

The Challenge in Diagnosing and Managing Heterotopic Interstitial Pregnancy in Natural Conception

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ABSTRACT

Heterotopic interstitial pregnancy in natural conception is very rare. Definitive diagnosis is made by systematic pelvic ultrasound. Simultaneous viable conception observed in both intra- and extra-uterine is pathognomonic of heterotopic interstitial pregnancy. We report a 34-year-old woman primigravida at 10 weeks' amenorrhoea who underwent evacuation of retained product of conception for missed miscarriage. Intraoperatively, minimal product of conception was retrieved. Bedside pelvic ultrasound showed cystic mass at right superolateral part of uterine fundus suspicious of interstitial pregnancy. Cornual resection was performed via laparotomy. Histopathological examination showed presence of product of conception and interstitial pregnancy. Serum β -human chorionic gonadotropin dropped from 10,027 IU/l on day one post-ERPC to 210 IU/l at day three post-cornual resection. This case report highlighted the challenge in diagnosing heterotopic interstitial pregnancy conceived naturally. Timely diagnosis may avert dire consequences of massive haemorrhage from ruptured uterine cornua.

KEYWORDS: Heterotopic interstitial pregnancy; pelvic ultrasound; pelvic magnetic resonance imaging (MRI); cornual resection

INTRODUCTION

Heterotopic interstitial pregnancy (HIP) is a diagnosis made when both intrauterine and extrauterine interstitial pregnancy coexist [1]. Heterotopic pregnancy incidence is one in 30,000 naturally conceived pregnancies [2]. With interstitial pregnancy occurrence between 2.4 to 4% of all ectopic pregnancies, the incidence of HIP is said to be exceedingly rare [3-5]. On the other hand, HIP occurs in 80 – 92% of the time following artificial reproductive technology [6, 7].

The consequences of missing the diagnosis of HIP can be disastrous. Maternal mortality associated with interstitial pregnancy ranges from 2 – 2.5% [8]. About 4.8% women died at less than 24 weeks' gestation as a direct consequence of ectopic pregnancy as reported in Mothers and Babies: Reducing Risk through Audits and Confidential Enquiries across the UK (MBRRACE-UK) report 2016 [9]. The maternal death occurs as a result of massive haemorrhage due to

ruptured intramyometrial arcuate vasculature that supply the cornua of uterus occupied by the late diagnosed interstitial pregnancy [4, 9].

Fifty percent of HIP cases have no apparent risk factors, making it difficult to suspect the diagnosis in natural conception based of background risk on its own [5]. In pregnancies conceived via in-vitro fertilisation, background history of previous uni- or bilateral salpingectomy is a significant risk factor that is evident in about 40% of HIP diagnosed in such setting [6]. The use of large embryo transfer medium, relaxed uterus from suprphysiological presence of progesterone released by multiple corpus lutea [10], together with multiple embryo transfer or presence of tubal infertility contribute to the increased risk of HIP in pregnancy conceived via artificial reproductive technology [6].

A third of patients with HIP have no symptom at diagnosis, with remaining 29 – 68% of patients having per vaginal bleeding and/or abdominal pain [7,



11]. In the analysis of 55 cases diagnosed as heterotopic pregnancy, the symptoms of abdominal pain and/or per vaginal bleeding was observed to appear before day 27 post-embryo transfer in in-vitro fertilisation in 83% of the patient, with onset of symptoms detected the earliest at 5.8 weeks' gestation [11]. Subsequent analysis showed a gap of 0.5 weeks between the gestation at the appearance of the symptoms and the gestation at diagnosis of the heterotopic pregnancy [11].

The diagnosis of HIP is established between six to 14 weeks of gestation [11, 12]. Late diagnosis of HIP at 26 weeks' gestation has been reported in which the pregnancy was mistakenly labelled as dichorionic diamniotic twin at 12 weeks of gestation, only to be diagnosed as HIP as the concomitant interstitial pregnancy spontaneously ruptured [13]. The wide variation of timing at diagnosis of HIP can be ascribed to the fact that myometrium surrounding the interstitial pregnancy has greater distensibility, with abundance of blood supply from collateral of ovarian and uterine arteries, giving the interstitial pregnancy the opportunity to thrive longer than the more common tubal ectopic [8].

Routine ultrasound assessment in early pregnancy may not reveal the extrauterine pregnancy in the presence of intrauterine pregnancy [8]. The intrauterine pregnancy diverts the clinician's attention from looking for the extrauterine pregnancy causing a 'red herring effect' which make the diagnosis of heterotopic pregnancy particularly challenging for natural conception [14]. Simultaneous presence of viable intrauterine pregnancy and interstitial pregnancy pose management challenge in HIP. As a rule of thumb, the interstitial pregnancy needs to be terminated due to associated morbidity and mortality with ruptured interstitial pregnancy, whilst allowing the viable intrauterine pregnancy to be preserved [12].

CASE PRESENTATION

A 33-year-old primigravida had first positive pregnancy test at seven weeks' amenorrhoea and subsequently confirmed to have viable intrauterine pregnancy at her general practitioner. At 10 weeks' amenorrhoea, she started to have per vaginal bleeding and lower abdominal pain. She was diagnosed with missed miscarriage at early pregnancy assessment unit with

crown-rump length measurement in consistent with 7 weeks of gestation and no fetal cardiac activity (Figure 1). She agreed for conservative management given the miscarriage process had started. She presented three times to early pregnancy assessment unit with complain of passing some tissue-like material within the two-weeks period. No change of ultrasound finding of missed miscarriage at 12 weeks' amenorrhoea, hence we proceeded with evacuation of retained product of conception (ERPC). Intraoperatively, surprisingly minimal product of conception was retrieved. Bedside pelvic ultrasonography showed a cystic mass located at the right superolateral part of uterine fundus (Figure 2) which was suspicious for interstitial pregnancy, although other diagnoses including angular pregnancy and degenerating fibroid could not be excluded. Pelvic magnetic resonance imaging (MRI) was indicated to better define the cystic mass; the result revealed the 'presence of an ovoid mass abutting the endometrial cavity to the right of the uterine fundus in consistent with suspicion of interstitial pregnancy'.



Figure 1 Shows the initial pelvic ultrasound finding of missed miscarriage at 10 weeks' amenorrhoea. The crown-rump length measurement was of 7 weeks' gestation with no visible fetal cardiac activity.



Figure 2 Shows the pelvic ultrasound image of the cystic mass at the uterine fundus area. The absence of fetal pole, and irregularity of the cyst edge made it appear like degenerating fibroid.

We performed serial β -hCG and inpatient observation of her symptoms since she was stable. Immediate post-ERPC β -hCG reading was 10,027 IU/L followed by 6,726 IU/L on day two post-ERPC. The reading of β -hCG plateaued to 4,173 IU/L on day seven post-ERPC, the trend of which is elicited in Table 1.

Table 1 Serial β -hCG reading

Gestation (week+day)	Clinical event	β -HCG (IU/L)
12+2	D0 post-ERPC	10,027
12+4	D2 post-ERPC	6,726
12+6	D4 post-ERPC	6,602
13+6	D11 post-ERPC	4,173
14+5	D3 post-cornual resection	210

The patient was asymptomatic throughout the observation period hence we electively performed hysteroscopy, endometrial curetting, diagnostic laparoscopy proceeded to laparotomy and cornual resection at 14 weeks' amenorrhoea, two weeks after the ERPC. Normal endometrial cavity demonstrated at hysteroscopy excluded angular pregnancy and bicornuate uterus. At laparoscopy, a 5 x 5 cm bulging mass was visible at right superolateral part of uterine fundus. Given the huge mass size and the need for adequate tissue resection, we performed laparotomy

and cornual resection. The myometrium overlying the mass together with the gestational sac was resected, followed by 3 interrupted vertical mattress sutures for haemostasis. Intraoperative blood loss was 300 ml. β -hCG reading declined to 210 IU/L level on day three post-cornual resection. Histopathological examination (HPE) of the first endometrial curetting at ERPC revealed the presence of chorionic villi and decidua in consistent with product of conception. HPE of the resected uterine cornua resulted as interstitial pregnancy. The patient made good recovery at six weeks follow-up.

DISCUSSION

Systematic assessment of the pelvis with ultrasound is the first line imaging option for diagnosing HIP. Interstitial line sign observed at transverse plane of the uterine fundus in pelvic ultrasound has 80% sensitivity and 98% specificity for interstitial pregnancy, the finding of which can be difficult to recognize [4, 15]. Three-dimensional sonography can improve the detection of interstitial line with reasonable reliability though performing three-dimensional sonography is even more operator dependent than the usual two-dimensional ultrasound [16]. Alternatively, pelvic MRI provides better imaging to confirm the diagnosis of IP by demonstration of intact junctional zone between the interstitial pregnancy and the endometrial cavity [15]. However, MRI may not always be easily accessible and the use of gadolinium contrast in HIP should be avoided in the presence of viable intrauterine pregnancy [15]. In the setting of artificial reproductive technology, only half of the heterotopic pregnancy was detected at first routine ultrasound examination [7], although higher figure of 85% has been quoted in smaller studies that proposed for routine transvaginal ultrasound at day 27 after embryo transfer [11]. In the case report, pelvic MRI was utilised to further delineate interstitial pregnancy from other potential diagnosis such as angular pregnancy or degenerating fibroid. There was no contraindication for contrast use in the case report due to the intrauterine pregnancy being a miscarriage.

Medical management of the interstitial pregnancy involves aspirating the gestational sac content with or without instillation of feticide agents

such as methotrexate or potassium chloride [17, 18]. By opting for medical management, patient must be informed of the lengthy follow-up and risk of rupture of the interstitial pregnancy within the treatment period, in balance with the success rate of more than 90% [19].

Surgical option is indicated in the presence of \geq 4 cm gestational sac of the interstitial pregnancy. Cornual resection offers more favourable outcome than cornuostomy owing to the better haemostasis with cornual resection [20]. Cornuostomy has the advantage of preserving the integrity of uterine cornua and shorter operating time as compared to cornual resection [21]. Otherwise, both surgical techniques have comparable outcome in terms of persistent interstitial pregnancy (PIP) and pre- and post-surgery haemoglobin level [19]. Laparotomy holds the mainstay role in excision of interstitial pregnancy in haemodynamically unstable patient, where skilled laparoscopic surgeon or equipment is unavailable, and/or poor operative field secondary to presence of pelvic adhesions [7, 20]. Expectant management of the coexisting interstitial pregnancy is reserved for cases with absent fetal cardiac activity and small gestational sac size, with close surveillance in place, and takes small proportion of 5.8% [6, 12].

Serial β -hCG has roles in detecting persistent interstitial pregnancy and differentiating intrauterine pregnancy from ectopic pregnancy [11, 17]. The typical doubling of serial β -hCG reading with viable intrauterine pregnancy may pose false reassurance to the clinician, resulting in missing the concomitant interstitial pregnancy in HIP [6]. Serial β -hCG was performed in the case study to guide the management option. Plateauing trend of β -hCG level as observed in the case study provided two cornerstones; intrauterine pregnancy was mostly evacuated at ERPC, and that cystic mass at superolateral part of the uterine fundus was of pregnancy origin hence excluding the differential diagnosis of degenerating fibroid. β -hCG level was reduced from 4173 IU/L to 210 on day three post-cornual resection. There was no further β -hCG level taken following the latest reading to follow through the pregnancy hormone until non-pregnant level in order to detect persistent interstitial pregnancy. Six weeks post-cornual resection follow-up confirmed negative urine pregnancy test which was reassuring.

CONCLUSION

In conclusion, all medical practitioners should have high index of suspicion of heterotopic pregnancy despite absence of any risk factors for HIP. Earlier diagnosis of HIP permits more conservative approach such as medical management or less invasive surgical intervention which are associated with less risk of uterine rupture in future pregnancy. Therefore, timely intervention potentially allows concurrent intrauterine pregnancy to survive and more importantly, it will reduce risk of maternal morbidity and mortality.

Conflict of Interest

Authors declare none

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