

## Mini Review

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## Heterotopic Pregnancy

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### KEY CONTENT

- Heterotopic pregnancy is a rare but life-threatening condition
- Very few clinicians will come across this very serious gynaecological condition during their careers
- It is very difficult to diagnose and the patient may collapse and die during investigations
- Life-saving emergency laparotomy is essential in seriously sick patients

### LEARNING OBJECTIVES

- To increase awareness amongst clinicians about this rare condition
- To help in the diagnosis and management of this serious pregnancy complication
- To help save lives

### ETHICAL ISSUES

- The safety of the mother and the intrauterine fetus
- The removal of the extrauterine fetus to save the mother and the intrauterine fetus

**KEYWORDS:** Heterotopic pregnancy; Life-threatening; Risk factors; Life-saving; Maternal collapse and death; Emergency laparotomy.

### INTRODUCTION

Heterotopic pregnancy is a rare gynaecological condition whereby there is a presence of an intrauterine pregnancy and extrauterine pregnancy at the same time. It was first defined by Duverney in 1708 as an autopsy finding in a patient who had died of a ruptured ectopic pregnancy and had an intrauterine pregnancy.<sup>1</sup> Rarely an intrauterine twin gestation can co-exist with a heterotopic pregnancy or *vice versa*. Higher order heterotopic gestations are extremely rare.<sup>2</sup> This condition may cause diagnostic difficulties and the patient may collapse and die during investigations. Those occurring after fertility treatments may face ethical and emotional dilemma of having to lose one of their babies. It is a rare life-threatening condition that very few clinicians would come across during their careers. It is therefore an important clinical condition, hence the need to bring the subject prominence through a review article like this one.

### INCIDENCE

The reported incidence of heterotopic pregnancy in a spontaneous natural cycle is 1 in 30,000.<sup>3</sup> This is indeed very rare that some clinicians may never come across it during their careers. This poses a danger to the mother and the intrauterine pregnancy as very few clinicians will consider this diagnosis until it is too late. It is mostly likely to be outside the list of initial differential diagnoses. There is a direct increase in the incidence related to the number of embryos being transferred during *in vitro* fertilisation.<sup>4,5</sup> The incidence has increased to 2.9%<sup>1</sup> with ovulation induction and to 1% with assisted reproductive techniques.<sup>6</sup> Couples undergo-

ing such processes must be fully counselled on these risks. They may face the prospect of having to undergo transabdominal fetal reduction.<sup>4</sup>

### RISK FACTORS

Heterotopic pregnancy can have several aetiological factors. Risk factors associated with this type of gestation include a history of pelvic inflammatory disease, previous surgery, pelvic trauma, congenital uterine malformations and the use of assisted reproductive techniques.<sup>7</sup> These factors may act singularly or together to cause the condition. About 1% of the pregnancies are ectopic of which, 95-97% are in the fallopian tube, the ampullary portion being the most common accounting for 80%, the isthmic portion accounts for 10%, fimbrial region 5% and cornual and interstitial regions 2-4%.<sup>8</sup> Other sites for ectopic implantation include ovarian, cervical and abdominal cavity.

### CLINICAL FEATURES

Heterotopic pregnancy can be asymptomatic in up to 54% of cases<sup>1</sup> or present with a haemodynamically compromised patient. Since it is a rare condition clinicians must be alert to seek it out in patients presenting to them. Clinicians must maintain a high index of clinical suspicion in any female patient of reproductive age group presenting with features suggestive of an abnormal pregnancy with or without risk factors.

The patient may present with a history of 6-8 weeks of amenorrhoea, lower abdominal pains, shoulder tip pain, fainting, dizziness and urinary symptoms. They can also present with atypical symptoms of epigastric pains and vomiting<sup>9</sup> and may be improperly treated for gastrointestinal diagnoses. There may be confusion with the diagnosis of ovarian hyperstimulation syndrome especially in patients that have recently undergone *in vitro* fertilisation. This syndrome can present with similar symptoms.

In a compromised patient, there may be pallor, tachycardia, tachypnoea, hypotension/hypovolemia, abdominal tenderness/distension and guarding<sup>1,10-12</sup> and the patient may collapse and die especially with a ruptured heterotopic pregnancy. This is a dire gynaecological emergency. Prolonged cardiovascular compromise can result in multi-organ failure necessitating a multidisciplinary team approach. The intrauterine fetus will demise with the mother.

### INVESTIGATIONS

Diagnosis of heterotopic pregnancy is difficult in that the clinical symptoms can be scanty/vague or the intrauterine gestation can mislead clinicians. Those patients suspected to have this diagnosis must be promptly investigated. Transvaginal ultrasonography in heterotopic pregnancy has a sensitivity of only 56%.<sup>5</sup> The presence of an intrauterine gestation does not exclude an ectopic gestation.<sup>13,14</sup> The use of colour Dop-

pler scans can improve the chance of diagnosing it.<sup>15</sup> Clinicians should relentlessly investigate further patients complaining of undetermined pelvic/abdominal pains despite a scan report confirming an intrauterine gestation. A life-threatening heterotopic pregnancy may be co-existing. At the same time a scan report can be falsely reassuring.

The use of  $\beta$ -hCG serum assaying is difficult in heterotopic pregnancy as the intrauterine gestation obscures the ectopic gestation.<sup>16</sup> The use of magnetic resonance imaging of the pelvis may be used to assist in the diagnosis.<sup>16,17</sup>

A diagnostic laparoscopy, without uterine instrumentation remains a gold standard procedure<sup>18</sup> where there is clinical diagnostic doubt and the patient is clinically stable. If the patient deteriorates during the procedure the laparoscopy should be converted to a laparotomy. It is contraindicated in patients that are haemodynamically unstable and these need an emergency life-saving laparotomy.

In settings, where there are limited investigative resources, clinicians must practice pure medicine of; a detailed history, physical examination and make life-saving decisions such as prompt recourse to exploratory surgery.

### MANAGEMENT

The management of heterotopic pregnancy must be decisive once the diagnosis has been made to save lives. The management of heterotopic pregnancy is laparoscopy<sup>7</sup> avoiding uterine instrumentation or laparotomy for the tubal pregnancy.<sup>19</sup> Emergency laparotomy is the life-saving option in patients with significant intra-abdominal haemorrhage or in a patient that is cardiovascularly compromised. An experienced anaesthetist and surgeon may be needed in a life-saving operation. Patients may need intra-operative and post-operative blood transfusions. They may be very sick needing admission to Intensive Care Unit/High Dependency Unit. In resource-challenged settings prompt laparotomy with basic investigations saves lives.

At surgery findings vary from un-ruptured tubal ectopic implantations to various degrees of haemoperitoneum<sup>10</sup> depending on the length of bleeding after the rupture<sup>10-12</sup> of the heterotopic pregnancy. At times, bleeding is found to be coming from the fimbrial end with a tubal pregnancy still intact. Specimens obtained should be sent for histological confirmation of ectopic implantation.

Medical therapy with methotrexate is highly effective with rates of 88.1% on single dose regimes and 92.7% on multi-dose regimes.<sup>1,20,21</sup> This has the advantage of avoiding risks associated with surgery, preserves the tube and has less need for hospitalisation. It is suitable for stable patients, those with small gestational sacs <3.5 cm on scan, no free fluid, absence of fetal cardiac activity and a compliant patient to follow-up.<sup>1</sup> The use of folinic acid as an antagonist to methotrexate helps reduce side

effects of methotrexate especially if high doses of methotrexate are used.<sup>21</sup>

Complete resolution of an ectopic pregnancy takes 2-3 weeks but can take as long as 6-8 weeks.<sup>20</sup> Serial scans and  $\beta$ -hCG levels would confirm this resolution.<sup>20,21</sup> Patients may find this long and become apprehensive hence counselling is crucial.

Other medical treatments described in the literature include the use of hyperosmolar glucose ultrasound-guided injection into the heterotopic pregnancy.<sup>22</sup> The use of ultrasound-guided intracardiac injection of potassium chloride can allow the intrauterine pregnancy to progress.<sup>23</sup> Nonsurgical management with transvaginal ultrasound-guided injection of potassium chloride and methotrexate into a cervical pregnancy resulted in a successful outcome.<sup>24</sup> Such management strategies are few as most cases described in the literature have been managed either by laparoscopy or laparotomy. There are no randomised trials comparing medical treatment versus surgical treatment.<sup>1</sup>

Expectant management has also been described but is rarely used as it needs intense monitoring,<sup>25</sup> and leaves the patient to potential harm if tubal rupture occurs without warning leading to catastrophic haemorrhage and maternal and intrauterine fetal death. Ectopic gestations can suddenly rupture leading to instant collapse and demise within minutes. Few clinicians and patients may be willing to embark on this option. Meticulous counselling and record keeping would be needed if catastrophic results were to occur.

## PROGNOSIS

The prognosis for the intrauterine fetus following both medical and surgical treatment of the ectopic gestation is good.<sup>1,2,7</sup> In a comparative review of 80 cases with heterotopic pregnancy treated surgically the survival rate of the intrauterine pregnancies was 68.7%.<sup>15</sup> The rate of live births in heterotopic triplets is around 60% but in one review the rate of live births was 92.3%.<sup>26-28</sup> These figures can be useful in counselling patients and reassuring them about the good chances of the normally-sited pregnancy progressing well to term deliveries.

## CONCLUSION

Heterotopic pregnancy is a very rare life-threatening clinical condition. It poses great clinical diagnostic difficulties. Very few clinicians worldwide will come across this serious complication during their training and careers. It can contribute to maternal morbidity and mortality and loss of the intrauterine fetus. It can happen in a natural cycle<sup>29,30</sup> and in women without risk factors. In patients who present in acute forms where investigations such as ultrasound scans are not possible to do, uterine instrumentation should be avoided at laparoscopy.<sup>30</sup>

Therefore, clinicians must remain vigilant in seeking

and promptly treating this dangerous condition. Clinicians must carry out life-saving emergency laparotomy if there is diagnostic doubt in the face of a clinically sick patient with an acute abdomen despite having an intrauterine pregnancy. The history and clinical findings must be taken into great consideration ahead of scan reports. It is better to make a retrospective diagnosis in a live patient.<sup>30-32</sup> than a post-mortem diagnosis with a loss of lives like what Duverney found in 1708.<sup>1</sup> In modern practice, we are backed up by modern diagnostic and therapeutic strategies.<sup>13</sup>

## CONTRIBUTION OF AUTHORSHIP

This paper was the sole work of Mr. Ngwenya.

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