CASE REPORT

Immune Thrombocytopenic Purpura Associated with Pulmonary Tuberculosis

Kiminori Tsuro1, Hideyuki Kojima1, Akira Mitoro1, Hitoshi Yoshiji1, Masao Fujimoto1, Masahito Uemura1, Yoshikawa Masahide2 and Hiroshi Fukui1

Abstract

A 22-year-old woman was admitted into our hospital because of generalized purpura and abnormalities in her chest X-ray. Isolated thrombocytopenia and elevated platelet-associated IgG levels were detected, while the bone marrow examination was normal. Mycobacterium tuberculosis was detected in the bronchoalveolar lavage fluid, and consequently she was diagnosed as having active tuberculosis. High-dose immunoglobulin therapy combined with anti-tuberculosis drugs not only rapidly and continuously corrected thrombocytopenia but also cured pulmonary tuberculosis. This case suggests a causal association between immune thrombocytopenia and tuberculosis as well as the safety and efficacy of the anti-tuberculosis drugs combined with high-dose immunoglobulin therapy.

Key words: pulmonary tuberculosis, immune thrombocytopenic purpura, anti-tuberculosis drugs, immunoglobulin therapy

(DOI: 10.2169/internalmedicine.45.1639)

Introduction

Tuberculosis has been recognized as a worldwide public health problem for many years, and it has various clinical forms. Many hematological derangements such as anemia, leukocytosis, or pancytopenia can occur in association with tuberculosis (1, 2). However, isolated thrombocytopenia is rare, and most commonly occurs via a non-immune mechanism in the setting of pancytopenia that develops secondary to granulomatous infiltration of the bone marrow. We herein present a case of immune thrombocytopenic purpura associated with pulmonary tuberculosis in whom thrombocytopenia and tuberculosis were successfully treated with anti-tuberculosis drugs following high-dose immunoglobulin therapy. To our knowledge, this is the second reported case with tuberculosis presenting as immune thrombocytopenia in Japan (3). This case suggests that immune thrombocytopenia can be one of the hematological manifestations of tuberculosis in which anti-tuberculosis drugs combined with high-dose immunoglobulin therapy may be available.

Case Report

In March 1997, chest X-ray was performed on a 22-year-old Japanese woman during a health check-up and revealed abnormal findings. She consulted a doctor because the generalized purpura occurred concurrently. Neither her past medical nor family history was noteworthy. She was afebrile, and had neither respiratory symptoms nor body weight loss. Because a short course of glucocorticoids administered for toxic dermatitis resulted in a transient improvement of her purpura, she was transferred to our hospital for further examinations and treatment. On admission, she was alert and fairly well nourished. There was neither lymphadenopathy nor hepatosplenomegaly. Other than the generalized purpura mainly on her extremities and trunk, the physical examination was normal. Peripheral blood examination revealed isolated thrombocytopenia as follows: platelet count 0.2×10^10/μl. white blood count 5000/μl with 65% granulocytes, 25% lymphocytes, 5% monocytes, 3% eosinophils, and 1% basophils, red blood count 414×10^12/μl with hemo-

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Received for publication November 7, 2005; Accepted for publication April 22, 2006

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Figure 1. Roentgenographic examination of the chest. A chest radiograph demonstrating infiltrative shadows without cavitation in the upper lobes of the bilateral lungs (A). This finding was confirmed on computed tomography (B, C).

globin 12.3 g/dl. The erythrocyte sedimentation rate (ESR) was 106 mm/hour, and the coagulation profiles including prothrombin time, APTT, fibrinogen, and fibrin degradation product were within the normal limits. The serum platelet-associated IgG levels were elevated at 310.5 ng/platelet. The anti-nuclear antibody and anti-DNA antibody were mildly elevated, but the other auto-antibodies were negative, and the complementary bodies were within the normal limits. Bone marrow examination revealed normocellularity of all cell lines with normal maturation. Megakaryocytes were normal in both number and morphology, and there was no granuloma. Polymerase chain reaction did not detect tuberculosis DNA in the bone marrow. Tuberculin skin test was too strongly positive to form hematoma and ulcer in the skin. Mycobacterium tuberculosis was detected in the bronchoalveolar lavage fluid. Chest X-ray demonstrated infiltrative shadow without cavity in the upper lobes of the bilateral lungs, and this was confirmed on computed tomography (Fig. 1). From these clinical, microbiological, and roentgenographic findings, she was diagnosed as having immune thrombocytopenia together with active tuberculosis 16 days after the admission.

The clinical course is shown in Fig. 2. Although glucocorticoids have been generally used for immune thrombocytopenia, our patient was treated with high-dose immunoglobulin but not with glucocorticoids because of the possibility of aggravating the active tuberculosis. When high-dose immunoglobulin was administered for 5 days, the systemic purpura rapidly disappeared along with recovery of the platelet count. The anti-tuberculosis therapy consisting of isoniazid, rifampin, and ethambutol was also started together with the immunoglobulin from the day of admission. Thereafter, the platelet count was continuously corrected despite the estimated transient effect of immunoglobulin for thrombocytopenia. The serum platelet-associated IgG levels were also normalized. Moreover, ESR was normalized, and the follow-up chest X-ray and tomography also revealed improvement in the infiltrative shadow. Although the anti-tuberculosis drugs were discontinued after 9 months, neither thrombocytopenia nor tuberculosis recurred.

Figure 2. Clinical course. The high-dose immunoglobulin therapy rapidly corrected the platelet count together with disappearance of the systemic purpura. The following anti-tuberculosis drugs induced continuous normalization of the platelet count despite the withdrawal of immunoglobulin. The serum platelet-associated IgG levels and the erythrocyte sedimentation rate were also normalized. Although the anti-tuberculosis drugs were discontinued after 9 months, neither thrombocytopenia nor tuberculosis recurred.

Discussion

Various hematological abnormalities including anemia,
leukopenia, and pancytopenia have been described in tuberculosis (1, 2). However, isolated thrombocytopenia via an immune mechanism is an extremely rare manifestation of tuberculosis. Glasser et al. (1) surveyed 3507 patients with tuberculosis and reported that all but one case with thrombocytopenia occurred in the context of pancytopenia or leukopenia. Maartens et al. (2) also showed that 25 of 109 patients with miliary tuberculosis were associated with thrombocytopenia, but they showed other hematological abnormalities. To our knowledge, only 17 reports describing 26 cases with immune thrombocytopenia associated with tuberculosis have been described in the world literature (Table 1) (3-18).

The mechanism of tuberculosis-related thrombocytopenia is unclear. However, there is some evidence to suggest 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 (19). Moreover, purified protein derivative of tuberculin may be a nonspecific B-lymphocyte stimulator (20). Jurak et al. (7) reported two cases of thrombocytopenia associated with tuberculosis that occurred simultaneously in a mother and her son. Because anti-platelet antibodies were detected in the serum of both patients, they speculated that Mycobacterium tuberculosis could stimulate a colony of lymphocytes directed against autologous platelets and might produce anti-platelet antibodies. Boots et al. (9) 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 process. Our patient suffered from isolated thrombocytopenia and active tuberculosis coincidentally. The platelet-associated IgG was detected in her serum, and high-dose immunoglobulin therapy rapidly corrected the platelet count. The following anti-tuberculosis drugs induced enduring normalization of the platelet count despite the withdrawal of immunoglobulin. Because serum platelet-associated IgG can be detected in some conditions other than immune thrombocytopenia such as liver cirrhosis and chronic thyroiditis, the increased platelet-associated IgG is not always connected with the diagnosis of immune thrombocytopenia. However, the normal megakaryocyte count in the bone marrow indicates the platelet destruction in the peripheral circulation and the prominent effect on thrombocytopenia with high-dose immunoglobulin therapy indicates an immune process in thrombocytopenia. Considering that the present patient was previously healthy and suffered from no disease other than tuberculosis, this case provides further evidence to suggest that tuberculosis was the most likely cause of immune thrombocytopenia.

Table 1 shows the clinical features of 26 cases with immune thrombocytopenia associated with tuberculosis that have been described in the world literature (3-18). Most of these patients were of Middle Eastern and Asian descent. Tuberculosis-related immune thrombocytopenia was distributed across all ages and females predominated slightly. The presenting manifestation of tuberculosis was pulmonary tuberculosis in 8 cases (31%), lymphadenitis in 8 cases (31%), and miliary tuberculosis in 7 cases (27%). The platelet count was under 1.0×10^4/μl in 16 cases (62%) and under 10×10^4/μl in all cases. Anti-platelet antibody was detected in 5 of 7

### Table 1. Clinical Course of 26 Cases with Immune Thrombocytopenia Associated with Tuberculosis

<table>
<thead>
<tr>
<th>Race/reported country</th>
<th>Number of patients</th>
<th>Type of tuberculosis</th>
<th>Platelet count (x10^4/μl)</th>
<th>Anti-platelet antibody</th>
<th>Treatments other than anti-tuberculosis drugs</th>
<th>Response to treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japanese/Apex (our case)</td>
<td>1</td>
<td>22/F</td>
<td>pulmonary</td>
<td>0.2</td>
<td>positive</td>
<td>γ-globulin</td>
</tr>
<tr>
<td>Kazakhstan/Turkey</td>
<td>1</td>
<td>6/F</td>
<td>pulmonary</td>
<td>0.8</td>
<td>negative</td>
<td>γ-globulin, corticosteroid</td>
</tr>
<tr>
<td>Kolkata/India</td>
<td>1</td>
<td>61/F</td>
<td>lymphadenitis</td>
<td>3.8</td>
<td>no mention</td>
<td>none</td>
</tr>
<tr>
<td>Thai/Thailand</td>
<td>1</td>
<td>66/F</td>
<td>pulmonary</td>
<td>1.3</td>
<td>no mention</td>
<td>corticosteroid</td>
</tr>
<tr>
<td>African/Italy</td>
<td>1</td>
<td>56/F</td>
<td>lymphadenitis</td>
<td>0.1</td>
<td>no mention</td>
<td>corticosteroid</td>
</tr>
<tr>
<td>African-American/USA</td>
<td>1</td>
<td>48/F</td>
<td>miliary</td>
<td>0.5</td>
<td>negative</td>
<td>γ-globulin, corticosteroid</td>
</tr>
<tr>
<td>Benin/Africa</td>
<td>1</td>
<td>6/F</td>
<td>lymphadenitis</td>
<td>0.2</td>
<td>no mention</td>
<td>corticosteroid</td>
</tr>
<tr>
<td>Moroccan/Spain</td>
<td>1</td>
<td>70/M</td>
<td>miliary</td>
<td>0.8</td>
<td>negative</td>
<td>γ-globulin, corticosteroid</td>
</tr>
<tr>
<td>No mention/Saudi Arabia</td>
<td>9</td>
<td></td>
<td>abscesses</td>
<td>1.4</td>
<td>no mention</td>
<td>none</td>
</tr>
<tr>
<td>Japanese/Apex</td>
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<td>56/M</td>
<td>pulmonary</td>
<td>0.7</td>
<td>positive</td>
<td>γ-globulin, corticosteroid, spinctectomy</td>
</tr>
<tr>
<td>No mention/India</td>
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<td>36/M</td>
<td>lymphadenitis</td>
<td>4.6</td>
<td>no mention</td>
<td>corticosteroid</td>
</tr>
<tr>
<td>Thai/Thailand</td>
<td>1</td>
<td>60/M</td>
<td>pulmonary</td>
<td>0.5</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>No mention/India</td>
<td>1</td>
<td>56/M</td>
<td>lymphadenitis</td>
<td>2.9</td>
<td>no mention</td>
<td>corticosteroid</td>
</tr>
<tr>
<td>Korean/USA</td>
<td>2</td>
<td></td>
<td>pulmonary</td>
<td>0.4</td>
<td>positive</td>
<td>corticosteroid, vincristine, spinctectomy</td>
</tr>
<tr>
<td>Indian/USA</td>
<td>2</td>
<td></td>
<td>splenectomy</td>
<td>0.0</td>
<td>negative</td>
<td>corticosteroid, spinctectomy</td>
</tr>
<tr>
<td>Chinese/Canada</td>
<td>1</td>
<td>74/F</td>
<td>miliary</td>
<td>0.1</td>
<td>no mention</td>
<td>corticosteroid, vincristine</td>
</tr>
<tr>
<td>Greek/Canada</td>
<td>1</td>
<td>73/F</td>
<td>lymphadenitis</td>
<td>0.8</td>
<td>no mention</td>
<td>corticosteroid</td>
</tr>
</tbody>
</table>

DOI: 10.2169/internalmedicine.45.1639
tested cases (71%). All patients were treated with anti-tuberculosis drugs, commonly in combination with corticosteroid, immunoglobulin or vincristine. In most cases, the platelet count recovered and the clinical course of tuberculosis was satisfactory. However, corticosteroids may aggravate tuberculosis occasionally (3, 4). Moreover, it is well recognized that tuberculosis sometimes occurs during the corticosteroid therapy for immune thrombocytopenia, suggesting a possibility of latent infection with Mycobacterium tuberculosis (21). On the other hand, the high-dose immunoglobulin therapy can achieve transient but reliable improvement of thrombocytopenia without deterioration of tuberculosis. Isolated thrombocytopenia associated with tuberculosis is uncommon but may be life threatening due to the marked bleeding tendency. In the case of severe thrombocytopenia associated with tuberculosis, therefore, high-dose immunoglobulin treatment combined with anti-tuberculosis drugs may be safe and effective.

In summary, we reported a case of immune thrombocytopenia associated with active tuberculosis successfully treated with anti-tuberculosis drugs following high-dose immunoglobulin therapy. It is necessary to consider tuberculosis as one of the causes of immune thrombocytopenia in areas with high endemicity of tuberculosis.

References


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