Weber-Christian Disease Developing into Mediastinitis and Pleuritis with Massive Pleural Effusion

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Abstract

A 53-year-old man visited our hospital complaining of high fever. Chest computed tomography showed left pleural effusion and mediastinitis. He developed painful red subcutaneous nodules in his bilateral lower extremities. Thoracoscopy-assisted exploratory excision showed visceral pleura thickening; panniculitis in the periaortic area was histologically proven. The patient was treated with corticosteroid therapy which immediately reduced the fever. Subsequent imaging examinations after corticosteroid therapy showed improvement of mediastinitis and pleural effusion. This case reminds us that Weber-Christian disease (WCD) should be included in the differential diagnosis of mediastinitis although WCD is rarely associated with thoracic involvement.

Key words: panniculitis, pleurisy, thoracoscopy, exploratory excision, periaortitis

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Introduction

Weber-Christian disease (WCD) is a rare inflammatory disorder of subcutaneous adipose tissue (1-6). It is also known as idiopathic relapsing febrile lobular non-suppurative panniculitis and is characterized by recurrent subcutaneous inflammatory painful nodules, fever, and malaise due to systemic inflammation (5, 6). In severe cases, the inflammation can involve the lungs, heart, gastrointestinal tract, spleen, kidneys, and adrenal glands. WCD can develop into pleuritis with pleural effusion (7) or mediastinitis. Herein, we report the rare case of a man diagnosed with WCD developing into mediastinitis and pleuritis, and successfully treated with corticosteroid therapy.

Case Report

The patient was a 53-year-old Japanese man, 170 cm tall and weighing 69.0 kg. He visited our hospital complaining of high fever and progressive dyspnea of several days duration. He did not have any remarkable past history of illness. On admission, the patient’s body temperature was 38.1°C, blood pressure was 121/78 mmHg, and radial pulse rate was 116 beats/min and regular. He had neither anemia nor jaundice. A physiological examination revealed percussion dullness over the lower left chest. Abdominal palpation revealed no tenderness. He had no joint pain, muscle weakness or myalgia. He had no oral ulceration. There were no skin or nail lesions including butterfly erythema, discoid rash, heliotrope eyelids, scleroderma, sclerodactylia or pitting scar.

Laboratory findings included a red blood cell count of 427×10^4/μL, a white blood cell count of 9,350/μL (normal range [NR]; 3,500-8,500), and a platelet count of 31.1×10^4/μL. The hemoglobin concentration was 13.0 g/dL. Aspartate aminotransferase (AST) was 130 IU/L (NR; 10-35), alanine aminotransferase (ALT) was 132 IU/L (NR; 7-42), lactate dehydrogenase (LDH) was 372 IU/L (NR; 120-240), alkaline phosphatase (ALP) was 558 IU/L (NR; 110-360), and γ-glutamyltranspeptidase (γ-GTP) was 160 IU/L (NR; 5-40). On renal function tests, blood urea nitrogen (BUN) and creatinine levels were normal. C reactive protein was 24.2 mg/dL (NR; <0.3 mg/dL) and the erythrocyte sedimentation...
rate was 105 mm/h. Total protein was 6.4 g/dL (NR; 6.5-8.0 g/dL), and serum albumin was 3.2 g/dL (NR; 3.9-4.9 g/dL). Serum amylase and lipase were within normal range. The immunoglobulins, IgG and IgA and IgM were normal. Moreover, he did not have skin lesions that were suggestive of systemic sclerosis or dermatomyositis. A 18F-Ga-citrate scintigraphy showed no obvious abnormal hot spots. Bone marrow aspiration revealed no tumor cell involvement. A clinical diagnosis of WCD with massive pleural effusion due to pleuritis was made, based on these image findings, immunological examinations, histological findings of skin biopsy and exclusion of diseases causing panniculitis such as connective tissue diseases, infectious diseases or malignancies. The patient underwent a thoracoscopy-assisted exploratory excision because of the continuation of fever, dyspnea and progression of pleural effusion after admission. During thoracoscopy, visceral pleura was hard and visceral pleura thickening was observed (Fig. 5). A thoracoscopic biopsy was performed from the periaortic area. Histological examination of the biopsy specimens from the periaortic region revealed an infiltration of inflammatory cells (lymphocytes and neutrophils), foam cells and some fibroblasts (Fig. 6). Those inflammatory cells included both CD3 positive-lymphocytes and CD20 positive-lymphocytes. There was no tumor cell involvement. The histological diagnosis was compatible with panniculitis change in the periaortic region. The patient was treated with pulse corticosteroid therapy (intravenous methylprednisolone, 1 g/day for 3 days) and followed with oral administration of prednisolone (80 mg/day), which immediately reduced the fever and dyspnea. His mediastinitis, pleural effusion and red subcutaneous nodules were resolved. He remains now disease free for 18 months after corticosteroid administration under a maintenance dose of corticosteroid of 4 mg/day.

Discussion

WCD, first described in 1892 by Pfeifer (9), was delineated further in Weber’s 1925 report of a case of relapsing non supplicative nodular panniculitis (10). After Christian stressed the importance of fever in this syndrome in 1928 (11) it became known as Weber-Christian disease (5). The major symptoms are painful cutaneous nodules and accompanying fever. Other constitutional symptoms include malaise, arthralgia, hepatosplenomegaly, anorexia and weight loss (12). The prognosis of WCD is extremely variable. In patients with only cutaneous involvement, the prognosis is good. On the other hand, lobular panniculitis associated with prominent visceral involvement occasionally results in a poor prognosis and may eventually lead to right gluteal - coxal region (Fig. 2A) and around the left kidney (Fig. 2B). He developed painful red subcutaneous nodules in his bilateral lower extremities, right gluteal region and right coxal region on day 5 (Fig. 3). The skin biopsy specimen obtained from subcutaneous nodule revealed a finding of fat degeneration with foamy cells and an infiltrate of mononuclear cells (Fig. 4). Neither tumor cell involvement nor a finding of phagocytosis was seen in the skin biopsy specimen. The patient did not fulfill the established criteria for systemic lupus erythematosus (SLE) (8).
death (5). Major causes of death are sepsis, hepatic failure, hemorrhage, and thrombosis (4, 13).

Although WCD can involve any fat tissue of the body, mediastinitis and/or pleuritis with pleural effusion are rare complications of this systemic panniculitis. Kumagai-Kurata et al (7) described that pleural effusion occurred in 4 of 323 patients (1.2%) with WCD in their literature review. Achten et al (14) reported a fatal case of idiopathic liquefying panniculitis in which bilateral pleural involvement with oily fluids seemed to have been the cause of death. A MEDLINE search of the literature, revealed only 3 cases of WCD associated with mediastinitis and/or pleuritis in the last 35 years including the present case (7, 14) (Table 1). There have been a few reports of histologically proven mediastinitis or...
pleuritis with WCD (7). Two cases (Kumagai-Kurata’s case and present case) underwent thoracoscopy and the histological findings of panniculitis were present in 2 cases in Table 1. The thoracic complications of WCD might occasionally lead to severe clinical problems as in the present case. Thus, the sooner diagnosis and treatment, the better. Pleural biopsy is taken into consideration as a diagnostic modality when patients have abnormal findings suggesting pleuritis such as pleural effusion or pleural thickening. However, pleural biopsy may be missed as in the present case. Moreover, pleural biopsy can obtain the specimens only from parietal pleura. Thoracoscopy is also a useful diagnostic modality for pleural lesion, and it is available for thoracic biopsy. Kumagai-Kurata et al (7) reported a first WCD case with pleural effusion who was thorascopically examined and histologically documented pleural involvement of the disease. We also performed a thorascopy-assisted exploratory excision in the present case, and panniculitis change in the periaortic area was histologically proven. Thorascopic biopsy and thoracoscopy was useful for the observation of the visceral pleura and histological confirmation of the panniculitis in the mediastinum in the present case.

The differential diagnosis for WCD with thoracic involvement includes connective tissue diseases such as SLE or systemic sclerosis, infectious diseases, malignancies including cytophagic histiocytic panniculitis, and subcutaneous panniculitis-like T-cell lymphoma (SPTCL). Although the present patient was weakly positive for ANA, we could not attain a definite diagnosis of connective tissue diseases. Cultures of blood, urine and pleural effusion showed no bacteria or fungi. As far as we could examine, we could not find any evidence of malignant disease including lymphoma or cytophagic histiocytic panniculitis in the present case. The ADA level of pleural effusion was over 50 U/L in this case. This high level of ADA was not compatible with the decreased level of pleural effusion ADA due to malignancy. Kumagai-Kurata et al (7) described that the ADA level and percentage of CD4+ T-cells in pleural exudates are significantly correlated, and the ADA level is presumed to be a marker of cell mediated immunity. The high level of pleural effusion ADA might suggest that T cell-mediated immune response play a role in the pathogenesis of pleuritis in the present case. Recently, there were some reports describing that EBV-infected SPTCL (15, 16). Since serum EBV-DNA was negative, there was small likelihood that EBV infection affected his clinical course, although we did not perform EBV-encoded RNA in situ hybridization with thorascoposcopic skin biopsy specimens. Thus, we made the clinical diagnosis of idiopathic panniculitis.

WCD with prominent visceral involvement needs early treatment because of its progressive nature. Immunosuppressive agents such as cyclosporin A (CsA) or high dose-corticosteroids have been tried as treatment modalities (5-7, 12). However, a standardized treatment has yet to be established. There have been several reports in which corticosteroid treatment resulted in insufficient outcome (5-7, 17). Miyasaka (4) mentioned that corticosteroids are often effective to treat acute attacks of the disease, but are occasionally accompanied with unsatisfactory results. CsA is classified as a calcineurin inhibitor predominantly inhibiting interleukin-2 (IL-2) production and transduction of antigen-recognition signals in activated T cells (18, 19). Pongratz et al (6) reported a case of corticosteroid-resistant WCD; in that case, leflunomide, methotrexate and sulfasalazine were not effective, only CsA was responsive. CsA is an available, useful treatment modality for corticosteroid-resistant WCD (4, 5). In the present case, corticosteroid treatment was very effective and he improved rapidly following corticosteroid treatment. However, we should pay attention to recurrent inflammation in the future. This patient remains alive without disease 18 months after thoracic biopsy. In our opinion, we should carefully follow-up with CT images or serum inflammation markers and, if recurrent inflammation is identified, this patient will in the future undergo re-treatment with high-dose corticosteroids or CsA therapy. The treatment for WCD with thoracic complications to date has not been established and thus, further studies and accumulation of long-term follow-up cases are necessary. The pathogenesis of WCD also remains unknown. It has been related to an immunologically mediated reaction to diverse antigenic stimuli because of an association in some patients with elevated levels of circulating immune complexes (5, 17). Iwasaki et al (5) reported the successful treatment of WCD with CsA with normalization of increased serum interferon γ and soluble IL-2 receptor suggesting that some relationship may exist between T cell-mediated im-

**Table 1. Summary of 3 Cases of Weber-Christian Disease Associated with Mediastinitis and/or Pleuritis**

<table>
<thead>
<tr>
<th>Author</th>
<th>Age</th>
<th>Sex</th>
<th>Mediastinitis</th>
<th>Pleuritis</th>
<th>Pleural effusion</th>
<th>Histological findings of the biopsy specimen</th>
<th>Therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Achten</td>
<td>34</td>
<td>Female</td>
<td>Not described</td>
<td>+</td>
<td>+</td>
<td>Not described</td>
<td>Not described</td>
</tr>
<tr>
<td>Kumagai-Kurata</td>
<td>19</td>
<td>Male</td>
<td>Not described</td>
<td>+</td>
<td>+</td>
<td>Panniculitis in the pleura</td>
<td>Oral corticosteroid + cyclosporin A</td>
</tr>
<tr>
<td>Present case</td>
<td>53</td>
<td>Male</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>Panniculitis in the periaortic region</td>
<td>Oral corticosteroid</td>
</tr>
</tbody>
</table>
mune response and systemic inflammation in regard to the etiology of WCD. Pongratz et al (6) also mentioned that T cell-mediated immune response play an important role in the pathogenesis of WCD since his patient only responded to CsA. We thought that therapeutic response to high-dose corticosteroid or CsA in the patients with WCD also support the hypothesis. Further studies on the pathogenesis of WCD are required.

In conclusion, we report a rare case of WCD which progressed to mediastinitis and pleuritis with massive pleural effusion. This case reminds us that WCD should be included in the differential diagnosis of thoracic inflammation although WCD is rarely associated with thoracic complications.

The authors state that they have no Conflict of Interest (COI).

References