig. 4: MRI T2 WI. Shows hemoperitoneum (clotted blood) as intermediate signals anterior and superior to the uterus.



