

Thrombocytopenia caused by albendazole in a patient with Sjögren's syndrome: A case report

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Abstract

Sjögren's syndrome (SS) is an autoimmune disease characterised by a chronic inflammatory response mainly localised to the lachrymal and salivary glands. Haematological abnormalities are common, although they rarely have clinical significance. Here, we report a patient with SS and thrombocytopenia caused by albendazole. Haematological abnormalities such as thrombocytopenia are seen in approximately 5-15% of SS patients; however, this disease is usually asymptomatic and can often be recovered to normal levels with corticosteroids. If it is not, we should keep in mind other reasons for the thrombocytopenia, such as drug use.

Key words: Thrombocytopenia, albendazole, Sjögren's syndrome

Introduction

Sjögren's syndrome (SS) is an autoimmune disease characterised by a chronic inflammatory response that is mainly localised to the lachrymal and salivary glands (1). Beside its autoimmunity, SS affects the mucous membranes, and has related laboratory tests. It is characterised by xerostomia (dry mouth), xerophthalmia (dry eyes), and lymphocytic infiltration of the exocrine glands (2). However, it sometimes involves extra-glandular organs, which leads to systemic disorders. Despite the limited clinical significance, haematological abnormalities are very common. Chronic diseases like lymphopenia, leucopenia and anaemia have been most commonly noted. Thrombocytopenia is not usual, but can be treated successfully with prednisolone (3).

Thrombocytopenia can be observed in patients who are receiving drugs for different reasons. The most frequent drug-oriented reason for thrombocytopenia is the use of oral anticoagulants like heparin; there are also some other rare triggering drugs such as salazopyrine, and antihypertensive drugs (alpha-metildopa) (4-6). Although there are a limited number of reports on this topic, albendazole as an anti-helminthic can also cause thrombocytopenia (7). On the other hand, symptomatic thrombocytopenia related to Sjögren's Syndrome is extremely rare. We herein report a case study concerning a patient with Sjögren's syndrome (SS) who has thrombocytopenia caused by albendazole.

Case Presentation

A 25 year-old female patient was referred to our rheumatology clinic with petechia and a thrombocyte count of $18 \times 10^3 \text{ mm}^3$, who reported eye and mouth dryness and arthralgia. She was hospitalised for investigation in July 2010. Blood tests revealed that the patient had thrombocytopenia ($15 \times 10^3 \text{ mm}^3$), anti-nuclear antibody (immune-fluoresan antibody) positivity (1/320; speckled pattern) and anti-SS-A (Anti-Ro): 132; however, anti-SS-B was negative. The measurement of lachrymal secretory capacity with Schirmer's tear test was positive (3 mm per 5 min, bilaterally) and salivary gland biopsy was consistent with a focus score of 3. As a result of these findings, she was diagnosed with Sjögren's Syndrome and was treated with methylprednisolone (60 mg/day). On the eighth day of the treatment, the platelet count was $100 \times 10^3 \text{ mm}^3$; because of her elevated platelet levels, she was discharged with methylprednisolone (60 mg/day; reducing to 4 mg/week), hydroxychloroquine (400 mg/day) and azathioprine (100 mg/day). Following the fifth month of the treatment period, after a retrospective evaluation of the blood tests, azathioprine was stopped and treatment with methylprednisolone (8 mg/day) and hydroxychloroquine (400 mg/day) was continued. In December 2010, she was admitted to the hospital emergency department with abdominal pain and diagnosed with hepatic cysts. In order to overcome problems resulting from the hepatic cyst, an operation was performed. Following the operation, the patient received albendazole (10 mg/kg/day) for the treatment of hepatic hydatid cysts. Prior to the operation, blood tests were normal: haemoglobin (Hb): 10.9 gr/dL, and platelet count: $283 \times 10^3 \text{ mm}^3$. However, one month after the operation, while she was being treated with albendazole, the patient was re-admitted to the emergency department with prolonged menstrual bleeding, fatigue, and the complaint of gum bleeding. Laboratory tests demonstrated that her Hb was 3.5 gr/dL and her platelet count was $8 \times 10^3 \text{ mm}^3$. The patient had 5 units of packed red blood cells and, following physical examination, she was giv-



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Submitted: 24.12.2013

Accepted: 20.01.2014

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en methylprednisolone (100 mg/day) for three days by an external rheumatology clinic. Abdominal ultrasound showed a 5 cm hydatid cyst in the liver; for that reason, after consultation with a surgeon, the patient continued to receive albendazole (10 mg/kg/day) for 3 days. Control platelet levels were low ($12 \times 10^3 \text{ mm}^3$) and she continued with methylprednisolone, at a dose of 250 mg/day, for the following 2 days. Then, she was referred to our rheumatology clinic with a low platelet level ($13 \times 10^3 \text{ mm}^3$) and menstrual bleeding, most probably due to the high dose of corticosteroids taken within the previous 5 days. In the first laboratory test held in our clinic, we noted thrombocytopenia with a platelet count of $18 \times 10^3 \text{ mm}^3$ and Hb of 11.6 gr/dL. The blood smear examination indicated hypo-chromic, normocytic erythrocytes, normal leukocytes and marked thrombocytopenia with normal platelet morphology. Abdominal ultrasonography showed a normal spleen. All of the serologic tests including Human Immunodeficiency Virus (HIV), Hepatitis B Virus (HBV), Hepatitis C Virus (HCV), Epstein-Barr virus (EBV), and Parvovirus (B19, CMV) were negative. Folate, ferritin, and vitamin B₁₂ levels were also normal.

Anti-nuclear antibody (ANA) 1/320 speckled pattern in immunofluorescence antibody assay (IFA) was positive and anti-Ro (SsA) antibody was strongly positive. The direct and indirect coombs tests and anti-platelet IgG determinations were negative. We started prednisolone (60 mg/d) and hydroxychloroquine (400 mg/d). Bone marrow investigations showed increased megakaryocytic, and slightly megaloblastic changes in the granulocytic series and that blast was 2% with a mild erythroid hypoplasia. Because the platelet levels were around $18 \times 10^3 \text{ mm}^3$, albendazole treatment was stopped. The blood test was repeated on a daily basis and on the eighth day of the treatment, platelet levels were $141 \times 10^3 \text{ mm}^3$ and menstrual bleeding had stopped. Following the normalisation of the platelet levels, the patient was discharged with 8 mg/d corticosteroids and 400 mg/d hydroxychloroquine. On routine control visits, blood tests were all normal.

Discussion

Sjögren's syndrome is a chronic autoimmune disorder associated with B lymphocyte hyper-reactivity. Haematological manifestations like anaemia are common in patients with SS and leucopenia is the most frequently seen symptom. The prevalence of anaemia is almost 11% and thrombocytopenia is 5-15% (8). Thrombocytopenia in SS is rarely occurs following treatment with corticosteroids. As was observed in our patient, cytopenias in SS patients are usually mediator-induced. The current patient had bleeding manifestations as a result of the thrombocytopenia.

Drug-induced thrombocytopenia (DIT) is a common clinical disorder, and the rapid iden-

tification and removal of the offending agent is vitally important. Despite the diverse types, heparin-induced thrombocytopenia (HIT) is the most important and most frequent drug-induced, immune-mediated type of thrombocytopenia. However, other drugs like sulfasalazine and antihypertensives (alpha-methyl dopa) can rarely cause thrombocytopenia as well. Albendazole can also cause thrombocytopenia, but this is not often reported.

Albendazole is a member of the benzimidazole compounds, and is used as a drug for the treatment of a variety of human echinococcosis. Pharmacologically, it targets beta-tubulin to inhibit helminth microtubule formation and is used at a dose of 10 mg/kg/d for 30 days; if necessary, the treatment can be extended. Adverse reactions to albendazole include gastrointestinal symptoms and elevated liver enzymes; as a result, close monitoring of liver enzyme levels is strictly advised. During the first 30 days of treatment there would be some other rare adverse events including headache, alopecia, anaphylactic shock, fever, leucopenia and thrombocytopenia (9). Steiger et al. (10) showed that treatment with albendazole in patients with hydatid disease was found to induce major side effects, including hepatotoxicity, neutropenia, and alopecia. One case of albendazole-induced megakaryocyte thrombocytopenic purpura was reported; the patient was a 25 year-old woman without any other chronic diseases, who had been taking albendazole (13 mg/kg/d) for hepatic and pulmonary cysts for 5 months and had reported gum bleeding and prolonged menstrual bleeding, but negative serologic tests and a normal spleen were reported. In the bone marrow biopsy, there were no megakaryocytes and a normal appearance of the granulocytic and mild erythroid hyperplasia. The albendazole treatment was terminated after two months, physical examination and laboratory investigation results were within normal limits in the post-treatment period. However, as in our case, the bone marrow examination revealed a remarkable increase in megakaryocytes (7).

One case of aplastic anaemia associated with albendazole therapy has been reported. A 71 year-old woman with portal hypertension and possibly hypersplenism had pancytopenia and hypoplasia following the albendazole treatment for hepatic hydatidosis (9). Opatrny reported one death associated with albendazole-induced pancytopenia. The patient was a 68 year-old man diagnosed with Child-Pugh class B cirrhosis and complicated grade 2 oesophageal varices. On the sixteenth day of albendazole treatment, the patient was hospitalised with septic shock with severe pancytopenia and the patient was initially resuscitated. However, he died after 10 days with no marrow recovery (11).

Consequently, haematological abnormalities like thrombocytopenia can be observed in approximately 5-15% of SS patients. Generally, patients are asymptomatic and levels can be recovered to normal with corticosteroids. Despite the use of corticosteroids, if the patients' scores do not reach normal limits, other reasons for thrombocytopenia, such as drugs, need to be considered. To the best of our knowledge, this is the first case of thrombocytopenia with increased megakaryocytes and further clinical trials need to be performed to prove albendazole-induced thrombocytopenia.

Ethics Committee Approval: N/A.

Informed Consent: Written informed consent was obtained from the patient who participated in this case.

Peer-review: Externally peer-reviewed.

Author contributions: Concept - Y.P.; Design - P.A.; Supervision - İ.H.T.; Resource - Y.P.; Data Collection&/or Processing - P.A.; Analysis&/or Interpretation - İ.H.T.; Literature Search - İ.H.T.; Writing - P.A.; Critical Reviews - Y.P.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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