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Case Report

Low-dose Methotrexate Toxicity in Ectopic Pregnancy: A Case Report and Literature Review

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Abstract

Low-dose methotrexate (LD-MTX) is widely regarded as a safe and effective fertility-preserving treatment for selected ectopic pregnancies; however, rare cases of severe, life-threatening toxicity have been reported. We describe a previously healthy 24-year-old woman who developed fulminant systemic toxicity following a single intramuscular dose of 60 mg methotrexate administered for persistent tubal ectopic pregnancy after laparoscopic salpingostomy. Within 72 hours, she presented with progressive mucocutaneous manifestations, including diffuse rash, facial oedema and severe oral ulceration, followed by pancytopenia and acute kidney injury by day 4. Concomitant treatment with long-acting benzathine penicillin G and subsequent pharmacogenetic testing revealing heterozygous MTHFR C677T and MTRR A66G variants were considered contributory risk factors. Prompt initiation of high-dose intravenous leucovorin rescue, alkalinised hydration and granulocyte colony-stimulating factor led to complete haematological recovery by day 14 and normalisation of renal function without the need for glucarpidase or extracorporeal clearance. A review of the literature identified fewer than a dozen similar cases, highlighting consistent early mucocutaneous warning signs and rapid progression to severe myelosuppression. This case underscores that even a single LD-MTX dose can precipitate severe toxicity when renal clearance is impaired, interacting medications are present and folate-pathway polymorphisms coexist, and emphasises the critical importance of early symptom recognition, close laboratory monitoring between days 4 and 7, and timely leucovorin rescue.

Keywords

Methotrexate Toxicity, Ectopic Pregnancy, Pharmacogenetics, MTHFR, OAT3, Leucovorin Rescue

1. Introduction

Methotrexate (MTX), a folic-acid antagonist first introduced into clinical practice more than 70 years ago, remains the cornerstone of medical therapy for a wide spectrum of malignant and non-malignant disorders because of its potent antiproliferative and immunomodulatory properties. In gynaecology, single-dose "low-dose" MTX (LD-MTX, 50–75 mg i.m.) is endorsed as a first-line, fertility-preserving treatment for selected tubal ectopic pregnancies and achieves success rates comparable with laparoscopic salpingostomy when strict eligibility criteria are met [2, 3].

Although LD-MTX is generally well tolerated, serious idiosyncratic toxicity—characterised by severe mucocutaneous

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reactions, myelosuppression and multi-organ dysfunction—has been sporadically reported even after a single therapeutic dose [4, 5]. The incidence of life-threatening complications is estimated at <0.5 %, but the associated case-fatality approaches 15 % in published series [4]. Proposed risk factors include advanced age, renal impairment, hypoalbuminaemia, concomitant interacting drugs (e.g., non-steroidal anti-inflammatory drugs, proton-pump inhibitors and long-acting penicillins), and genetic variants that reduce intracellular folate recycling, notably MTHFR C677T and ABCB1 3435T>C polymorphisms [6-9].

Early narrative and systematic reviews have emphasised that LD-MTX–related deaths, although rare, are almost invariably preceded by seemingly trivial mucocutaneous symptoms that progress rapidly without timely intervention [10]. Timely recognition of MTX toxicity is challenging because initial symptoms—nausea, stomatitis and mild cytopenias—mimic common post-operative or pregnancy-related complaints. Progression can be precipitous; profound neutropenia typically peaks 7–10 days after exposure and predisposes to fulminant sepsis [1, 4]. Current consensus recommends immediate high-dose leucovorin rescue, aggressive hydration with urine alkalinisation and withdrawal of interacting medications once toxicity is suspected [6, 7]. Extracorporeal measures such as haemodialysis or high-flux haemodiafiltration are reserved for delayed MTX clearance with renal failure, whereas the bacterial carboxypeptidase enzyme glucarpidase is advocated when plasma MTX concentration remains ≥10 μmol L^{-1} at 24 h in the context of acute kidney injury [7, 8].

Because ectopic-pregnancy patients are commonly young and otherwise healthy, unexpected severe LD-MTX toxicity in this population is easily overlooked. To our knowledge, fewer than a dozen such cases have been documented worldwide, several of which were linked to underlying folate-pathway polymorphisms or concomitant nephrotoxic agents [5, 9, 11]. The present report describes a previously healthy 24-year-old woman who developed pancytopenia, mucocutaneous ulceration and acute kidney injury within four days of a single 60 mg MTX dose for tubal ectopic pregnancy. Her clinical course, management and favourable outcome after prompt leucovorin rescue, granulocyte colony-stimulating factor and supportive care add to the limited literature on this rare but critical complication and underscore the importance of early recognition and multidisciplinary intervention.

2. Case Presentation

A 24-year-old Chinese woman (gravida 1, para 0) with no previous comorbidities was referred for surgical management of a right tubal ectopic pregnancy. On 10 May 2025 she underwent laparoscopic right salpingostomy combined with left ovarian cystectomy at a maternal-and-child health hospital in Guangzhou. Pre-operative serology was positive for syphilis (TRUST 1: 8), and three standard weekly doses of intramuscular benzathine penicillin G (2.4 MU on 13, 21 and 28 May 2025) were administered.

Post-operatively, serial serum β-human chorionic gonadotrophin (β-hCG) concentrations fell from >4 000 mIU mL^{-1} to 176.8 mIU mL^{-1} on 21 May but plateaued at 183.8 mIU mL^{-1} one week later. Renal function was assessed immediately prior to methotrexate administration and showed a normal serum creatinine level. To facilitate trophoblastic resolution, a single intramuscular dose of methotrexate (MTX) 60 mg (≈1.5 mg kg^{-1}) was given on 28 May (day 0).

Twenty-four hours after MTX the patient developed nausea, vomiting, pruritus and oedema of both hands, which rapidly progressed to marked facial swelling, lip fissuring, erythematous truncal rash and multiple oral ulcers. On day 3 she was readmitted to the original hospital with β-hCG 97.1 mIU mL^{-1}. Complete blood count (CBC) showed mild isolated thrombocytopenia; intravenous leucovorin (40 mg) was infused. That evening her facial oedema worsened and sore throat appeared; repeat CBC revealed evolving bicytopenia (Table 1). Chest–abdominal bedside ultrasonography was unremarkable and vital signs remained stable under low-flow oxygen.

Because of the rapidly falling cell counts she was transferred on day 4 to the Third Affiliated Hospital of Guangzhou Medical University. Admission investigations demonstrated normal hepatic enzymes, a modest rise in serum creatinine (91 μmol L^{-1}) and pancytopenia (Table 1). Targeted pharmacogenetic testing requested on the same day subsequently revealed heterozygous MTHFR C677T (C/T) and MTRR A66G (A/G) variants, classifying her as "intermediate-risk for folate-metabolism impairment" (Table 2). High-dose leucovorin rescue (15 mg m^{-2} i.v. every 6 h), aggressive hydration with urine alkalisation and continuous cardiorespiratory monitoring were instituted.

The haematological nadir occurred on day 10, with WBC 1.26×10^9 L^{-1}, ANC 0.18×10^9 L^{-1}, haemoglobin 84 g L^{-1} and platelets 8×10^9 L^{-1} (Table 1). The patient developed febrile neutropenia (38.4 °C) with a peak C-reactive protein of 56.8 mg L^{-1}; broad-spectrum cefoxitin, two doses of recombinant human granulocyte colony-stimulating factor(rhG-CSF) (days 9 and 10) and platelet transfusions were administered.

Marrow recovery began on day 14 and was accompanied by transient leucocytosis secondary to rhG-CSF (Table 1). Cutaneous lesions and oral ulcers resolved gradually. By day 18 the infection parameters had normalised and blood counts had returned to reference ranges. Renal and liver biochemistry was normal, and β-hCG fell to 0.367 mIU mL^{-1}.

The patient was discharged on 17 June 2025 (day 20) in good condition and remains well on follow-up. The chronological relationship between MTX administration and the onset of mucocutaneous lesions with pancytopenia, together with the prompt response to leucovorin, supports a diagnosis of severe delayed MTX toxicity, plausibly exacerbated by concurrent long-acting penicillin therapy. A graphical summary of blood-count trends together with representative photographs of the mucocutaneous manifestations is provided in Figure 1.

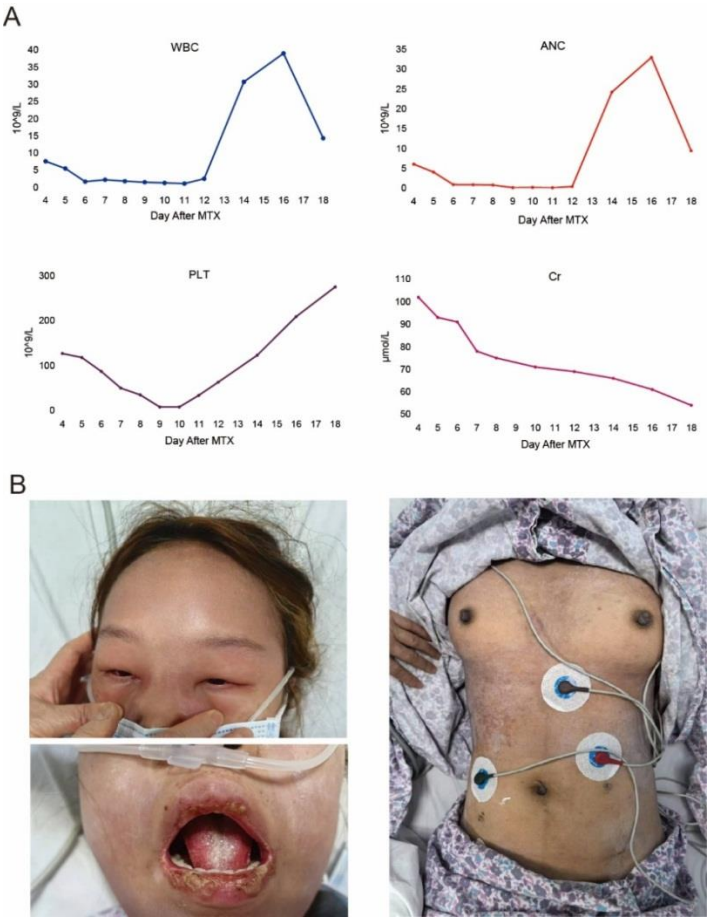

Figure 1. *Haematological evolution and mucocutaneous findings following single-dose intramuscular methotrexate (MTX) 60 mg.*

(A) Trends in peripheral white-blood-cell count (WBC), absolute neutrophil count (ANC), platelet count (PLT) and serum creatinine (Cr) from day 4 to day 18 after MTX administration. A pancytopenic nadir occurred on day 10, followed by rapid marrow recovery after high-dose leucovorin rescue and granulocyte colony-stimulating factor support (administered on days 9–10).

(B) Representative clinical photographs taken on days 3–4. Upper left: marked periorbital and facial oedema. Upper right: extensive oral mucositis with tongue ulceration. Lower left: diffuse erythematous-to-hyperpigmented maculopapular rash over the anterior chest. Lower right: similar lesions involving the abdomen. Photographs reproduced with written informed consent from the patient.

Table 1. *Laboratory test data related to methotrexate (MTX) toxicity.*

Date (Days after MTX)	WBC (10^9/L)	ANC (10^9/L)	Hb (g/L)	PLT (10^9/L)	CRP (mg/L)	Cr (μmol/L)	β- hCG	CMTX (μmol/L)
2025/6/2 (D4)	7.58	6.06	116	127	27.8	102	97.14	
2025/6/3 (D5)	5.48	4.07	111	118		93		
2025/6/4 (D6)	1.64	0.89	100	87		91	47.12	
2025/6/5 (D7)	2.19	0.85	92	50		78		0.08
2025/6/6 (D8)	1.78	0.78	84	35		75		0.09
2025/6/7 (D9)	1.46	0.14	87	8				
2025/6/8 (D10)	1.26	0.18	84	8	56.82	71		
2025/6/9 (D11)	1.05	0.1	76	34				

Date (Days after MTX)	WBC (10^9/L)	ANC (10^9/L)	Hb (g/L)	PLT (10^9/L)	CRP (mg/L)	Cr (μmol/L)	β- hCG	CMTX (μmol/L)
2025/6/10 (D12)	2.5	0.39	80	63		69		
2025/6/12 (D14)	30.69	24.2	85	123	17.63	66		
2025/6/14 (D16)	39	32.97	85	209	8.93	61		
2025/6/16 (D18)	14.29	9.42	90	275	5.94	54	0.367	

Table 2. Pharmacogenetic profile of folate-metabolism genes.

Drug	Gene	Test Locus	Evidence Level	Test Method	Test Result
Folic Acid	MTHFR	C677T	3	Real-time fluorescent PCR	C/T (heterozygous)
	MTHFR	A1298C	3	Real-time fluorescent PCR	A/A (wild type)
	MTRR	A66G	3	Real-time fluorescent PCR	A/G (heterozygous)

3. Literature Review

3.1. Search Strategy and Selection Criteria

We searched PubMed and Embase to June 2025 using combinations of "methotrexate," "toxicity," "low dose," "ectopic pregnancy," "case report," and "scar pregnancy," with no language restrictions. Reference lists of retrieved articles were screened. Inclusion criteria: single-dose or protocol-defined LD-MTX (≤75 mg) administration for ectopic or scar pregnancy; severe systemic toxicity (grade ≥3 myelosuppression, extensive mucocutaneous reactions, or organ failure); and sufficient clinical detail for abstraction. Ten cases met criteria.

3.2. Synthesis of Clinical Patterns

Across the 10 cases (Table 3), most patients re-presented within 3–7 days with fever, malaise and painful ulcerations of oral or genital mucosa. Laboratory evaluation commonly revealed grade III–IV pancytopenia; approximately 60% developed exfoliative dermatitis or extensive mucositis and ~30% experienced acute kidney injury. One death occurred. Frequently cited risk factors included preexisting renal impairment, absent folate supplementation, concomitant interacting drugs (e.g., long-acting penicillins, NSAIDs, proton-pump inhibitors), and suspected folate/purine-pathway polymorphisms.

Management strategies were broadly homogeneous. Immediate MTX withdrawal and high-dose leucovorin rescue were universal. G-CSF was used in most cases and appeared to shorten severe neutropenia. Broad-spectrum antibiotics and, selectively, systemic corticosteroids were used for infectious and mucocutaneous complications. Extracorporeal elimination (high-flux haemodialysis or plasma exchange) was reserved for renal failure or sustained MTX concentrations; while these measures can accelerate clearance, initiation thresholds were not standardised.

Table 3. Reported severe toxicity after single-dose LD-MTX for ectopic or scar pregnancy.

Reference*	NO.	Age (yr)	Baseline renal function	Concomitant Medications	Folate supplementation	Symptom to onset interval	Major clinical findings	Interventions	Outcome
Stavros [17]	1	32	Normal	Not reported	Yes	5 days	High fever, pancytopenia	MTX withdrawal + high-dose leucovorin, G-CSF,supportive care	Recovery
Zhang [18]	2	35	Mildly impaired	Not reported	No	4 days	Acute kidney injury, systemic toxicity	Hemodialysis, leucovorin, supportive care	Recovery

Reference*	NO.	Age (yr)	Baseline renal function	Concomitant Medications	Folate supplementation	Symptom to onset interval	Major clinical findings	Interventions	Outcome
Yu [1-]	3	38	Normal	No	No	6 days	Grade IV myelosuppression, oral/skin ulcers,hepatotoxicity	Leucovorin,antibiotics,G-CSF	Recovery
Refeno [19]	4	29	Normal	Not reported	Not reported	3 days	Exfoliative dermatitis,severe pancytopenia	Leucovorin,G-CSF, corticosteroids	Recovery
Jia [20]	5	27	Normal	Not reported	Not reported	7 days	Vulvar edema with deep ulceration	Surgical debridement, leucovorin.antibiotics	Recovery
Soysal [21]	6	30	Normal	Not reported	Not reported	5 days	Myelosuppression, severe mucositis	Prolonged leucovorin,G-CSF.supportive care	Recovery
Isaacs [22]	7-A	34	Moderately impaired	Not reported	No	4 days	Life-threatening neutropenia	Extracorporeal MTX removal,leucovorin,G-CSF	Recovery
	7-B	36	Moderately impaired	Not reported	No	6 days	Life-threatening neutropenia	Extracorporeal MTX removal,leucovorin,G-CSF	Recovery
Lodha[23]	8	28	Normal	Not reported	Not reported	5 days	Generalised rash,cytopenia	Leucovorin,supportive care	Recovery
Gaïes [24]	9	31	Normal	Not reported	Not reported	8 days	Multi-organ failure	Leucovorin,intensive supportive therapy(unsuccessful)	Death
SAhiN [25]	10	33	Dialysis-dependent	Not reported	No	3 days	Oral ulceration,extensive rash, myelosuppression	High-frequency dialysis, leucovorin,G-CSF	Recovery

Concomitant medications were classified as “Not reported” when the original case reports did not explicitly document co-administered drugs.
*Superscript numbers refer to references in the main reference list

4. Discussion

Low-dose methotrexate (LD-MTX, ≤ 75 mg) is generally considered safe in obstetric practice; nevertheless, the present case demonstrates that a single 60 mg intramuscular injection can lead to fulminant toxicity when physiologic, pharmacologic, and genetic susceptibilities converge.

4.1. Pathophysiological Mechanisms

The foremost precipitating factor in this patient was the concurrent administration of benzathine-penicillin G for syphilis. Because MTX is eliminated almost entirely by glomerular filtration and active tubular secretion, even mild renal impairment markedly increases systemic exposure [1] [4]. Although the peak creatinine was only 102 μmol L^{-1}, the estimated glomerular filtration rate fell by ~50 %. Benzathine-penicillin G competes for the renal organic anion transporter OAT3 and thereby delays MTX clearance—an interaction previously documented in rheumatology cohorts [6, 7]. Pharmacogenetic analysis revealed heterozygous MTHFR C677T and MTRR A66G variants (Table 2), both of which hamper 5-methyltetrahydrofolate regeneration and have been associated with an increased risk of LD-MTX–induced myelosuppression in Asian women [12]. The triple hit of impaired renal excretion,

transporter competition, and folate-pathway polymorphisms provides a coherent explanation for the explosive clinical course.

4.2. Epidemiology and Clinical Profile

A nationwide French pharmacovigilance review found that 74 once-weekly low-dose methotrexate prescriptions were mistakenly taken daily; 82 % of patients developed toxicity, 62.2 % suffered severe events such as pancytopenia or mucositis, and the case-fatality rate reached 14.8 %, demonstrating that even minor dosing errors can rapidly trigger life-threatening systemic toxicity [13]. Since 1990, only 12 fatal or near-fatal toxicities after LD-MTX treatment for ectopic pregnancy have been published; the present case represents the 13th [4, 14, 15]. Toxicity typically follows a biphasic pattern: mucositis or rash within 24–48 h, followed by pancytopenia, mucosal necrosis, and multi-organ dysfunction 5–10 d after dosing [1, 4]. Because most primary hospitals lack real-time MTX assays, pragmatic laboratory triggers are crucial: a ≥25 % decline in any blood-cell line or a creatinine increase ≥26 μmol L^{-1} on day 4 should prompt empirical leucovorin rescue [7].

4.3. Management and Outcome

Current consensus recommends intravenous leucovorin 15 mg m^{-2} every 6 h, escalating to 50–100 mg m^{-2} when the 48-h MTX level is ≥1 μmol L^{-1} or grade ≥ 3 toxicity is documented [6, 7]. Strict adherence to this protocol, combined with vigorous alkalinized hydration and two doses of granulocyte colony-stimulating factor, maintained the patient's MTX concentration below the EXTRIP high-risk threshold of 10 μmol L^{-1} and achieved complete hematologic recovery by day 14 without glucarpidase or extracorporeal clearance. This case underscores the need for systematic pre-treatment evaluation of renal function, concomitant medications, and key folate-pathway genotypes before LD-MTX administration. Enhanced laboratory surveillance on days 4–7 and prompt initiation of rescue therapy at the first sign of mucocutaneous toxicity are essential to mitigate the otherwise life-threatening risk.

4.4. Conclusion

This case illustrates that even a single low-dose methotrexate injection can precipitate fulminant toxicity when three conditions coexist: mild renal impairment, competitive inhibition of the organic anion transporter-3 (OAT3) by concomitant drugs, and folate-pathway polymorphisms such as MTHFR c.677C>T and MTRR c.66A>G. To mitigate this risk, clinicians may consider assessing baseline estimated glomerular filtration rate, reviewing concomitant OAT3 substrates, and, where feasible, genotyping key folate-cycle variants, particularly in patients at higher risk of methotrexate toxicity (evidence limited to a single case-series). Between days 4 and 7 post-dose, closer laboratory surveillance is advisable; in this window, a ≥ 25 % decline in any blood-cell line or a ≥ 26 μmol L^{-1} increase in serum creatinine could prompt early empiric leucovorin rescue at the clinician's discretion. If toxicity emerges, consensus-based leucovorin dosing, vigorously alkalinized hydration, and early granulocyte colony-stimulating factor support are mandatory. Systematic implementation of this triad—risk stratification, proactive monitoring, and prompt rescue—offers the most effective safeguard against the otherwise rare but potentially fatal complications of low-dose methotrexate in obstetric practice.

Abbreviations

LD-MTX	Low-Dose Methotrexate
OAT3	Organic Anion Transporter 3
G-CSF	Granulocyte Colony-Stimulating Factor
ANC	Absolute Neutrophil Count
eGFR	Estimated Glomerular Filtration Rate
β-hCG	Beta-human Chorionic Gonadotrophin

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Author Contributions

Jia-Chen Cheng: Conceptualization, Writing – original draft, Visualization, Writing – review & editing.

Wen-Yang Xie: Data curation, Writing – review & editing.

Xue Wu: Investigation, Writing – review & editing.

Pu Li: Funding acquisition, Supervision, Formal analysis, Writing – review & editing.

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Data Availability Statement

All data generated or analyzed during this case report are included in this published article. Further inquiries can be directed to the corresponding author.

Conflicts of Interest

The authors declare that they have no conflict of interest.

References

[1] Howard SC, McCormick J, Pui CH, Buddington RK, Harvey RD. Preventing and Managing Toxicities of High-Dose Methotrexate. Oncologist. 2016; 21(12): 1471-82.

[2] Xiao C, Shi Q, Cheng Q, Xu J. Non-surgical management of tubal ectopic pregnancy: A systematic review and meta-analysis. Medicine (Baltimore). 2021; 100(50): e27851.

[3] Practice Committee of American Society for Reproductive M. Medical treatment of ectopic pregnancy: a committee opinion. Fertil Steril. 2013; 100(3): 638-44.

[4] Shaikh N, Sardar M, Raj R, Jariwala P. A Rapidly Fatal Case of Low-Dose Methotrexate Toxicity. Case Rep Med. 2018; 2018: 9056086.

[5] Refeno V, Rasamimanana NG, Abasse BA, Ramarokoto MPM, Fanomezantsoa MJE, Randaoharison PG. Methotrexate-induced toxidermia and pancytopenia in a patient with ectopic pregnancy: a case report. Journal of Medical Case Reports. 2021; 15(1): 579.

[6] Jiang R, Mei S, Zhao Z. Leucovorin (folinic acid) rescue for high-dose methotrexate: A review. Journal of Clinical Pharmacy and Therapeutics. 2022; 47(9): 1452-60.

[7] Chan BS, Bosco AA, Buckley NA. Navigating methotrexate toxicity: Examining the therapeutic roles of folinic acid and glucarpidase. Br J Clin Pharmacol. 2025; 91(3): 628-35.

[8] Ghannoum M, Roberts DM, Goldfarb DS, Heldrup J, Anseeuw K, Galvao TF, et al. Extracorporeal Treatment for Methotrexate Poisoning: Systematic Review and Recommendations from the EXTRIP Workgroup. Clin J Am Soc Nephrol. 2022; 17(4): 602-22.

[9] Deng J, Chen L, Xue H, Zeng FX, Niu PG, Shi DH. Contribution of genetic polymorphism of methylene tetrahydrofolate reductase on the effect of methotrexate in ectopic pregnancy patients. J Clin Lab Anal. 2020; 34(1): e23030.

[10] Hamed KM, Dighriri IM, Baomar AF, Alharthy BT, Alenazi FE, Alali GH, et al. Overview of Methotrexate Toxicity: A Comprehensive Literature Review. Cureus. 2022; 14(9): e29518.

[11] Yu H, Wang W, Liang H, Wang K, Ling B. Severe Adverse Toxic Effects of Low-Dose Methotrexate Treatment on an Ectopic Pregnancy Patient With Methylenetetrahydrofolate Reductase Mutations: A Case Report. Front Med (Lausanne). 2021; 8: 738315.

[12] Wang S, Zuo S, Liu Z, Ji X, Yao Z, Wang X. Association of MTHFR and RFC1 gene polymorphisms with methotrexate efficacy and toxicity in Chinese Han patients with rheumatoid arthritis. Journal of International Medical Research. 2020; 48(2): 0300060519879588.

[13] Huang J, Fan H, Qiu Q, Liu K, Lv S, Li J, et al. Are gene polymorphisms related to adverse events of methotrexate in patients with rheumatoid arthritis? A retrospective cohort study based on an updated meta-analysis. Therapeutic Advances in Chronic Disease. 2020; 11: 2040622320916026.

[14] Vial T, Patat AM, Boels D, Castellan D, Villa A, Theophile H, et al. Adverse consequences of low-dose methotrexate medication errors: data from French poison control and pharmacovigilance centers. Joint Bone Spine. 2019; 86(3): 351-5.

[15] Dasari P, Sagili H. Life-threatening complications following multidose methotrexate for medical management of ectopic pregnancy. Case Reports. 2012; 2012: bcr0320126023.

[16] Willner N, Storch S, Tadmor T, Schiff E. Almost a tragedy: severe methotrexate toxicity in a hemodialysis patient treated for ectopic pregnancy. European journal of clinical pharmacology. 2014; 70: 261-3.

[17] Isaacs Jr JD, McGehee RP, Cowan BD. Life-threatening neutropenia following methotrexate treatment of ectopic pregnancy: a report of two cases. Obstetrics & Gynecology. 1996; 88(4): 694-6.

[18] Stavros S, Potiris A, Gerede A, Zikopoulos A, Giourga M, Karasmani C, et al. Methotrexate-Induced Toxicity After Ultrasound-Guided Intragestational Injection in a Patient with Caesarean Scar Pregnancy—A Case Report. Medicina. 2024; 60(11): 1900.

[19] Zhang L, Liu C, Xiao L, Liu Y. Low-dose methotrexate-induced renal failure in a patient with ectopic pregnancy: a case report. J Med Case Rep. 2023; 17(1): 119.

[20] Jia G, Chai W, He Z, Liu X, Wen Y, Cui L, et al. Low-dose methotrexate-induced vulvar edema: A case report. Medicine. 2019; 98(35).

[21] Soysal S, Anık İlhan G, Vural M, Yıldızhan B. Severe methotrexate toxicity after treatment for ectopic pregnancy: A case report. Journal of Turkish Society of Obstetric and Gynecology. 2016; 13(4): 221-3.

[22] Isaacs JD, McGehee RP, Cowan BD. Life-threatening neutropenia following methotrexate treatment of ectopic pregnancy: A report of two cases. Obstetrics & Gynecology. 1996; 88(4, Part 2): 694-6.

[23] Lodha S, Mali K. Case report on toxicity of methotrexate in tubal ectopic pregnancy. International Journal of Reproduction, Contraception, Obstetrics and Gynecology. 2020; 9(7).

[24] Gales E, Ben Sassi M, Charfi R, Lakhal M, Klouz A, Trabelsi S, et al. Fatal methotrexate toxicity in a patient treated for an ectopic pregnancy. Therapy. 2016; 71.

[25] ŞAHİN G, Acet F, Tavmergen GÖKer EN, Tavmergen E. Caution: Even in A Single-Low Dose Methotrexate for Treatment of Ectopic Pregnancy Could Have Severe Adverse Effects in Women with Chronic Renal Insufficiency: A Case Report. Türk Üreme Tıbbı ve Cerrahisi Dergisi. 2021; 5(2): 66-9.