

Heterotopic pregnancy following in-vitro-fertilization: a clinical dilemma in a low resource setting

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Abstract

Background: Heterotopic pregnancy occurs when both intra-uterine and ectopic pregnancies co-exist simultaneously. Its occurrence in natural conception is quite rare, however, it is more frequently encountered following assisted conception especially when multiple embryos are transferred [1,2,3]. Diagnosis in its early stage has been reported to be a dilemma due to the concomitant presence of an intra-uterine gestation posing significant challenges with management and clinical outcome [4,5]. Prognosis is noted to vary based on the time of diagnosis and option of management deployed [5], however live birth rates of about 66.7% has been reported in literature [6]. This case report highlights the clinical dilemma associated with a heterotopic pregnancy following In-Vitro-Fertilization (IVF) in a low resource setting.

Case presentation and management: A 35-year-old G3P1⁺¹ (1 alive) civil servant who had IVF on account of secondary infertility of 3 years duration. She had spontaneous vertex delivery of a life female neonate 6 years prior to presentation and left total salpingectomy following ruptured ectopic gestation about 3 years earlier. There was a history of pelvic inflammatory disease on at least 2 occasions. A hysterosalpingogram (HSG) revealed absent left tube and patent right tube with peritubal adhesions. She had IVF using the long protocol. 8 metaphase II oocytes were aspirated and inseminated with her husband's sperm. She had 2 blastocysts transferred and a pregnancy test done 2 weeks after was positive. An obstetric scan done at 6 weeks revealed an intra-uterine gestation compatible with her date and a concomitant right tubal ectopic gestation. She had transvaginal injection of potassium chloride as part of conservative management. Resolution of the ectopic occurred, however she developed right haematosalpinx and persistent lower abdominal pain. She subsequently had right total salpingectomy at a gestational age of 8 weeks. She continued luteal support till 14 weeks and pregnancy remained

uneventful. She had an elective caesarean section at 38 weeks and was delivered of a healthy male neonate.

Conclusion: Heterotopic pregnancy following IVF in a low-income setting can be catastrophic. It poses a unique challenge due to the dilemma occasioned by the risk of conservative over surgical management of the ectopic whilst preserving the intra-uterine gestation. Encouraging elective single embryo transfer (eSET) at IVF is an important preventive measure, often difficult to enforce in a low resource setting.

Keywords: - Dilemma, Heterotopic Pregnancy, In-Vitro-Fertilization, Low-resource

Résumé

Contexte : La grossesse hétérotopique survient lorsque des grossesses intra-utérines et extra-utérines coexistent simultanément. Son occurrence dans la conception naturelle est assez rare, cependant, elle est plus fréquemment rencontrée après la conception assistée surtout lorsque plusieurs embryons sont transférés [1,2,3]. Le diagnostic à un stade précoce a été signalé comme un dilemme en raison de la présence concomitante d'une gestation intra-utérine posant des défis importants pour la gestion et les résultats cliniques [4,5]. Il est noté que le pronostic varie en fonction du moment du diagnostic et de l'option de prise en charge déployée [5], cependant des taux de naissances vivantes d'environ 66,7 % ont été rapportés dans la littérature [6]. Ce rapport de cas met en évidence le dilemme clinique associé à une grossesse hétérotopique après une fécondation in vitro (FIV) dans un environnement à faibles ressources.

Présentation et prise en charge du cas : Un fonctionnaire G3P1+1 (1 vivant) de 35 ans ayant eu une FIV pour infertilité secondaire d'une durée de 3 ans. Elle a accouché spontanément d'un nouveau-né de sexe féminin 6 ans avant la présentation et a quitté la salpingectomie totale après une rupture de gestation ectopique environ 3 ans plus tôt. Il y avait des antécédents de maladie inflammatoire pelvienne à au moins 2 reprises. Une hystérosalpingographie (HSG) a révélé l'absence de tube gauche et un tube droit perméable avec des adhérences périfimbriales. Elle a eu une FIV en utilisant le protocole long. 8

ovocytes en métaphase II ont été aspirés et inséminés avec le sperme de son mari. Elle a eu 2 blastocytes transférés et un test de grossesse fait 2 semaines après était positif. Un scanner obstétrical réalisé à 6 semaines a révélé une gestation intra-utérine compatible avec sa date et une gestation ectopique tubaire droite concomitante. Elle a reçu une injection transvaginale de chlorure de potassium dans le cadre d'une prise en charge conservatrice. La résolution de l'ectopique s'est produite, mais elle a développé un hématosalpinx droit et des douleurs abdominales basses persistantes. Elle a ensuite subi une salpingectomie totale droite à un âge gestationnel de 8 semaines. Elle a continué le soutien lutéal jusqu'à 14 semaines et la grossesse est restée sans incident. Elle a eu une césarienne électorale à 38 semaines et a accouché d'un nouveau-né de sexe masculin en bonne santé.

Conclusion : Une grossesse hétérotopique après FIV dans un milieu à faible revenu peut être catastrophique. Elle pose un défi unique en raison du dilemme occasionné par le risque d'une gestion conservatrice plutôt que chirurgicale de l'ectopique tout en préservant la gestation intra-utérine. Encourager le transfert électif d'un seul embryon (eSET) lors de la FIV est une mesure préventive importante, souvent difficile à appliquer dans un environnement à faibles ressources.

Mots clés : - *Dilemme, Grossesse hétérotopique, Fécondation in vitro, Faible ressource*

Introduction

Heterotopic pregnancy refers to the simultaneous occurrence of both intra-uterine and ectopic gestations. The incidence following natural conception is estimated to be about 1 in 30,000 pregnancies [7], however with increasing resort to IVF, there has been a disproportionate increase among women who had assisted conception with values as high as 1 in 100 pregnancies [8,9,10]. The most common site for an ectopic gestation both in spontaneous and IVF heterotopic pregnancies is the fallopian tube [11]. Clinical presentation of heterotopic gestation includes vaginal bleeding (54%), abdominal pain (72%) and occasionally asymptomatic (24%) [12], especially if diagnosed early. There exists an inherent dilemma with management especially following a well intentioned and desired pregnancy such as that following In-Vitro- Fertilization. Prompt diagnosis and institution of appropriate management is critical to improving the clinical outcome of the pregnancy as delays have been associated with increased

morbidity and mortality for both mother and intra-uterine gestation [10,13]. This case report seeks to highlight the challenges of management in a low resource setting against the background of infertility.

Case

A 35-year-old G3P1⁺ (1 alive) civil servant who had IVF on account of secondary infertility of 3 years duration. She had spontaneous vertex delivery (SVD) of a life female neonate 6 years prior to presentation. She had a history of left total salpingectomy following ruptured ectopic gestation about 3 years prior to presentation. She also had pelvic inflammatory disease on at least 2 occasions which were managed with broad spectrum antibiotics. A hysterosalpingogram revealed absent left tube and patent right tube with perifimbrial adhesions. Her spouse was a 38-year-old self-employed man. His serological tests and semen analysis were essentially normal. In view of the long-standing infertility and tubal factor, the couple was counselled on the need for assisted conception.

She had IVF using the long protocol. Ovarian down-regulation was achieved using 0.5 IU Buserelin while oocyte stimulation was with 300IU FSH (Follicle Stimulating Hormone). Oocyte maturation was with 5,000 IU hCG (Human Chorionic Gonadotropin). Eight metaphase II oocytes were aspirated and inseminated with her husband's sperm. She had 2 blastocysts transferred and a pregnancy test done 2 weeks after was positive. An obstetric scan done at 6 weeks revealed an intra-uterine gestation compatible with her date alongside a concomitant right tubal ectopic gestation. She had transvaginal injection of potassium chloride into the ectopic gestation as part of conservative management. Resolution of the ectopic gestation occurred however, she developed right haematosalpinx with persistent lower abdominal pain necessitating exploratory laparotomy and right total salpingectomy at a gestational age of 8 weeks. Her post-operative condition was satisfactory, and she continued luteal support with cyclogest vaginal pessaries till 14 weeks. Pregnancy remained uneventful. She had an elective caesarean section at 38 weeks and was delivered of a healthy male neonate weighing 3.2kg. Mother and baby were discharged home on the 4th post-operative day to be followed up at the post-natal clinic.

Discussion

A heterotopic pregnancy is an undesirable outcome following advanced fertility management. It is known to occur spontaneously or following superovulation,

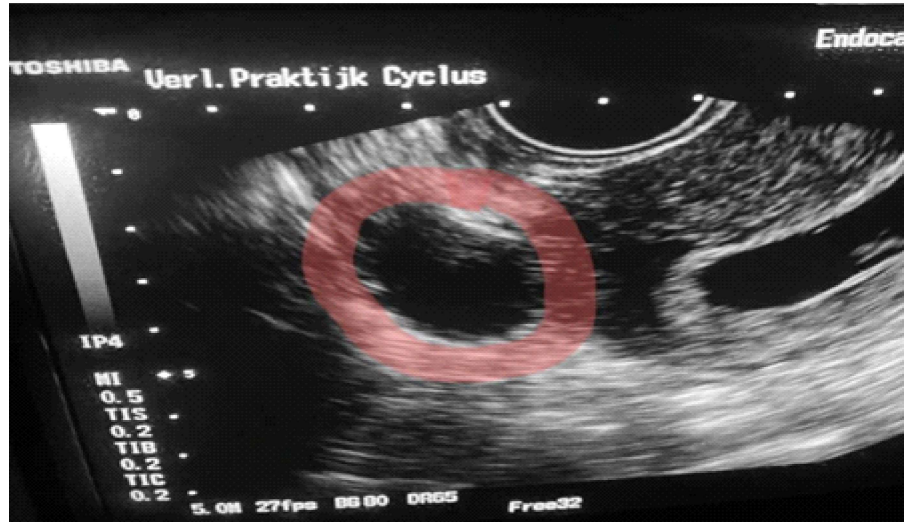


Figure 1: Viable intra-uterine gestation and right haematosalpinx (circled) following transvaginal injection of potassium chloride for embryo reduction in a heterotopic gestation.

with multiple embryo transfer at IVF. With increasing deployment of assisted reproductive techniques (ART) for the management of infertility, the incidence of heterotopic pregnancy has gradually risen with a current estimation of 1 in 100 pregnancies [10]. Heterotopic pregnancy was first described in France by Duverney in 1708 during a post-mortem examination [14] and was associated with several risk factors including tubal disease. In-vitro-fertilization presents a unique opportunity for simultaneous intra-uterine and extra-uterine implantations to occur and the earliest report of a heterotopic pregnancy following IVF was by Yovich *et al* in 1985 [15] when a patient with underlying tubal disease had transfer of five 4-cell embryos. Heterotopic pregnancy has also been reported following gamete intra-fallopian transfer [16] and in extremely rare instances has occurred in caesarean section scars [17]. Implantation of the extra-uterine component of a heterotopic pregnancy on the left psoas muscle following frozen embryo transfer (FET) has been reported in literature [18].

Risk factors for heterotopic pregnancy include tubal pathologies which may arise from previous pelvic infections, tubal surgeries including sterilization and ectopic pregnancies [19]. This patient had a history of pelvic inflammatory disease (PID) and left total salpingectomy from a previous ruptured ectopic gestation. The negative impact of pelvic infections on tubal function cannot be overemphasized and often leads to both structural and physiological dysfunction. Other important risk factors for heterotopic pregnancy include pelvic endometriosis,

pelvic abnormalities, use of progestogens and adhesions arising from pelvic surgeries. Following IVF, risk factors predisposing to heterotopic pregnancy include, multifetal transfer, direct injection of the embryo(s) into the fallopian tube, replacement of embryos with large volume of media, improper placement of embryo transfer catheter (less than 10mm below the surface of the uterine fundus) and uterine contractions post embryo transfer [20, 21]. Our patient had IVF on account of tubal disease and had 2 blastocysts transferred, factors that may have predisposed her to a heterotopic pregnancy.

Diagnosis in a resource-constrained environment may prove challenging due to low levels of suspicion often accompanying the presence of a viable intrauterine gestation. This is further compounded by imaging difficulties due to enlarged ovaries post superovulation at IVF which may mask the presence of an ectopic. There is a compelling need for continuous development of expertise in pelvic imaging especially by fertility specialist in developing countries such that early detection is possible. This patient had an early diagnosis made at 6 weeks gestational age.

Conservative (non-surgical) management was the initial choice because the diagnosis was made quite early and there were no symptoms or complications. Treatment options generally depend on the severity of presentation, viability of the intra-uterine gestation, location of the ectopic gestation and the expertise and facilities available for treatment. Trans-vaginal injection of potassium chloride (KCL) was the method of choice considering the presence

of a viable intra-uterine gestation. Hyperosmolar glucose and potassium chloride have been found suitable for non-surgical management of a heterotopic pregnancy, however, may be complicated by persistent trophoblastic activity [22]. Methotrexate administered either systemically or locally has been employed in the conservative management of ectopic pregnancies, however due to its embryotoxicity, it cannot be used in the presence of a viable intra-uterine pregnancy [22, 23].

This patient had exploratory laparotomy with right total salpingectomy on account of failed conservative management evidenced by progressive haematosalpinx after resolution of the ectopic tissue along with persistent lower abdominal pain. The cardinal principle for the management of heterotopic pregnancy is to quickly remove the extra-uterine pregnancy whilst maintaining the intra-uterine component [24]. In general terms, the least invasive method is preferable and where facilities exist for operative laparoscopy, this would have been the route of choice due to its minimally invasive nature and associated lower risk for miscarriage and preterm delivery [25].

Conclusion

Heterotopic pregnancy in a low-resource setting against a background of infertility managed via IVF can be unsettling. It poses a unique management challenge due to the dilemma occasioned by the risk of conservative over surgical management of the ectopic whilst avoiding miscarriage of the concomitant intra-uterine gestation. Early detection coupled with conservative management is a feasible first line option except there is failure and or progression to acute abdomen. Encouraging elective single embryo transfer (eSET) at IVF is an important preventive measure which is often difficult to enforce in a resource constraint setting where there is no insurance coverage for repeat IVF cycles such that treatment failure may constitute an economic catastrophe.

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