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Research Article

A Successful Methotrexate Management Of Pregnancy Of Unknown Location (Pul) With Associated Pre-Existing Leukopenia: A Case Study.

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Abstract

This report describes a 45-year-old female who was diagnosed with pregnancy of unknown location (PUL) and successfully treated with methotrexate (MTX), despite having minor leukopenia and neutropenia. Serial β-hCG levels plateaued without ultrasonography indicating the possibility of pregnancy. Following a hematology consultation, MTX was provided with close hematological monitoring, resulting in stable clinical results without problems.

Keywords: *Pregnancy of unknown location, methotrexate, ectopic pregnancy, transient leakopenia.*

INTRODUCTION

Pregnancy of unknown location (PUL) is diagnosed when no intrauterine or ectopic gestation is seen on transvaginal ultrasound despite a positive pregnancy test and elevated β-hCG [1].

This entity requires careful follow-up to prevent rupture from undetected ectopic pregnancy or unnecessary intervention in early intrauterine pregnancy [2].

Methotrexate (MTX) is a folate antagonist used as first-line treatment for selected cases of ectopic pregnancy and some PULs, provided the patient is stable, β-hCG levels are relatively low, and there are no contraindications [3]. MTX may cause myelosuppression,hepatotoxicity, and mucositis, making baseline laboratory evaluation essential [4].

Leukopenia and neutropenia are relative contraindications; most guidelines advise withholding MTX if ANC <1.0×10³/μL [3,5]. However, evidence is limited on MTX use in patients with mild pre-existing leukopenia. This report presents such a case, highlighting the role of multidisciplinary decision-making and close hematologic monitoring.

CASE PRESENTATION

A 45-year-old woman, gravida 8 para 5 (two prior first-trimester spontaneous abortions), presented to the early pregnancy assessment unit with amenorrhea of approximately 7 weeks by last menstrual period (25 January 2025). She reported no abdominal pain, vaginal bleeding, fever, or systemic symptoms. Her obstetric history included five uncomplicated spontaneous vaginal deliveries; she had no significant gynecologic or medical history and was on no regular medications.

On examination, she was afebrile, blood pressure 118/72 mmHg, pulse 84 bpm, and oxygen saturation 98% on room air. Abdominal and pelvic examination were unremarkable; there was no adnexal tenderness or palpable mass.

Initial laboratory investigations revealed β-hCG of 328 mIU/mL (16 March 2025), which dropped slightly to 295 mIU/mL (18 March) but then increased to 325 mIU/mL (20 March),

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demonstrating a plateau pattern. Complete blood count (CBC) showed leukopenia with WBC 3.15×10³/μL and absolute neutrophil count (ANC) 1.24×10³/μL. Hemoglobin was 13.2 g/dL,and platelets were 265×10³/μL. Renal and liver function tests were normal.

Transvaginal ultrasound performed twice, by different operators, demonstrated an empty uterus with thin endometrium, no adnexal mass, and no free fluid in the pelvis.

Given the plateauing β-hCG and absent intrauterine pregnancy, ectopic pregnancy was suspected. However, the patient's baseline leukopenia raised concerns regarding MTX administration. Hematology consultation was sought, and the assessment concluded that the leukopenia was mild, likely transient, and not associated with infection. Vitamin B12 and folate levels were within normal limits. The hematologist advised that MTX could be given with strict weekly CBC monitoring and readiness to initiate granulocyte colony-stimulating factor (G-CSF) if ANC fell below 0.5×10³/μL or if febrile neutropenia developed.

On 20 March 2025, the patient received a single intramuscular dose of MTX 79.5 mg (50mg/m²). She was counseled to avoid folic acid, NSAIDs, and pregnancy for at least 3 months.

Barrier contraception was advised. She was also instructed to report immediately if she developed fever, sore throat, mucositis, or abdominal pain.

Follow-up on day 4 post-MTX showed β-hCG 279 mIU/mL, WBC 3.35×10³/μL, ANC 1.01 ×10³/μL. The patient remained asymptomatic. Day 7 post-MTX revealed β-hCG 183 mIU/mL, ANC 0.77×10³/μL, but she remained afebrile with no signs of infection. No G-CSF was given.

By day 14, β-hCG had dropped to 54 mIU/mL, and ANC had started to recover. On 16 April 2025, β-hCG was <2.3 mIU/mL, WBC 3.87×10³/μL, ANC 1.74×10³/μL. The patient was discharged from both gynecology and hematology follow-up without complications.

DISCUSSION

MTX is an established treatment for selected ectopic pregnancies and PUL [1,3]. Baseline hematologic abnormalities, particularly neutropenia, may increase the risk of infectious complications [4,5]. Our patient had mild neutropenia at baseline, with ANC above 1.0×10³/μL, which is a threshold often considered safe for MTX in non-oncology settings when close monitoring is available [6,7].

The observed ANC nadir on day 7 (0.77×10³/μL) is consistent with the expected timing of MTX-induced myelosuppression [4]. The absence of clinical infection and spontaneous recovery without intervention aligns with previous reports of transient MTX-related neutropenia [5,8].

This case demonstrates that in a stable patient with mild pre-existing leukopenia, MTX may be used safely if there is hematology input, strict follow-up, and access to rescue therapies.

Avoiding unnecessary surgery in a hemodynamically stable patient also aligns with current recommendations favoring medical management in selected cases [3].

CONCLUSION

MTX may be considered in PUL with mild pre-existing leukopenia in tertiary care settings with specialist oversight and vigilant hematologic monitoring. Individualized assessment remains essential.

Author Contributions

- Hana Ahmad Albahi – Conceptualization, patient management, manuscript review.
- Yassir Abdulahd A Turkistani – Hematology evaluation, interpretation of laboratory findings, manuscript review.
- Renad M. Alsaedi – Data collection, manuscript drafting, literature review, reference formatting.

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Patient Consent and ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying data. The patient understood that personal identifiers would be removed, and anonymity would be maintained.

Ethical approval is waived according to Saudi Arabia Moh IRB guidelines regarding case reports.

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