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Case Report

Medical Management of Unruptured Ectopic Gestation with Successful Outcome at a Private Health Facility in Akure, South West Nigeria

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Abstract
Ectopic pregnancy is a public health issue and a life-threatening condition in Sub-Saharan Africa due to high risk of sexually transmitted infections. While surgical option of management is often advocated for cases of ruptured ectopic gestation, unruptured cases can be managed medically especially where fertility is of a major concern. The case presented is that of a 30-year old GIP0+0 who presented at a private health facility with mild right sided lower abdominal pain and spotting per vaginal of 2days duration at a gestational age of 7weeks and 2days, she was haemodynamically stable. A pelvic Ultrasound done showed a right sided gestational sac with no cardiac activity and an empty uterus. Serum β HCG done was 913mIU/ml. She was managed as a case of unruptured ectopic gestation with intramuscular methotrexate injections and she had a complete resolution of the ectopic gestation as evidenced by the disappearance of the symptoms and biochemical assessment of the level of serum β HCG which dropped to zero.

Keywords: Unruptured ectopic, Methotrexate, Private facility, Successful Outcome

INTRODUCTION
Ectopic pregnancy is a major cause of maternal morbidity and mortality especially in the first trimester of pregnancy [1]. It is commoner in Nigeria due to a high risk of sexually transmitted infections [2]. Currently, a high index of suspicion, serial serum β- Human Chorionic Gonadotrophin (β- HCG) assay coupled with transvaginal ultrasound can facilitate early diagnosis and treatment before rupture occurs [3]. Different modalities of management of unruptured ectopic pregnancy have been advocated which include surgical, medical and expectant [1]. While the surgical option is often indicated in cases of ruptured ectopic, the use of medical treatment may be considered in the unruptured cases with gestational sac of <3.5cm, no fetal cardiac activity seen on ultrasound and a quantitative serum β-HCG level of <5000 mIU/ml [1].

Methotrexate (MTX) is a folic acid antagonist that is highly toxic to rapidly replicating tissues, it achieves results comparable to surgery for the treatment of appropriately selected unruptured ectopic pregnancies and is used commonly as a drug of choice in the medical treatment of unruptured ectopic pregnancy [4]. Surgery is specifically indicated in cases of suspected tubal rupture and when methotrexate is contraindicated such as in patients with chronic liver disease, pre-existing blood dyscrasias, pulmonary disease, peptic ulcer disease and immunodeficiency. Additionally, patients who have sensitivity to methotrexate, that have an intrauterine pregnancy, or are breastfeeding are not candidates for methotrexate therapy [1].

Ideally, a candidate for medical management with MTX should meet the following criteria: hemodynamic stability, no severe or persistent abdominal pain, commitment to follow-up until the ectopic pregnancy has resolved, and must

have normal baseline liver and renal function test results. When the criteria described are fulfilled, treatment with MTX yields treatment success rates comparable to those achieved with conservative surgery [6].

Cases of unruptured ectopic gestation requiring medical treatment are mostly managed in a teaching hospital setting to enhance knowledge and for prompt intervention if rupture occurs. However, this case presented was diagnosed and fully managed at a private facility with regular follow up visits by the patient. It is presented to emphasize the fact that with high index of suspicion, adequate facilities in place for monitoring and with good compliance to treatment and follow up patients who present early with unruptured ectopic gestation and who meet all the conditions for medical management may be considered for such treatment.

CASE REPORT

This case was a 30-year old $G_1P_0^{+0}$ married lady whose last menstrual period was on the 22nd of December 2022 and she presented with amenorrhoea of 7weeks and 2days, spotting per vaginal and mild right sided abdominal pain at a private facility in Akure (Skye Hospital) on the 10th of February 2023. Pregnancy was said to have been spontaneously conceived and desired. She had done urine pregnancy test 2weeks after her missed period which was positive. She developed the symptoms 2days prior to presentation at the facility but there was no associated dizziness nor fainting spell, no passage of fleshy materials but pain was said to radiate to her back. There was no use of any abortificient agents. There were no urinary symptoms nor change in bowel habits. No associated fever nor vomiting. She was managed for pelvic inflammatory disease at the same facility 4 weeks earlier with antibiotics when she complained of having foul smelling vaginal discharge, fever and lower abdominal pain and she had antibiotics treatment for 2weeks based on the high vaginal swab for microscopy, culture and sensitivity result. She menstruated for 4days in a regular cycle of 28days. She was aware of contraception but had never used any. She was not aware of pap smear. She was not a known hypertensive nor diabetic, not a known sickle disease patient and had never been transfused. She was married in a monogamous family setting to a 35-year old Naval officer, she never took alcohol nor smoked cigarettes. There was no history of allergy to any drug.

On examination she was afebrile, not pale, not jaundiced, not in any obvious respiratory distress, not dehydrated, acyanosed and had no pedal oedema. Cardiovascular examination revealed a blood pressure of 120/60mmHg, pulse rate of 92beats/minute and heart sounds I & II with no murmurs. Respiratory examination findings showed a respiratory rate of 24cycles/minute and the chest was clinically clear. Abdominal examination showed a flat abdomen which moved with respiration with mild tenderness on the right iliac fossa. The liver, spleen, kidneys and the uterus were not palpably enlarged. Vaginal examination showed minimal altered blood on her pad, no active bleeding per vagina, normal vulva and vaginal, cervical os was closed with no palpable lesion, cervical excitation tenderness was negative and the uterus was about 6weeks size on bimanual palpation, pouch of douglas was not bulging; gloved fingers were stained with minimal altered blood. Rectal examination done showed empty rectum and no abnormality on the pelvic side wall.

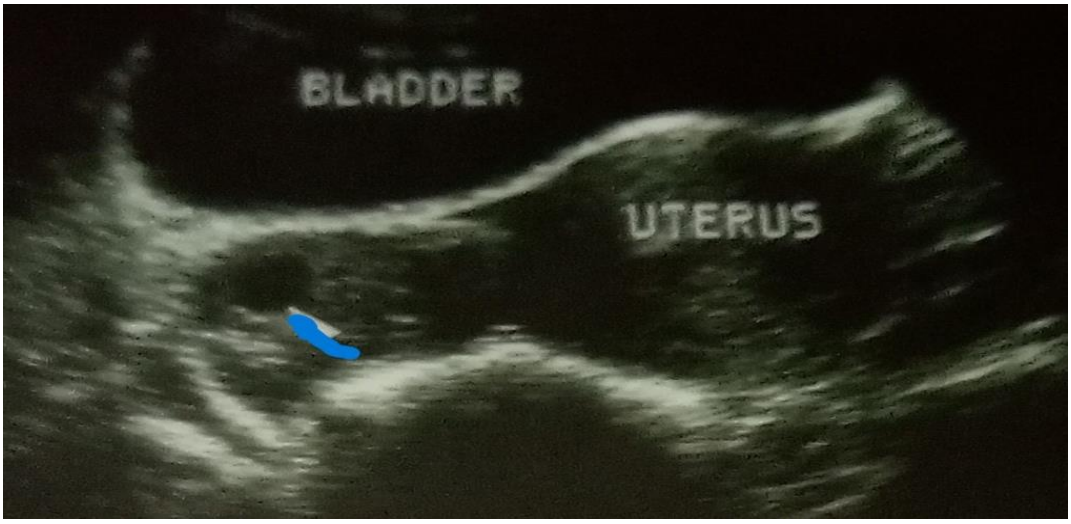
Investigations done included a packed cell volume (PCV) which was 35%, Serum pregnancy test which was positive, serum β-HCG which was 913mIU/ml and an Ultrasound which showed an empty anteverted uterus, a right sided adnexal mass which measured 3.2 x2.4cm with no cardiac activity and no haemoperitoneum. See picture below (Ultrasound Image1).

Based on her history, the examination findings, serum β HCG result and the Ultrasound findings she was counselled for medical treatment with methotrexate and she further had the following investigations done: Full blood count, Liver function test and electrolyte, urea and creatine which were all within normal range. She was screened for HIV and hepatitis B surface antigen which were not reactive.

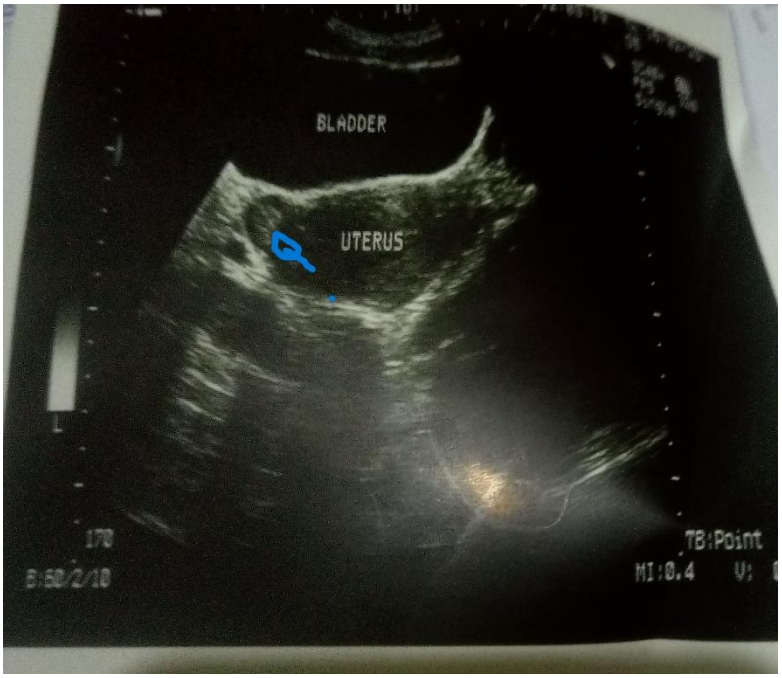
She was managed on outpatient with alternate day intramuscular methotrexate injections at 50mg/m^2 on the 11th, 13th and 15th of February 2023. Her vital signs remained stable throughout her visits. She had no symptoms suggestive of methotrexate toxicity.

On the 17th of February 2023 she noticed that the spotting per vaginal and the abdominal pain had subsided and she was asked to do a repeat serum β HCG which was zero, her repeat PCV was still 35%. She also had a repeat Ultrasound done on the same day which was normal with no adnexal mass seen as shown below (Ultrasound Image 2). Her vital signs were stable and there were no significant findings on examination. She was reassured and further counselled on the symptoms of methotrexate toxicity. She was given a week appointment to have a repeat β- HCG. On the 24th of February 2023, she presented to the facility for check-up, she had no complaint, there were no significant findings on examination, her vital signs remained stable and a repeat serum β- HCG done was still zero. She was finally discharged and counselled to present early if she misses her period again.

Ultrasound Image 1:



Ultrasound Image 2



DISCUSSION

This was a case of an unruptured ectopic gestation with an antecedent history of pelvic inflammatory disease prior to conception which was successfully managed medically with methotrexate at a private health facility.The use of methotrexate to treat unruptured ectopic pregnancy was first cited in 1982 where several protocols of administration was advocated including single dosing and the use of multiple doses of methotrexate with the concomitant use of leucovorin rescue necessitating multiple hospital visits by the patient that could affect convenience [7] .Therefore, in an attempt to increase efficacy and maintain convenience, a novel protocol was introduced in 2007 which is the two-dose protocol that maximized the dose of methotrexate without the need for leucovorin rescue [8] as was done in this case.

In deciding whether a patient is a suitable candidate for medical management, it is essential to evaluate factors that could be associated with success and failure rates. According to Menon et al in 2007, women with HCG values of > 5,000mIU/ml, an ultrasound with moderate-large free fluid, fetal cardiac activity, continuous increase in serum HCG over a 48-hour period have all been associated with failure of medical management [9]. A study by Mol et al recommends single dose methotrexate for those with HCG values of <1,500mIU/ml and multi-dose methotrexate for those with HCG values of ≤ 3,000mIU/ml, however the study did not establish a cut off value of HCG at which success could be

achieved with methotrexate [10]. The success rate of medical treatment of unruptured ectopic gestation with methotrexate decreases with increasing levels of serum HCG.The decision to proceed with medical or surgical management still depends on the clinician's discussion with the patient.

Additional considerations in the choice of patients who can receive medical therapy for unruptured ectopic gestation is compliance and follow up visits. The use of methotrexate necessitates multiple office visits and surveillance of HCG values for weeks. A second often unrealized drawback is that women can be falsely reassured that the treatment for the ectopic pregnancy is complete at the time of the first injection which may interfare with the necessary follow up visits. One study assessing compliance of methotrexate therapy noted that only 45.5% of patients completed follow-up which was defined as documented resolution of the level of HCG to zero, only 19.7% completed the appropriate follow-up which was defined as declining HCG levels on day 4, day 7 and weekly until levels declined to zero while a total of 24% required surgery [11]. Patients who are non-compliant with visits may not be appropriate candidates for methotrexate treatment, as this may put them at greater risk for adverse events. This patient was compliant with all her visits during which her vital signs were continuously checked for signs of rupture and the level of HCG was monitored until complete resolution, these contributed to the reported success in the outcome.

When administering methotrexate therapy for unruptured ectopic gestation, it is essential to remain aware of the risk and its side effects. A major risk of medical treatment with methotrexate is rupture of the ectopic gestation and this has been reported in 7-14% of cases [12]. The rate of increase in the level of the HCG is a predictor of rupture which is an important sign to watch out for during the follow up visits. Similarly, the sside effects of methotrexate should not be overlooked. The most common side effects are mild and include nausea, vomiting, stomatitis, diarrhoea, and elevated liver function tests. Severe side effects of methotrexate such as nephrotoxicity, interstitial pneumonitis and alopecia dermatitis are not common because of the dose and the short duration of use. These side effects were not seen in this patient, this was also probably because of the short duration of use.

CONCLUSION

Patients who present with unruptured ectopic gestation especially where fertility is of major concern, who can comply with medication and follow up and who have no contraindication to methotrexate may be considered for medical treatment. However, it is important to remember that there could be a risk of rupture while choosing a medical treatment modality and this requires careful patient selection. Therefore, while considering medical treatment of unruptured ectopic gestation, there should be a clear documentation of the diagnostic and management strategies with clinical, sonographic and biochemical assessment of the patient.

CONFLICTS OF INTEREST: None declared.
CONSENT: Consent was taken from this patient to publish this report.

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