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CASE REPORT

Fertility-preserving Management of Cervical Ectopic Pregnancy in a Nigerian Teaching Hospital

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Summary

Cervical Ectopic Pregnancies (CEPs) are commonly associated with adverse outcomes due to diagnostic and treatment challenges. This report describes the successful management of an initially misdiagnosed CEP. A 30-year-old $G_4P_2^{+1}$(Alive 2) presented to the Obafemi Awolowo University Teaching Hospitals Complex (OAUTHC), Ile-Ife, Nigeria, with vaginal bleeding following 11 weeks amenorrhea. The patient was haemodynamically stable, with minimal bleeding *per vaginam*, and ultrasonography had previously diagnosed complete miscarriage. However, transvaginal ultrasonography demonstrated classical hour-glass uterus. The ballooned cervix contained a gestational sac and foetal node without cardiac activity. The patient was managed with a single dose of intramuscular methotrexate injection. Her serum B-HCG concentration declined from 460.8mIU/ml at presentation to <5mIU/ml on the 10th day post-methotrexate injection, with a complete clinical and ultrasonographic resolution of the features. A high index of suspicion and appropriate ultrasonographic skills are necessary for prompt diagnosis of a CEP. Medical management could minimise the risk of intractable haemorrhage and hysterectomy.

Keywords: Cervical Ectopic Pregnancy, Conservative management, Hysterectomy, Methotrexate, Transvaginal ultrasonography.

Introduction

Ectopic pregnancies are the leading cause of maternal mortality in the first trimester. The risk of adverse outcomes following ectopic pregnancies is increased in Low- and Middle-Income Countries (LMICs) with high maternal mortality ratios, such as Nigeria, due to suboptimal healthcare-seeking attitudes and delayed diagnosis. Cervical Ectopic Pregnancy (CEP) is a rare variant first reported in 1817, with an incidence as low as 1 in 95,000 pregnancies. [1] It occurs when the product of conception, at the blastocyst stage, implants directly within the endocervical canal. [2] The condition is important due to its rarity and the high propensity for massive haemorrhage, the need for extirpative surgeries to secure haemostasis, as well as the need for massive blood transfusion. Until recently, CEPs are almost always associated with loss of fertility due to life-saving procedures such as emergency hysterectomy. [3]

Opinions vary about the ideal treatment modality for patients with CEPs, as the rarity of

the condition precludes the possibility of a clinical trial. However, experience in the management of CEPs continues to build, as case reports and series on surgical and medical options are published in the medical literature. In this index report, the successful fertility-preserving medical management of a CEP that was initially misdiagnosed as complete miscarriage is presented.

Case Description

A 30-year-old $G_4P_2^{+1}$ (Alive 2) woman presented to the Early Pregnancy Unit (EPU) of the Obafemi Awolowo University Teaching Hospitals Complex, Ile-Ife, Nigeria, with recurrent vaginal bleeding after 11 weeks of amenorrhoea. There was associated passage of blood clots, but there was no foetal tissue or vesicle. Her previous deliveries were by Caesarean sections, and she had vacuum aspiration of retained products in her last pregnancy for a first-trimester miscarriage. Previous transabdominal ultrasonography at another centre had reported an empty uterine cavity and normal adnexa, with a resultant diagnosis of a complete miscarriage. At presentation, she was haemodynamically stable, and abdominal examination was unremarkable. Speculum vaginal examination revealed an enlarged, bluish cervix with a closed external os and minimal bleeding. An ectopic pregnancy was suspected based on the symptomatology. Further, transvaginal ultrasonography demonstrated a bulky uterus with the classical "hour-glass" appearance (Figure 1).

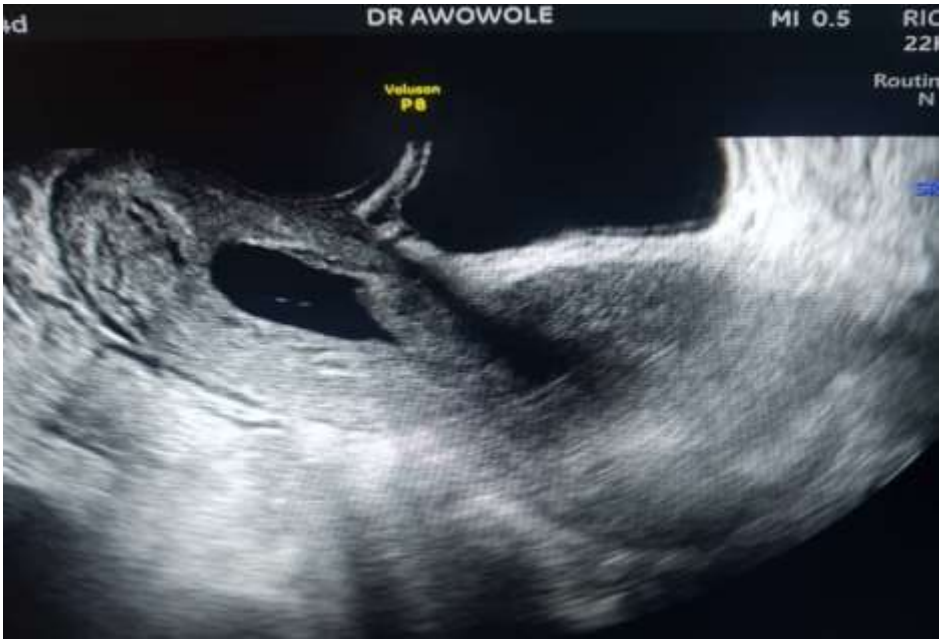

Figure 1: Ultrasonographic image of the gestational sac within the cervical canal, conferring the "hour-glass" appearance on the uterus.

The endometrial cavity was empty, with an endometrial thickness of 10.2 mm. There was no adnexal mass. The ballooned-out cervical canal contained a regular gestational sac (Figures 1 and 2). There was a yolk sac and a foetal node with Crown Rump Length (CRL) equivalent to 7 weeks gestation. There was no demonstrable foetal cardiac pulsation. The internal cervical os

above the gestational sac was closed, with a thin rim of endocervix between the internal os and the proximal part of the sac. The tissue "sliding sign" was negative. The haematocrit was 12g/dL, while the serum Human Chorionic Gonadotropin (β-HCG) concentration was 460.8IU/L. A diagnosis of CEP was made based on these findings. After extensive counselling, during which she confirmed her desire for fertility preservation, she was managed medically with a single dose of 86mg intramuscular methotrexate injection (at a dose of 50mg/m^2 body surface area).

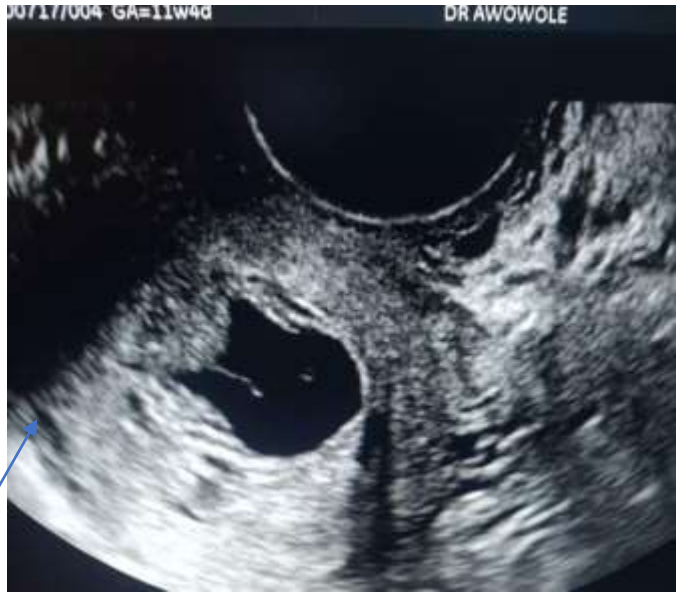

Figure 2: Axial section showing the gestational sac and the foetus, with a concentric ring of cervical tissue around it. (Arrow indicates the foetus and the umbilical cord).

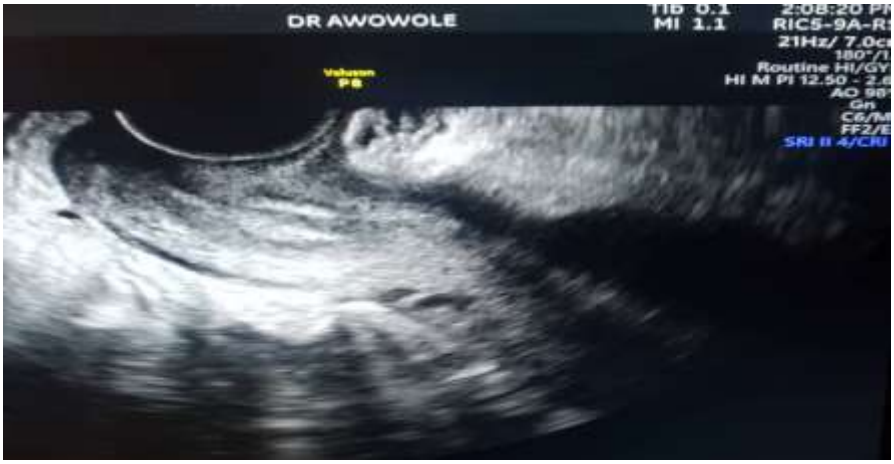

Figure 3: Remodelled cervix with a minimal decidual reaction on day 12 after methotrexate therapy

The woman had moderate bleeding, which was self-limiting, and passage of products of conception *per vaginam* in the first three days following the injection. Her haematocrit remained unchanged, and she was discharged home on the fourth day. The serum concentration of β-HCG became undetectable (<5mIU/ml) ten days after the injection, with complete resolution of symptoms. A repeat transvaginal ultrasonography on the 12th day after methotrexate injection revealed a remodelled cervix with minimal decidual reaction (Figure 3). She was advised to use contraception for at least 4 to 6 months to limit the risk of teratogenicity and to present early in her subsequent pregnancy for localisation of the pregnancy.

Ethical consideration

This case report is completely anonymised. Therefore, an Institutional Research Board approval was unnecessary. However, the patient gave consent for the publication of the images.

Discussion

The incidence of ectopic pregnancy has been increasing due to the effect of assisted reproductive technology. Other risk factors include previous uterine curettage, previous caesarean sections, and endometritis. [4] In many instances, however, a predisposing factor may not be identifiable. This patient had two previous caesarean sections and one uterine evacuation following a miscarriage. Therefore, a caesarean scar ectopic pregnancy was a possibility in her. Nevertheless, the diagnosis of Caesarean scar ectopic pregnancy was not entertained after the ultrasonography, which showed that the gestational sac was surrounded by a concentric ring of thick cervical tissue. In contrast, a caesarean scar ectopic pregnancy would have been embedded on the anterior wall of the cervix, with a thin rim of intervening myometrial tissue (<3mm in thickness) between the sac and the bladder. [5]

In 1911, Rubin proposed the pathologic criteria for the diagnosis of CEP, including intimate attachment of the placenta to the cervix, visible cervical glands on the site of attachment of the trophoblastic tissues, the attachment of the trophoblast below the level of the uterine vessels or the anterior and posterior peritoneal reflections on the uterus, and lastly, absence of foetal elements and trophoblastic tissues from the corpus uteri.[6] The utilisation of these criteria is only feasible after histopathological examination of a hysterectomy specimen, understandably, as most patients with CEPs ended up with an inevitable hysterectomy. To facilitate clinical diagnosis without the need for recourse to pathologic specimens, Palmaan and McElin published a set of clinical criteria for diagnosing CEP. These included uterine bleeding without cramping pain following a period of amenorrhea, hourglass-shaped uterus, partially opened external os, closed internal os and firmly adherent products of conception within the endocervix. [7]

The introduction of high-resolution ultrasonography and high-performance β-HCG assay has improved the diagnosis of CEP, which was often diagnosed previously following intractable haemorrhage during an attempt at surgical evacuation for unrecognised cases, as earlier reported by Palmaan and McElin. Despite these, cases of cervical ectopic pregnancies are still misdiagnosed as complete miscarriage as observed in the index patient due to the finding of the empty uterine cavity and normal adnexa on ultrasonography. Therefore, appropriate sonographic skills are essential to the timely diagnosis of CEPs before significant haemorrhage ensues. CEPs may also be misdiagnosed as the cervical stage of an ongoing miscarriage. However, the ultrasonographic

criteria proposed by Raskin in 1978, [8] with modifications by Timor-Tritsch *et al.* [5] and Jurkovic *et al.* [9] help avoid this pitfall. These criteria include an empty uterine cavity with a barrel-shaped cervix, a gestational sac that is below the level of the internal cervical os, the intact cervical canal between the endometrium and gestational sac, absence of the 'sliding sign', and blood flow around the gestational sac using colour Doppler; all of these features were identified in the patient during transvaginal ultrasonography Apart from the earlier-mentioned, other diagnostic criteria for CEP have been published, further emphasising the inherent diagnostic difficulties. [10]

Surgical and conservative medical modalities of management of CEPs have been described, with various modifications based on expertise and the available technology. Surgical options include suction evacuation with or without cervical curettage, hysteroscopic visualisation and endocervical resection, and cervical amputation. Primary dilatation and curettage may be associated with a 40% risk of hysterectomy, though adjunctive measures can mitigate this. [9] Adjunctive methods of limiting intra- and post-procedural bleeding include intracervical single or double-balloon tamponade, cervical cerclage, femoral artery catheterisation with internal iliac artery or uterine artery embolisation, and ligation of the descending branch of the uterine artery. [5] Nevertheless, many patients experienced significant haemorrhage during surgical management, with eventual recourse to hysterectomy. [11]

Since the report of conservative medical management of CEP using methotrexate in 1953, there have been many reports of successful use of methotrexate and other trophotoxic agents. This option is the first line, especially when the patient is not bleeding actively and fertility preservation is desired. Methotrexate with or without adjunctive foeticide is the most commonly used agent and may be administered systemically (usually intramuscularly) or locally via intracervical or ultrasound-guided intra-amniotic instillation. [12] While overall success rates of 80-90% have been reported with methotrexate, [12] there is currently no evidence on the route or dose that is most effective. Hung *et al.* reported that decreased success of methotrexate therapy might be recorded in CEPs with gestational age >9 weeks, serum β-HCG level >10,000 mIU/mL, viable foetus and CRL >10 mm. [13] Multiple doses of methotrexate may, therefore, be needed in such cases. The index patient was carefully evaluated, and none of these criteria was present. Thus, this may explain her rapid response to the single dose of methotrexate that was administered. Other medical options include local injection of potassium chloride, prostaglandins, mifepristone, actinomycin-D, and etoposide. A combined approach of uterine artery embolisation with systemic methotrexate administration has also been described with a good outcome. [10] The response of patients with CEP to conservative management should be monitored, using a combined plan of care that involves clinical evaluation, serial serum β-HCG assay and transvaginal ultrasonography until the symptoms resolve completely. [5]

Conclusion

CEP may present a diagnostic dilemma. A high index of suspicion and appropriate sonographic skills are required for prompt diagnosis and management to minimise the associated morbidities. Conservative management with methotrexate in appropriately-selected women is associated with a high success rate and fertility preservation.

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and follow-up. The final manuscript was critically reviewed and approved by all the authors.

Conflict of Interest: None.

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