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Case Report

Dermatomyositis Complicated by Thrombotic Thrombocytopenic Purpura

Maria A. Sawdyk, MD,* and Jeffrey Jundt, MD†

A 65-year-old woman who had a documented history of dermatomyositis was hospitalized for evaluation of a syncopal attack. During the course of her stay, she experienced progressive neurologic dysfunction, hemolytic anemia, and thrombocytopenia. A clinical diagnosis of thrombotic thrombocytopenia purpura (TTP) was made, and therapy was initiated with glucocorticoids, plasmapheresis, plasma infusion, and antiplatelet medication. The pathogenesis of TTP has not been clearly elucidated. However, reports in the literature have postulated immune damage of the endothelium with demonstration of IgM and complement deposits as the origin of the condition. Further, there are reported cases of TTP associated with collagen disorders such as systemic lupus erythematosus, rheumatoid arthritis, polyarteritis nodosa, and Sjögren’s syndrome. To our knowledge, this represents the first known case of an association of TTP with dermatomyositis. Because of the implication of an immunologic pathogenesis for these disorders, this association is worth noting.

Thrombotic thrombocytopenic purpura (TTP) was originally described by Moschowitz in 1925 (1). Since that time more than 300 cases have been reported, but the etiology remains unclear. Recent studies show that extensive microthrombi formation involving many internal organs is responsible for the clinical symptomatology of hemolytic anemia, thrombocytopenia, fever, neurologic symptoms, and renal abnormalities. These microthrombi are believed to form as a result of vascular damage (2,3), but their actual pathogenesis is still debated. Many mechanisms for vascular damage have been postulated including toxins (4), viruses (4), immune complexes (5-8), platelet aggregating factor (9), mechanical damage (10), and abnormalities of endothelial function (11,12).

The association of TTP with recognized immunologic disorders has great significance if one postulates an immunologic mechanism for TTP. Thus far, the disorder has been described in association with Sjögren’s syndrome (13), systemic lupus erythematosus (14-17), rheumatoid arthritis (18), and polyarteritis nodosa (19). However, there have been no reports of TTP associated with dermatomyositis, but we present such a case. Because of the implication of an immunologic pathogenesis for these disorders, their association in this patient is worth noting.

Case Report

A 65-year-old woman was admitted for evaluation of a syncopal episode. Her past medical history was significant for dermatomyositis, hypertension, and type II diabetes mellitus.

The dermatomyositis diagnosis was established in 1975 at which time the patient presented with proximal muscle weakness and skin changes of the face, upper arms and back. Creatine phosphokinase (CPK) and aldolase levels were elevated, and an electromyogram (EMG) showed myopathic changes in the right and left quadriceps. Findings of biopsy of muscle from the left quadriceps were consistent with a diagnosis of myositis, and results of biopsies of skin from the right midback and right outer arm were consistent with the diagnosis of dermatomyositis (Figs 1,2). Findings of repeat biopsies of skin in 1980 and 1982 were also consistent with this diagnosis. CPK and aldolase values were elevated in early 1982, and findings of repeat EMG were consistent with the ongoing inflammatory features of myopathy. Corticosteroid therapy of various doses produced subjective clinical improvement.

At admission, medications included hydrochlorothiazide (25 mg every morning), lente insulin (30 units every morning), and prednisone (20 mg every day).

The patient was moderately obese and had hyperpigmented scaling patches on the extensor surfaces of the arms and shoulders. No Gottron’s papules or heliotrope rash were noted, and no petechial or ecchymotic lesions were seen on initial examination. Proximal muscle strength was minimally decreased.

The day after admission the patient became confused, her temperature rose to 38°C, and her hemoglobin level was dropping. Schistocytes and thrombocytopenia were seen on the peripheral blood smear (Fig 3). Based on the triad of hemolytic anemia with microangiopathic changes in erythrocytes, thrombocytopenia, and fluctuating neurologic abnormalities described by Moskowitz (1), we made the clinical diagnosis of TTP.
Dermatomyositis Complicated by TTP

Fig 1
Biopsy of skin in 1980. Findings were histologically compatible with dermatomyositis.

Fig 2
Muscle biopsy from quadriceps 1980. Infiltrative accumulation of inflammatory cells is seen.

Fig 3
Peripheral blood smear showing markedly decreased platelets and moderate amounts of schistocytes.
Sawdyk and Jundt

Table

<table>
<thead>
<tr>
<th>Date</th>
<th>Clinical</th>
<th>Hemoglobin (g/dL)</th>
<th>Platelets (thousand/mm³)</th>
<th>Blood Products Transfused</th>
<th>Prothrombin Time/Partial Thromboplastin Time (seconds)</th>
<th>Fibrinogen (mg/dL)</th>
<th>Fibrin Degradation (µg/mL)</th>
<th>Blood Urea Nitrogen (mg/dL)</th>
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<tr>
<td>7/26</td>
<td>Syncopal episode</td>
<td>9.5</td>
<td>7</td>
<td></td>
<td>15/30</td>
<td>315</td>
<td>10</td>
<td>31/1.1</td>
</tr>
<tr>
<td>7/28</td>
<td>Delirious</td>
<td>7.5</td>
<td>12</td>
<td>10 units platelets; 4 units fresh frozen plasma; 2 units packed red blood cells</td>
<td>30/110</td>
<td>236</td>
<td>10</td>
<td>14/0.9</td>
</tr>
<tr>
<td>7/30</td>
<td>Seizures; 2° disseminated intravascular coagulation</td>
<td>10.0</td>
<td>16</td>
<td>10 units platelets; 5 units fresh frozen plasma</td>
<td>17/110</td>
<td>76</td>
<td>80</td>
<td>23/2.6</td>
</tr>
<tr>
<td>7/31</td>
<td>Opens eyes; moves extremities</td>
<td>6.9</td>
<td>124</td>
<td>10 units platelets; 2 units fresh frozen plasma</td>
<td>19.5/110</td>
<td>188</td>
<td>80</td>
<td>16/1.7</td>
</tr>
<tr>
<td>8/2</td>
<td>Moves all extremities; responds to commands</td>
<td>9.9</td>
<td>115</td>
<td>4 units fresh frozen plasma</td>
<td>15/36</td>
<td>218</td>
<td>10</td>
<td>20/1.3</td>
</tr>
<tr>
<td>8/4</td>
<td>Alert; responding; 2° pneumonia</td>
<td>11.4</td>
<td>49</td>
<td>4 units fresh frozen plasma</td>
<td>15/30</td>
<td>263</td>
<td>20</td>
<td>20/1.0</td>
</tr>
<tr>
<td>8/5</td>
<td>Alert; responding; pneumonia progressing</td>
<td>10.6</td>
<td>12</td>
<td>10 units platelets; 4 units fresh frozen plasma</td>
<td>17/36</td>
<td>221</td>
<td>20</td>
<td>60/2.5</td>
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<tr>
<td>8/6</td>
<td>Hypotension; seizures; cardiac arrest</td>
<td>6.8</td>
<td>15</td>
<td></td>
<td>27/110</td>
<td>198</td>
<td>20</td>
<td>85/4.1</td>
</tr>
</tbody>
</table>

Therapy included high doses of corticosteroids (2 g methylprednisolone sodium succinate every four hours), plasmapheresis with plasma replacement (Table), and antiplatelet agents (100 mg dipyridamole every six hours). The clinical course consisted initially of progressive neurologic deterioration leading to coma and seizures. Likewise, the thrombocytopenia and hemolytic anemia persisted. Indeed, with the intense hemolysis, a secondary disseminated coagulopathy was triggered. However, by the sixth day the patient exhibited significant neurologic improvement as well as signs of stabilization of her hematologic parameters with concurrent correction of the disseminated coagulopathy. Unfortunately, secondary pneumonia disrupted this course, leading to the patient's final demise. Specific details are listed in the Table. Autopsy findings revealed multiple microcirculatory hyaline thrombi, most pronounced in portions of the brain, heart, and kidney (Figs 4,5). These histologic changes have been described previously in cases of TTP (20).

This form of therapy in TTP has led to remissions in 60% to 80% of cases. Improvement is achieved consistently when glucocorticoids, platelet inhibitors, and plasma exchange transfusions are used in combination (21).

Discussion

A variety of etiologies of TTP have been postulated and investigated. These include: the presence of a platelet aggregating factor (9), deficiency of a naturally occurring inhibitor of a platelet aggregating factor (12), abnormalities of endothelial function (11), and an immune etiology, which has been suggested because of the apparent association of TTP with disorders of autoimmune origin (13-19).

Because our patient experienced TTP several years after she had been treated for dermatomyositis, we would like to pursue the possible association of the disorders by an immunologic pathogenesis.

In 1972, Mant and his associates (5) described immunofluorescent studies done on autopsy specimens from a patient who died of TTP. IgM and complement and fibrin were demonstrated in the vicinity of the endothelium and in small-blood-vessel thrombi in multiple organs. Subsequently, Weisenburger and associates (6) demonstrated a case of TTP with deposition of IgM and C3 in small vessels using immunofluorescent studies. Meister and colleagues (7) reported circulating immune complexes in a patient who had TTP. These complexes cleared with plasma-exchange therapy, and the patient's condition returned to normal. Garvey and Freedman (8) demonstrated complement activation that induced complement coating of both platelets and red blood cells in their patient who had TTP. These complexes cleared with plasma-exchange therapy, and the patient's condition returned to normal. Garvey and Freedman (8) demonstrated complement activation that induced complement coating of both platelets and red blood cells in their patient who had TTP.
Dermatomyositis Complicated by TTP

Fig 4
Autopsy specimen of heart showing smaller arterioles thrombosed.

Fig 5
Autopsy specimen of kidneys demonstrating the presence of small thrombi within glomerular tufts. Mild degree of nephrosclerosis is seen.
had hemolytic uremic syndrome and TTP. These reports all supported the concept of a possible primary immunologic etiology for the vascular damage that occurs in patients who had TTP.

Immunoglobulin concentrations and complement staining of muscle tissue have been evaluated in patients who had dermatomyositis. Whitaker and Engel (23) studied biopsy specimens of muscle tissue from 36 patients who had inflammatory myopathies and described deposits of IgG, IgM, and/or C3 within morphologically abnormal muscle fibers in 21 of the patients. These findings were most frequently associated with cases of childhood dermatomyositis. The deposits were noted in small vein walls and, less frequently, in small artery walls in agreement with previously noted morphologic vascular alterations.

The deposits of immunoglobulin IgM and C3, alone or in combination, were detected in the walls of blood vessels not just in the endomysium. This observation suggests that these findings are not simply a nonspecific change but represent a primary vascular abnormality. Consequently, the study implies that (at least) childhood dermatomyositis may be associated with an abnormal immune response.

During this patient’s illness, laboratory evidence also demonstrated disseminated intravascular coagulation (DIC). This secondary phenomenon has been studied previously in other patients who had TTP. Jaffe and associates (24) studied the coagulation parameters in 12 patients who had TTP and found coagulation abnormalities consistent with disseminated intravascular coagulation in three.

An evaluation of the clinical course and coagulation data in Jaffe’s series does not support the concept that DIC played a primary pathogenetic role in TTP. When present, DIC appeared to be a secondary phenomenon related to exacerbation of the hemolytic process with subsequent release of red-blood-cell fragments. Additional evidence against DIC as a primary mechanism for TTP was suggested by the failure of heparin administration to influence the course of the disease. Our patient also received heparin therapy with no apparent effect on the outcome.

References


