Rheumatology: Current Research
ISSN: 2161-1149

Kaydok and Salbas, Rheumatology (Sunnyvale)
2018, 8:2
DOI: 10.4172/2161-1149.1000236

Case Report Open Access

Thrombocytosis Development due to the Use of Methotrexate in a Patient with Rheumatoid Arthritis

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Received date: March 23, 2018; **Accepted date:** May 07, 2018; **Published date:** May 10, 2018

Abstract

Rheumatoid arthritis is a systemic rheumatic disease that affects various organs and systems. In the course of rheumatoid arthritis, various blood disorders including thrombocytosis (>400.000/mm^3), an increase in the platelet count are observed. Methotrexate is a disease-modifying agent used in the treatment of Rheumatoid Arthritis and various rheumatic diseases. During methotrexate treatment, hematologic problems such as leukopenia, anemia, and thrombocytopenia are observed generally due to bone marrow suppression. In our case report, we aimed to present a 56 year-old patient who has arthritis of both hands and was diagnosed with rheumatoid arthritis and whose platelet values were initially within normal limits and then increased up to the level of 808.000/microliter despite a clinical and laboratory suppression in the disease activity after the initiation of methotrexate treatment, and quickly returned to normal values after the termination of methotrexate treatment. In conclusion, we think that the response of the blood profile to drugs may be very different, as in our case, and therefore, patients should be carefully monitored.

Keywords: Rheumatoid arthritis; Methotrexate; Thrombocytosis; Adverse reaction

Introduction

The platelet count is 150.000-400.000/mm^3 in adults. Thrombocytosis is caused by a platelet count exceeding 400.000 per milliliter [1]. According to the etiology, thrombocytosis is divided into two: primary (essential) and secondary (reactive) thrombocytosis. Primary Thrombocytosis (PT) is a rare myeloproliferative disorder that develops due to anomalies in the hematopoietic cells or anomalies in the thrombopoietin biology. Secondary thrombocytosis is mainly caused by a variety of diseases such as infections, chronic inflammation, tissue injury (trauma, surgery, burns) and malignancies [2]. There are also rare cases of secondary thrombocytosis due to drugs. Rheumatoid arthritis is one of the most common rheumatic diseases, and in some cases, the hematologic alterations such as anemia of chronic disease, leukopenia, thrombocytopenia, and pancytopenia occur [3]. During the activation phase of rheumatoid arthritis, thrombocytosis may occur [4]. Side effects such as leukopenia, thrombocytopenia, and pancytopenia are frequently encountered as the hematologic side effects of methotrexate, commonly used in the treatment of rheumatoid arthritis. In this case report, we aimed to present the investigation of a case in which pure thrombocytosis was observed despite the suppression of the activity of the disease and which has not previously been described in the literature.

Case Report

A 56-year-old female patient with the diagnosis of rheumatoid arthritis for 15 years previously used methotrexate, but discontinued it voluntarily. At the time of admission, both wrists, both the 2nd PIP joints and the 3rd MCP joints of the patient were tender, and the MCP joints of the 2nd digit on both hands were swollen. The patient's erythrocyte sedimentation rate (ESR) was 48 and the CRP was 28. The patient's platelet and hemoglobin values were within normal limits (382.000/ml and 12.1 mg/dl, respectively). The treatment of prednisolone 10 mg/day and oral methotrexate 10 mg/week was initiated. A significant improvement was found in the complaints of the patient at the 4th week control.

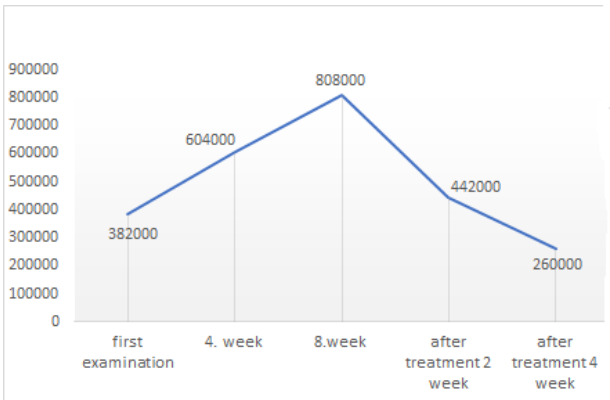

Figure 1: Changes in Platelets Count.

The CRP was decreased to 7.8, the ESR was decreased to 30 and the platelet count was 604.000/ml. The patient's prednisolone treatment was gradually reduced and discontinued within 2 weeks, and methotrexate treatment was maintained in the same way. The patient's clinical condition was good at the 8th-week control and the DAS 28-CRP score was decreased from the baseline value of 4.92 to 3.28. In laboratory tests, the CRP was decreased to 3.1, the ESR was decreased to 28. However, as no cause to explain the thrombocytosis was detected in the patient with a platelet count of 808,000/mm^3, methotrexate treatment was discontinued and 10 mg prednisolone was initiated. The patient was closely followed up, the platelet count was found to have

decreased to 442.000/ml[2] weeks later, and to 260.000/ml at the end of 4th week (Figures 1 and 2). Leflunomide treatment was planned for the patient and no hematologic disorder was observed during the follow-up for 6 months.

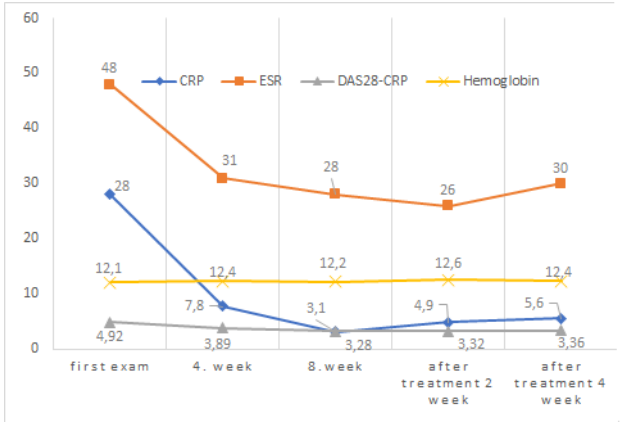

Figure 2: CRP, ESR, DAS28 and Hemoglobin Levels.

Discussion

According to the causes, thrombocytosis is examined in two different groups: primary (essential) and secondary (reactive). Primary thrombocytosis is a rare myeloproliferative disorder that develops due to anomalies in the hematopoietic cells or anomalies in the thrombopoietin biology. Secondary thrombocytosis (reactive thrombocytosis) is mainly caused by a variety of diseases such as infections, chronic inflammation, tissue injury (trauma, surgery, burns) and malignancies [2,5,6]. One of the rare causes of secondary thrombocytosis (ST) is drugs. The diagnosis of thrombocytosis induced by drugs is challenging in the presence of other diseases. The cases that developed thrombocytosis due to drugs such as G-CSF, beta-lactam antibiotics, miconazole, vinca alkaloids, iron therapy, enoxaparin, antipsychotic drugs, adrenaline, glucocorticoids, retinoic acid, ciprofloxacin have been reported [7-12]. Mechanisms such as elevation of endogenous IL-6, other cytokines or catecholamines, increased megakaryocytes, increased splenic mobilization, prolonged platelet life-span have been suggested in the etiopathogenesis of ST [9].

The most common hematological findings in patients with rheumatoid arthritis are anemia, leucopenia and thrombocytosis. In a cohort study investigating laboratory abnormalities in patients with early arthritis, the frequency of thrombocytopenia was reported as 0.97% and the rate of thrombocytosis as 14.7% [3,4]. Thrombocytosis occurs during the active disease period. It correlates well with the disease activity and reaches the normal ranges during the remission period [6]. Reactive thrombocytosis is common in RA. It has been reported in a study that thrombocytosis may occur in 16% of patients [5]. In these cases, clinical findings such as joint swelling and increased pain, as well as an increase in the acute phase reactants, especially in the serum CRP levels, are commonly detected. In our case, a severe thrombocytosis was detected despite the clinical improvement of the patient's complaints and no increase in the serum CRP level. The use of methotrexate has been considered as the cause of thrombocytosis since there was no acute pathology such as bacterial infection, anemia, trauma or surgery that would explain thrombocytosis in our case, and it was observed that thrombocytosis was improved within a few weeks by the discontinuation of the drug.

Conclusion

Although hematologic findings such as leukopenia and thrombocytopenia are observed due to the use of methotrexate in rheumatic diseases, reactive thrombocytosis that occurred due to the use of methotrexate and that has not been previously described due to the use of methotrexate in the literature was detected in our case. The platelet count returned to the normal limits by the discontinuation of the methotrexate treatment. We, therefore, consider that thrombocytosis may not only indicate the disease activation in rheumatoid arthritis but may rarely occur due to drugs, as in our case.

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