Juvenile rheumatoid arthritis presented with thrombocytopenia

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SUMMARY: Koç A, Kösecik M, Tatlı MM, Ataş A. Emiroğlu HH. Juvenile rheumatoid arthritis presented with thrombocytopenia. Turk J Pediatr 2000; 42: 162-164.

Leukopenia and thrombocytopenia are rare findings in systemic onset juvenile rheumatoid arthritis (S-JRA), and if present, bone marrow (BM) examination is necessary to exclude malignant diseases. We report here a 13.5-year-old boy with S-JRA who had severe thrombocytopenia and mild leukopenia, without arthritis, at the onset of the disease. BM was hypercellular with increased numbers of myeloid precursors and megakaryocytes. After treatment with acetylsalicylic acid, leukocyte and platelet counts returned to normal levels, and after two months chronic arthritis developed.

Key words: systemic onset juvenile rheumatoid arthritis, thrombocytopenia, fever.

Anemia, leukocytosis and thrombocytosis are frequently seen hematological disorders in systemic onset juvenile rheumatoid arthritis (S-JRA)[1,2]. It has been known that leukocyte and platelet counts are increased, especially in the active stage of disease[2,3]. Leukopenia and thrombocytopenia are very rare in S-JRA, and if present, bone marrow (BM) examination is necessary to exclude malignant diseases such as leukemia[1,4,5].

We report here a child with S-JRA who had thrombocytopenia at the onset of the disease.

Case Report

A 13.5-year-old boy was admitted to the hospital with a one-month history of fever and headache. He had no history of other complaints. He had been treated with ampicillin-sulbactam and paracetamol with a diagnosis of sinusitis for two weeks, without any improvement.

Physical examination revealed a body temperature of 37 °C, weight at the 10th percentile and height at the 25th percentile for age. The liver was palpable 1.5 cm and the spleen 2.5 cm below the respective costal margins. The other systems were normal. Laboratory investigations showed hemoglobin (Hb) 11.6 g/dl, white blood cell (WBC) count 4400/mm^3 (60% neutrophils, 34% lymphocytes, 2% monocytes and 2% eosinophils), platelet count 130,000/mm^3, anti-streptolysin O (-), c-reactive protein (CRP) (++), rheumatoid factor (-), erythrocyte sedimentation rate 36 mm/h, serum albumin 3.7 g/dl, globulin 3.9 g/dl. Chest radiograph was normal and serological tests for brucella and salmonella were negative. Throat, urine, stool and blood cultures showed no pathogen bacteria.

In the follow-up, daily spikes of fever with rapid returns to normal levels were shown. On the 7th day, complete blood count revealed Hb 10.2 g/dl, WBC 3600/mm^3 (55% neutrophils, 42% lymphocytes, 3% monocytes), and platelet counts 39,000/mm^3. In peripheral blood (PB) smear, there were only a few platelets with normal erythrocyte and leukocyte morphology. Prothrombin and activated partial thromboplastin times, and hepatic function tests were in normal limits. Urine analysis was also normal. On 8th day, no platelet was shown in PB smear, so bone marrow (BM) aspiration was performed to explain thrombocytopenia and exclude a malignant disorder. BM was hypercellular with an increased number of both myeloid precursors and megakaryocytes as seen in immune thrombocytopenias (ITP), and so malignancy was excluded.

The diagnosis of S-JRA was made on the 10th day in view of daily spikes of fever, transient erythematous rash on the trunk and arms, and

the absence of other diseases, although no arthritis had been documented. Therefore, acetylsalicylic acid (100 mg/kg/day) was given both for the diagnosis and treatment. After acetyl-salicylic acid was started, the fever disappeared and after 10 days, platelet and WBC counts returned to normal levels[6]. About two months later, arthritis developed at the right knee and right wrist. The chronic progress of the arthritis confirmed the diagnosis of S-JRA. The patient was treated with naproxen with clinical benefit. During the past 2.5 year follow-up, he has had only intermittent arthritis at knees, wrists and ankles which could be controlled with naproxen therapy, without joint deformity.

Discussion

We report a patient with S-JRA associated with severe thrombocytopenia and mild leukopenia. Acute ITP is the major cause of thrombocytopenia in childhood and is frequently associated with viral illness or immunization one to three weeks prior to presentation[7]. The PB and BM findings of this patient resembled ITP, but the fever could not been explained by ITP alone.

Disseminated intravascular coagulation (DIC) and hemolytic uremic syndrome (HUS) may be the causes of thrombocytopenia in a patient with high fever[7], but these disorders were excluded by normal PB smear findings (except thrombocytopenia), normal urine analysis and normal coagulation tests. Thrombocytopenia may be seen in bacterial and viral infections[3,7], but the physical examination and laboratory investigations did not reveal any infectious disease, and there were no medications known to be the cause of thrombocytopenia[7], at least during the 15 days prior to thrombocytopenia being found. Thrombocytopenia with increased numbers of BM megakaryocytes may be seen in systemic lupus erythematosus (SLE), but the absence of other characteristic manifestations of SLE at the beginning of the disease and in the 2.5 years of follow-up excluded this probability[8]. Inflammatory conditions such as JRA may cause anemia by a different mechanism[9]. Inflammation was considered as the possible cause of mild anemia in this patient. There are a few reports of thrombocytopenia in S-JRA. Sherry et al.[10] reported three patients with S-JRA; they had transient thrombocytopenia seven, four and two years after diagnosis, in follow-up. Ewer et al.[3] reported a patient with S-JRA who developed pancytopenia due to bone marrow hypoplasia 21 days after her illness began. They suggested that autoimmunity might be a possible cause of pancytopenia, but also that acute hepatic dysfunction and side effects of medications (aspirin, co-trimaxazole) might be responsible. Thrombocytopenia has also been reported secondary to DIC in patients with S-JRA[11,12]. Scopelitis et al.[5] reported two cases of leukopenia in S-JRA, one had mild and the other had moderate thrombocytopenia. In the second patient, WBC and platelet counts increased promptly after the splenectomy. Our patient had thrombocytopenia at the onset of disease, and the had no other findings to support a diagnosis of DIC. He was also different from Ewer et al's. patients[3] because of the BM hypercellularity and no associations with medications. He was similar to Scopelitis et al's. cases[5], he also had mild leukopenia, lathough absolute neutrophil and lymphocyte counts were in normal limits[6].

Arthritis may be absent at presentation of S-JRA, and may not develop for months or even years, causing difficulty in diagnosis[1,13]. The diagnosis of S-JRA was delayed in this case because of the absence of arthritis at the onset of disease. But in the follow-up, S-JRA was suspected because of daily spikes of fever, transient erythematous rash, positive CRP, inversion of serum albumin/globulin ratio, and the absence of other disease[1,2,13]. Disappearance of fever with aspirin, and chronic arthritis, which began two months later, confirmed the diagnosis. Increased megakaryocytes in BM with peripheral thrombocytopenia indicate peripheral platelet destruction, like ITP. This condition suggests that autoantibodies might also be present against platelets in S-JRA, which is an autoimmune disease itself. The presented case has demonstrated that S-JRA should also be suspected in unexplained febrile situations associated with thrombocytopenia, although it is an unusual finding.

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