Immune thrombocytopenic purpura associated with pulmonary tuberculosis

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Over the past decade, tuberculosis has been recognized worldwide as a public health problem of increasing proportions. We report a patient who presented with epistaxis and generalized petechiae. The diagnosis was immune thrombocytopenia and the patient was treated with intravenous immunoglobulin and pulse steroid. The bleeding continued and thrombocyte level was low despite therapy. Chest X-ray and a computed tomography scan of the thorax showed right upper lobe opacities and bilateral interstitial infiltrates. The patient also had a history of close contact with an individual with active tuberculosis. The thrombocytopenia was resistant to standard therapy, but resolved after antituberculosis treatment. This report is the first case of a child with immune thrombocytopenia secondary to pulmonary tuberculosis.

Key words: immune thrombocytopenic purpura, pulmonary tuberculosis.

Tuberculosis is a disease that can be diagnosed and treated easily in developing countries[1]. However, diagnosis is occasionally difficult because of extraordinary presentations. Tuberculosis can present with monocytosis, leukocytosis, anemia or pancytopenia[2,3]. Thrombocytopenia in tuberculosis is usually the result of granulomatous infiltration of the bone marrow and often appears as a component of pancytopenia[4]. Immune thrombocytopenia (ITP) is a rare complication of tuberculosis. In the literature, ITP secondary to tuberculosis has been described in 22 adults and two children[4,5]. The coexistence of ITP and pulmonary tuberculosis was reported in the majority of adults, but all pediatric cases were associated with tuberculosis lymphadenitis[5,6].

Our patient is the first reported with ITP as a complication of pulmonary tuberculosis.

Case Report

A four-year-old boy presented to an otolaryngology clinic with the complaint of uncontrolled nose bleeding and widespread petechiae. Thrombocytopenia was detected through the blood studies and he was referred to our pediatric emergency unit after the bleeding was controlled. He had no past history suggestive of hematologic or liver disease and no consumption of drugs that would cause thrombocytopenia. His weight was 11 kg (3rd percentile) and height was 88 cm (3rd to 10th percentile). His vital signs included temperature 37.3°C, heart rate 138 beats/min and 2/6 pansystolic cardiac murmur, and respiratory rate 22 breaths/min. Chest examination was normal. Neither lymphadenopathy nor hepatosplenomegaly was present. He had extensive cutaneous petechiae and purpura all over the body.

The white blood cell count was 13.6x10^9/L, red blood cell count 4.14x10^9/L, hemoglobin 7.9 g/dl, hematocrit 26.6%, mean corpuscular volume 73.5 fl, platelet count 2x10^3/μl, and mean platelet volume 11 fl. The peripheral blood smear showed 54% lymphocytes, 32% polymorphonuclear leukocytes, 4% monocytes, hypochromic microcytic erythrocytes, and a remarkable paucity of platelets but no atypical cells. The erythrocyte sedimentation rate was 25 mm/h. Direct Coombs test was negative and reticulocyte count was 2.5%. Prothrombin

time and activated partial thromboplastin times were normal. Biochemical analysis and urine analysis were within normal limits. The purified protein derivative test was negative as was serology for human immunodeficiency virus (HIV).

Examination of a bone marrow aspirate showed erythroid hyperplasia and an increase in megakaryocytic cells. This finding was consistent with ITP (Fig. 1). The patient was given intravenous immunoglobulin (IVIG) 1 g/kg/day. After IVIG administration, the platelet count was 3 x 10^3/µl. Because of continuing epistaxis, tachycardia and low hematocrit level (from 26.9 to 21%), erythrocyte suspension was given. High-dose (30 mg/kg/day) steroid treatment was started because thrombocytopenia was resistant to IVIG therapy. The Otolaryngology Department was consulted because of continuing epistaxis. No vascular anomalies were found. Right upper lobe opacities and bilateral reticulonodular infiltrates were observed on the chest X-ray (Fig. 2). A computed tomography scan of the thorax showed alveolar consolidation, compensatory hyperinflation and atelectasis in the right upper lobe and bilateral reticulonodular lung infiltrates (Fig. 3). Pulmonary tuberculosis was considered in the differential diagnosis. Fasting gastric fluids were obtained for three consecutive days and tested for acid resistant bacilli, and the results were positive (Fig. 4). In the follow-up, his hematocrit level decreased to 25.9% and tachycardia continued, and

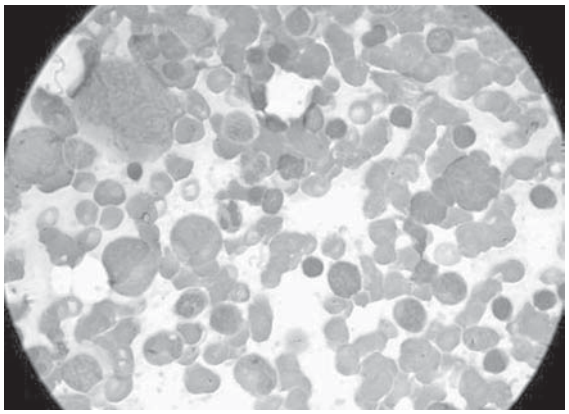

Fig. 1. Examination of bone marrow aspirate showed an increase in megakaryocytic cells.

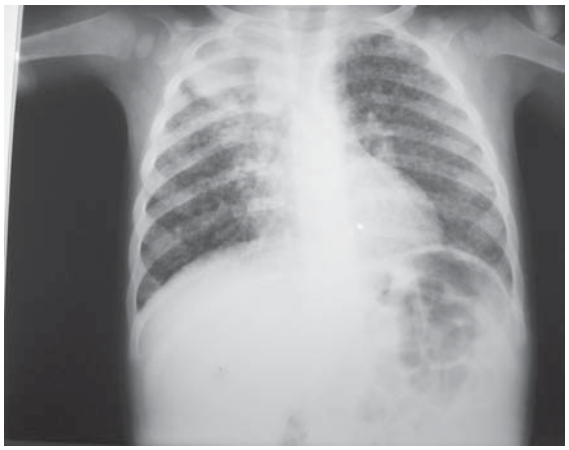

Fig. 2. Right upper lobe opacities and bilateral reticulonodular infiltrates were observed in the chest X-ray.

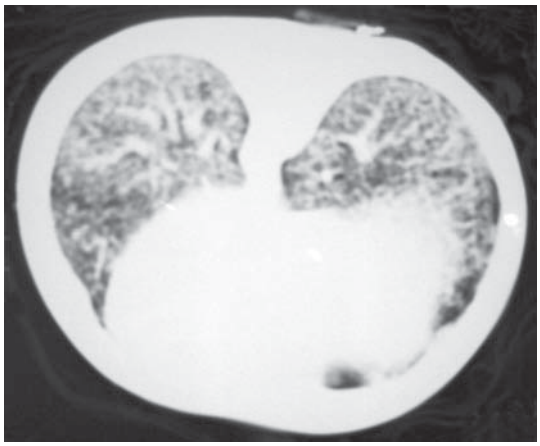

Fig. 3. Alveolar consolidation, compensatory hyperinflation, and atelectasis in the right upper lobe and bilateral reticulonodular infiltrates were observed in the thorax computed tomography scan.

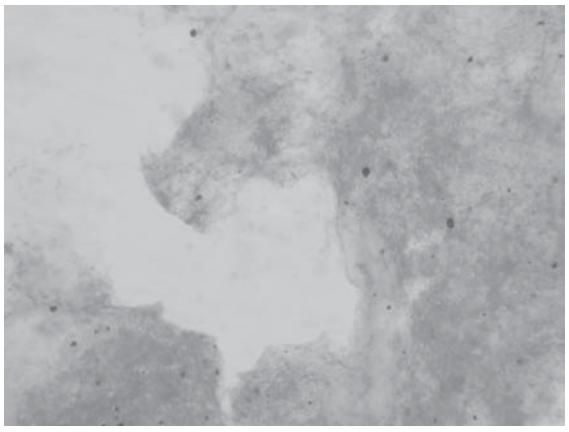

Fig. 4. Positive acid-fast bacilli are seen in the gastric fluid specimen.

erythrocyte suspension was given for the second time. After a three-day high-dose methylprednisolone treatment, his platelet count was 5 x10^3/µl. Although at first questioning the family history was nonspecific, when the parents were questioned again in detail, they reported that one of the patient's uncles who lived in the same house with them was hospitalized for antituberculosis therapy a month previously. Due to this close contact history and the radiological findings, the diagnosis was pulmonary tuberculosis and ITP. Antituberculosis treatment consisting of isoniazid (165 mg), rifampin (110 mg) and pyrazinamide (300 mg) was started. His family members were screened for tuberculosis, which was also detected in four of his brothers; they began antituberculosis therapy as well. After the first week of antituberculosis therapy, our patient's platelet count increased to 70 x 10^3/µl and no bleeding occurred. At the end of the first month, chest radiography showed resolution of the reticulonodular and right upper lobe infiltrations; the follow-up platelet counts were 152 x 10^3/µl. In the follow-up period, antituberculosis treatment was discontinued after nine months and ITP did not recur.

Discussion

Tuberculosis can be subclinical in children. In patients with primary pulmonary tuberculosis, physical examination can be normal despite abnormal radiological findings[1]. In our case under prophylaxis, the chest X-ray showed bilateral reticulonodular infiltrates and upper lobe opacities in the absence of clinical findings.

Diagnostic techniques for detecting tuberculosis in children are similar to those used for adults, but the types of specimens and their yields differ. Children rarely produce sputum; the first morning gastric fluid is the best clinical specimen in young children with suspected pulmonary tuberculosis, but is positive in only 30%-50% of all pediatric cases[7,8]. We could not get a sputum sample from our four-year-old patient but detected Mycobacterium tuberculosis in gastric fluid specimens.

Thrombocytopenia can result from three different mechanisms: increased breakdown, abnormal sequestration, and decreased production[9]. In tuberculosis, thrombocytopenia might be the result of decreased production due to bone marrow infiltration by the tuberculosis bacilli. Caseous granulomas are typically seen in a bone marrow biopsy[10]. Although pancytopenia and secondary myelosclerosis occur in the bone marrow aspirate, these are very rare in children[11]. In a study by Singh et al.[12] of 55 tuberculosis cases, thrombocytopenia was considered as a component of miliary tuberculosis. In pulmonary tuberculosis cases, they found thrombocytosis instead. Our patient had an increase in the size and number of megakaryocytic cells and erythroid hyperplasia in the bone marrow aspirate. Erythroid hyperplasia was considered to be the response to the blood loss due to continuing hemorrhage. Organomegaly and lymphadenopathy were not detected during the physical examination. Therefore, causes that infiltrate the bone marrow (leukemia, hemophagocytic syndrome, etc.) and diseases that cause peripheral thrombocyte breakdown (drugs, etc.) were ruled out in the differential diagnosis[9]. In our case, thrombocytopenia was considered to be the result of an immune response to pulmonary tuberculosis. Some evidence suggests that the immune process may play a major role in the pathophysiology of tuberculosis-related thrombocytopenia. Tuberculosis infection stimulates suppressor monocyte activity together with reduction of the T lymphocytes[13]. Jurak et al.[14] reported two cases of thrombocytopenia associated with tuberculosis that occurred simultaneously in a mother and her son. It was hypothesized that *M. tuberculosis* could stimulate a clone of B lymphocytes that might produce antibodies against autologous platelets. Boots et al.[15] also described a case of isolated thrombocytopenia complicating pulmonary tuberculosis. High-dose immunoglobulin treatment rapidly corrected the thrombocytopenia, and the platelet surface membrane IgG was detected by immunofluorescence and immunoblot studies. They concluded that isolated thrombocytopenia associated with tuberculosis was induced via an immune response.

A variety of modalities can be used to treat tuberculosis. Some authors have utilized antituberculosis treatment along with IVIG or steroids; others have used antituberculosis treatment alone[4,6,16-18]. In our case, initial diagnosis was ITP but the patient was resistant to ITP standard treatment. He responded better to antituberculosis therapy than IVIG and

steroid treatment. Additionally, Hernandez-Maraver et al.[19] described a 70-year-old patient with the complaints of mucosal bleeding and cough. The patient was started on therapy with the diagnosis of ITP but had no response to treatment. Caseous granulomas had been detected in the bone marrow biopsy that was repeated. Antituberculosis therapy was started and thrombocytopenia improved. Boots et al.[15] reported pulmonary tuberculosis and ITP in a 20-year-old patient who presented with rectal bleeding and thrombocytopenia. In our case, on the fourth day of antituberculosis therapy, platelet count returned to normal. On the other hand, thrombocytopenia in tuberculosis can be caused by use of rifampicin, pyrazinamide and ethambutol[20-22]. In our case, the platelet count rapidly increased with antituberculosis treatment. We did not observe drug-induced thrombocytopenia.

In conclusion, ITP is a rare complication of tuberculosis and may be fatal because of uncontrolled bleeding. If ITP is resistant to standard therapy, tuberculosis should also be considered in highly endemic areas such as Turkey.

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