CASE REPORT

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Pericardial Tamponade Due to Methotrexate Toxicity: A Case Report

Mustafa Ahmet Afacan[1], İsmail Tayfur[2], Burcu Genç Yavuz[1], Özlem Tataroğlu[3]

[1]*University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey*
[2]*University of Health Sciences Turkey, Sancaktepe Prof. Dr. İlhan Varank Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey*
[3]*University of Health Sciences Turkey, Kartal Dr. Lütfi Kırdar Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey*

Abstract

Methotrexate (MTX) is a folic acid analog that inhibits the growth of rapidly proliferating cells, such as bone marrow or cancer cells, through its anti-inflammatory and anti-proliferative properties. With these characteristics, using MTX for treating moderate or severe psoriatic arthritis results in a significant improvement in the health of patients with this condition. Although MTX has many side effects, pericardial tamponade is a very rare complication. Rapidly progressing tamponade is associated with high morbidity and mortality. Here, we present a case of pericardial tamponade in a 69-year-old female patient due to MTX use and its possible facilitating effect.

Keywords: Methotrexate, psoriatic arthritis, pericardial tamponade

Introduction

Psoriatic arthritis (PsA), a chronic inflammatory disease of the joints, develops in approximately 30% of psoriasis cases and can be accompanied by an extra-articular involvement [1]. Today, despite the availability of the development of new therapeutic agents, MTX remains the main treatment option for PsA due to its strong immunosuppression efficacy and tolerability [2,3]. As an immunosuppressant, weekly, low-dose MTX (7.5 to 25 mg) administered orally or subcutaneously shows great efficacy in PsA [4]. Recent studies have also highlighted the advantages of using methotrexate (MTX) alone or in combination therapy with a TNF-alpha inhibitor or cyclosporine A, resulting in better treatment outcomes and fewer side effects [5]. Although complications associated with MTX treatment have been frequently reported in the literature, pericarditis and pericardial effusion, which are also serositis complications, are quite uncommon ones [6]. Pulmonary toxicity has been well-described and may take various forms. Pulmonary infiltrates are the most commonly encountered form of MTX pulmonary toxicity, and these infiltrates resemble hypersensitivity lung disease.

Case Report

A 69-year-old female presented to the emergency department with dyspnea and syncope. Her anamnesis revealed that the patient had a diagnosis of PsA and had been receiving a single dose of 17.5 mg/week MTX for the last four months due to the lack of symptoms being uncontrolled by steroid treatment. It was also determined that the patient, who had not previously experienced respiratory problems, had complaints of dyspnea and cough for the last 10 days.

During the patient's physical examination in the emergency department, the Glasgow Coma scale remained at 13/15, she was tachycardic with a heart rate of 115 beats/min (sinus rhythm), and her initial blood pressure was 80/65 mmHg. At 72% SaO_2 in room air, she had a temperature of 36.7°C. The patient was observed to have jugular venous fullness, and her respiratory system examination revealed bilateral lung sounds that were more prominent on the right side, reduced breathing sounds, and fine crepitant rales. Additionally, there was 3+ pretibial pitting edema. The patient appeared cachectic and had lost 10 kg within the last two months.

Address for Correspondence: Mustafa Ahmet Afacan, University of Health Sciences Turkey, Haydarpaşa Numune Training and Research Hospital, Clinic of Emergency Medicine, İstanbul, Turkey
Phone: +90 216 336 05 65 **E-mail:** drmustafaahmet@hotmail.com **ORCID-ID:** orcid.org/0000-0003-1045-0681
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The results of laboratory parameters were as follows: pH 7.52, $PaCO_2$ 25.2 mmHg and PaO_2 56 mmHg in blood gas, D-dimer 3,143 ng/mL, total protein 3.7 g/dL, albumin 2.31 g/dL, C-reactive protein 11.2 g/dL, and white blood cell count 14,500 Ul, while the remaining blood parameters were within the normal ranges. An electrocardiogram was performed and showed sinus tachycardia with ST segment depression, best seen in V3-V6 leads. The patient was thought to have had a pulmonary embolism due to hypoxic, hypocarbic respiratory alkalosis, and syncope, but the contrast-enhanced thoracic computed tomography (CT) showed no pulmonary embolism. However, the sagittal and axial plane CT images showed a large pericardial effusion with a compressed small heart. A moderate-sized bilateral pleural effusion was also observed. The patient had clinical and hemodynamic findings consistent with pericardial tamponade (Figures 1, 2). Resuscitation was initiated with intravenous crystalloid and noradrenaline infusion with a target of 65 mmHg mean arterial blood pressure. With a preliminary diagnosis of tamponade, the patient was referred to the cardiology and cardiovascular surgery department where urgent left anterior thoracoscopic pericardiocentesis was performed and a 310 mL effusion was drained. The analysis of the patient's pericardial fluid showed an exudate with 3.2 g/dL total protein, 108 mg/dL glucose, 720 IU/L lactate dehydrogenase, and 1020 density. No pathogen was detected in the culture of the fluid and no malignant cells were detected in the cytological examination. Medical treatment was started, and the patient was discharged as healthy after 11 days of hospitalization.

Discussion

MTX can cause serious or life-threatening side effects, such as muscle weakness, shortness of breath, upper stomach pain, mouth sores, pneumonitis, and MTX-related liver disease, confusion, or seizures [6]. Acute pneumonitis is the most common pulmonary toxicity associated with MTX, although its pathogenesis has not yet been fully elucidated [7]. Apart from lung pathologies, the most feared complications of MTX therapy are chronic liver injury, cirrhosis, and portal hypertension [8]. However, pericardial tamponade due to MTX use that is described in the current case is a very rare complication and has only been reported in two cases in the literature.

Conditions that cause cardiac tamponade include malignancies, acute myocardial infarction, cardiac catheterization procedures, collagen tissue diseases, bacterial or viral infections, tuberculosis, and hypothyroidism [9]. No malignancy, infection, or thyroid dysfunction were detected in the current case. The normal findings of the patient in the control chest X-ray before medical treatment indicate that a clinical change occurred secondary to MTX treatment.

The mechanisms by which low-dose MTX exhibits its therapeutic effect have not yet been fully elucidated. However, renal excretion constitutes the main elimination pathway of MTX [8]. The drug is filtered by glomeruli and undergoes active tubular secretion and reabsorption [10]. Fifty percent of circulating MTX is bound to albumin and excreted by the urinary system at a rate of 65-80% within 12 h of ingestion [11]. The low albumin level of 2.31 g/dL in our patient may have changed the pharmacokinetics of MTX, resulting in a decrease in the excretion of the substance and leading to toxicity in the blood, despite the dose taken. The cachectic appearance of the patient may have been associated with hypoalbuminemia,

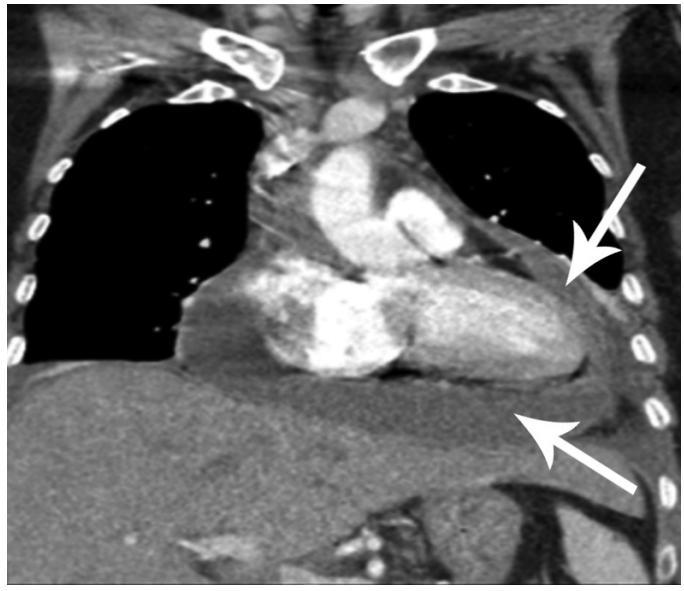

Figure 1. Thoracic computed tomography image in the sagittal plane showing pericardial effusion (arrows)

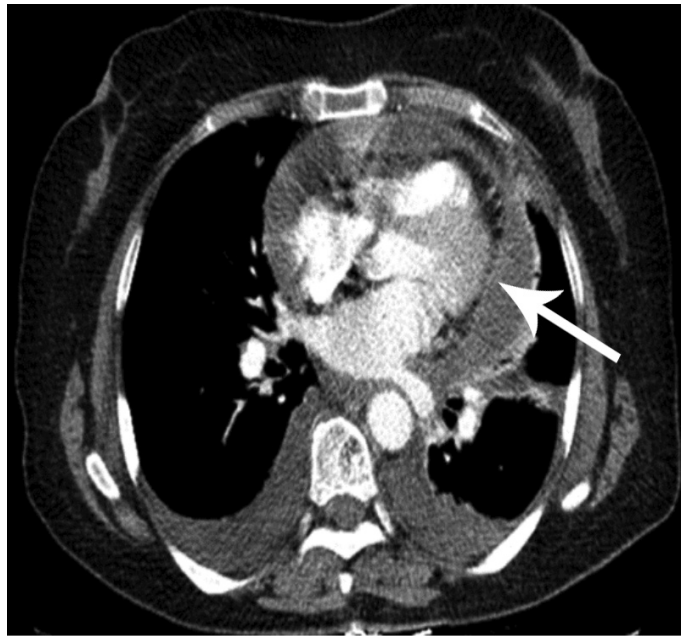

Figure 2. Thoracic computed tomography image in the axial plane showing pericardial and pleural effusion (arrow)

as well as a factor in facilitating MTX toxicity. We consider 17.5 mg/week MTX to be within the treatment dose limits and postulate that a low albumin level of 2.31 g/dL resulted in toxicity, leading to the development of pericardial tamponade.

Conclusion

The treatment of patients with PsA should be designed by taking into account the severity of the disease, response to previous treatments, and the presence of co-morbidities. The routine use of MTX in patients with hypoalbuminemia and cachexia may facilitate end-organ toxicity. We suggest that in this patient group, hypoalbuminemia should be resolved and the MTX dose should be reduced or included in a combination therapy to reduce the risk of unwanted end-organ toxicity, such as tamponade.

Ethics

Informed Consent: Patient consent was obtained.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: M.A.A., Concept: M.A.A., İ.T., Design: M.A.A., İ.T., B.G.Y., Ö.T., Data Collection or Processing: M.A.A., B.G.Y., Ö.T., Analysis or Interpretation: M.A.A., B.G.Y., Literature Search: M.A.A., B.G.Y., Writing: M.A.A., Ö.T.

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