

Iatrogenic Pancytopenia in Rheumatoid Arthritis Patients with Significant Joint Deformities: A Case Report from Sudan

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1. Abstract

1.1. Background

Pancytopenia is a condition marked by the decrease of all three myeloid cell lineages. Iatrogenic pancytopenia specifically denotes pancytopenia induced by a drug or a therapeutic intervention. Rheumatoid arthritis (RA) treatment may provoke this scenario.

1.2. Case Presentation

We describe the case of a 68-year-old Sudanese woman with rheumatoid arthritis who exhibited fatigue, dyspnea, and bruising. The patient underwent prolonged treatment with low-dose methotrexate. Blood tests indicated pancytopenia and normal renal function. The patient experienced joint abnormalities and, ultimately, iatrogenic pancytopenia. She received medical attention, including blood transfusions, and her pancytopenia resolved after discontinuation of therapy.

1.3. Conclusion

This case report emphasizes the need to monitor patients undergoing methotrexate therapy for pancytopenia.

2. Introduction

Rheumatoid arthritis (RA) is a persistent inflammatory disorder marked by inflammation of the joints and adjacent tissues. Although RA is a systemic condition, it predominantly impacts the joints, resulting in pain, inflammation, and rigidity. In advanced in-

stances, RA can result in considerable joint deterioration, resulting in abnormalities such as swan neck fingers [1]. The management of RA often entails a regimen of pharmaceuticals, comprising disease-modifying antirheumatic drugs (DMARDs) and corticosteroids. Even though these drugs effectively manage RA symptoms, they may also induce undesirable effects, such as pancytopenia, a disorder marked by a reduction in all three blood cell types: red blood cells, white blood cells, and platelets [2]. Iatrogenic pancytopenia is an uncommon yet severe consequence of RA treatment. Awareness of the risk factors for this syndrome and vigilant monitoring of patients for signs and symptoms are essential [3]. This case study attempts to elucidate the pancytopenia provoked by rheumatoid arthritis medication.

3. Case Presentation

A 64-year-old Sudanese woman with a 35-year history of rheumatoid arthritis reported to the rheumatology clinic with complaints of weariness, easy bruising, and dyspnea. Physical examination revealed several petechiae distributed across the upper torso. She has also experienced heightened bruising during the past few weeks. These contusions advanced to the exposed hemorrhagic ulcerations with minor trauma.

She had been administered methotrexate (7.5 mg) since the age of 29, demonstrating a proactive approach to her treatment. At 39 years of age, she commenced therapy with disease-modifying antirheumatic drugs (DMADs) and corticosteroids owing to their

efficacy in alleviating RA symptoms. However, they can also have detrimental effects. During physical examination, she exhibited pronounced joint deformities, notably swan neck fingers [Figure 1]. Upon admission, the patient's vital signs were as follows: pulse (68 bpm); respiratory rate (18 beats per minute); blood pressure (122/81); and temperature (37.7°C). The patient also presented with a significant condition of pancytopenia: WBC count, 2.5 (differential: polymorphonuclear neutrophils, 1.1; lymphocytes, 0.7; monocytes, 0.3); hemoglobin level 6.5, MCV 98, and platelet count, 97000. The additional laboratory results are presented in

Table 1. Her most recent CBC carried out two months ago, indicated WBC 5.6, Hb 10.0, and platelets 163. Bone marrow examination revealed a marked reduction in all cell populations, ruling out cancer and myelodysplasia. The chest X-ray revealed several dispersed pulmonary infiltrates. The patient received transfusions of packed red blood cells, platelets, and fresh frozen plasma. She was empirically initiated on broad-spectrum antibiotics for neutropenic fever, granulocyte colony-stimulating factor (G-CSF), and methotrexate was discontinued. She showed significant progress, with pancytopenia disappearing and nearly normal hematologic values within less than a week of follow-up, except for joint deformities.



Figure 1: Rheumatoid Arthritis Clinical Manifestations. Ulnar deviation of fingers and toes with joint swelling.

Table 1: Laboratory findings of the case.

| Variables | Case result | Normal or control |
|---|-------------|-------------------|
| White blood cells $\times 10^9/l$ | 2.5 | 4 – 10 |
| Red blood cells $\times 10^{12}/l$ | 1.77 | 3.5 – 5.5 |
| Hemoglobin g/dl | 6.5 | 11 – 15 |
| Hematocrit % | 17.4 | 35 – 45 |
| Mean Corpuscular Volume fl | 98.3 | 78 – 98 |
| Mean Corpuscular Hemoglobin pg | 36.7 | 26 – 35 |
| Mean Corpuscular Hemoglobin Concentration % | 37.0 | 30 – 36 |
| Red Distribution Width-CV % | 14.9 | 11.5 – 14.5 |
| Absolute lymphocyte count $\times 10^9/l$ | 0.7 | 1.0 – 4.3 |
| Absolute neutrophil count $\times 10^9/l$ | 1.1 | 1.5 – 7.0 |
| Absolute monocyte count $\times 10^9/l$ | 0.3 | 0.1 – 1.0 |
| Platelet count $\times 10^9/l$ | 97 | 150 – 400 |
| Mean Platelet Volume fl | 9.5 | 9 – 13 |
| Platelet Distribution Width fl | 11.8 | 9 – 17 |
| Platelet Large cell ratio % | 23.5 | 11 – 45 |
| Erythrocyte sedimentation rate, 1st hour mm/h | 93 | Up to 20 |
| Erythrocyte sedimentation rate, 2nd hour mm/h | 118 | Up to 30 |
| Bleeding time min | 2.7 | 2 – 7 |
| Clotting time min | 6.0 | 5 – 15 |
| Clot retraction % | 118 | 30 – 120 |
| Prothrombin time $second$ | 16.2 | 12 – 16 |
| Partial thromboplastin time $second$ | 39.4 | 26 – 43 |
| Thrombin time $second$ | 15.2 | 8 – 18 |
| Antithrombin % | 90 | 78 – 126 |

| | | |
|---|------|-------------|
| D-Dimer <i>mg/l</i> | 0.2 | Up to 0.3 |
| Von willebrand factor % | 121 | 50 – 160 |
| Creatinine <i>mg/dl</i> | 0.81 | 0.4 – 1.6 |
| Blood Urea <i>mg/dl</i> | 15.0 | 10 – 50 |
| Blood Urea Nitrogen <i>mg/dl</i> | 7.0 | 7 - 21 |
| Uric Acid <i>mg/dl</i> | 6.0 | 3.4 – 7.0 |
| Total Bilirubin <i>mg/dl</i> | 0.44 | 0.2 – 1.3 |
| Direct bilirubin <i>mg/dl</i> | 0.09 | Up to 0.25 |
| Total protein <i>g/dl</i> | 6.9 | 6.6 – 8.3 |
| Albumin <i>g/dl</i> | 3.7 | 3.5 – 5.5 |
| Alanine transaminase <i>U/l</i> | 18 | Up to 41 |
| Aspartate transaminase <i>U/l</i> | 28 | Up to 40 |
| Alkaline phosphatase <i>U/l</i> | 78 | Up to 115 |
| Glycosylated Hemoglobin % | 5.8 | 4.5 – 6.5 |
| Thyroid stimulating hormone $\mu\text{IU/ml}$ | 1.16 | 0.27 – 4.2 |
| Lactate dehydrogenase <i>U/l</i> | 1320 | 204 - 440 |
| Vitamin B12 level <i>pg/ml</i> | 212 | 197 – 997 |
| Folic acid level <i>ng/ml</i> | 6.6 | 2.7 – 20.0 |
| Ferritin level <i>ng/ml</i> | 79.8 | 13 – 250 |
| Iron level $\mu\text{mol/l}$ | 12.3 | 10.5 – 32.6 |

4. Discussion

Iatrogenic pancytopenia is an uncommon, yet severe consequence of rheumatoid arthritis treatment. The primary causative agents are DMARDs including methotrexate, leflunomide, and sulfasalazine. Additional medications, including nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids, may further facilitate the onset of pancytopenia [4]. Methotrexate, a potent folate inhibitor, is a key player in the treatment of many cancers, autoimmune disorders, and abortions. It is absorbed into cells via an active cellular uptake transporter and then expelled by an active efflux transporter. Once inside the cell, methotrexate's primary function is to inhibit dihydrofolate reductase (DHFR), an enzyme that catalyzes the conversion of dihydrofolate (DHF) to tetrahydrofolate (THF) [4, 5]. This mechanism of action is crucial for understanding the effectiveness of the drugs.

This medication's polyglutamylation extends its intracellular duration [6]. It immediately increases the amount inside the myeloid lineages and epithelial cells, which can cause ulcers and bleeding in patients [7]. Consequently, the patient may have exhibited infections and macrocytic anemia, as observed in this case. The absorption of low-dose oral and parenteral methotrexate (≤ 15 mg/week) is approximately equal; however, when the oral dosage surpasses 15 mg/week, absorption may decrease by up to 30% [8]. Although not prospectively examined in rheumatoid arthritis patients

on prolonged methotrexate therapy, the parenteral administration method is expected to have a significant impact in reducing the risk of hepatotoxicity. In a study that looked back, higher levels of transaminases were seen when the same people were administered methotrexate by mouth instead of IV [9].

Risk factors for iatrogenic pancytopenia include advanced age, renal dysfunction, previous bone marrow disorders, and the concurrent use of other drugs that may influence bone marrow activity. Owing to the underlying inflammatory process, individuals with pronounced joint abnormalities, such as swan neck fingers, may face a heightened risk [10]. The clinical manifestation of pancytopenia may be nonspecific, encompassing symptoms such as fatigue, weakness, dyspnea, easy bruising, and hemorrhage. The crucial role of diagnostic evaluation, which necessitates laboratory tests like a complete blood count and bone marrow biopsy, cannot be overstated [11]. The management of iatrogenic pancytopenia requires the cessation of the causative medicine and the provision of supportive care [12].

5. Conclusion

Iatrogenic pancytopenia is a rare but serious complication of RA treatment. It is important to be aware of the risk factors for this condition and to monitor patients closely for signs and symptoms. Early diagnosis and prompt treatment are essential to prevent complications.

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