Severe Restrictive Pulmonary Defect in a Patient with Adult-Onset Still's Disease*

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Adult-onset Still's disease is characterized by seronegative arthritis, fever, and an evanescent skin rash. Earlier reports have described pneumonitis and pleuritis as manifestations of this disease. We report a patient with adult-onset Still's disease with severe restrictive ventilatory impairment and evidence of respiratory muscle weakness who responded to corticosteroid and aspirin therapy.

Adult-onset Still's disease, as originally described, is characterized by fever, evanescent macular or maculopapular rash, polyarthritis, and negative serologic tests for rheumatoid factor and antinuclear antibodies. Lymphadenopathy, splenomegaly, pharyngitis, elevated liver transaminases, and pericarditis are often present. The erythrocyte sedimentation rate is typically elevated, and marked leukocytosis is invariably present. Progressive bony ankylosis of the carpal bones has been described with greater frequency in adult-onset Still's disease than in other arthritic conditions. Although pulmonary involvement characterized by pleuritis and pleural effusions has been reported, only two reports of adult-onset Still's disease associated with impairment of pulmonary function have appeared in the literature. We present a patient with adult-onset Still's disease who was found to have a severe restrictive defect.

Case Report

A 34-year-old black man developed fever (39.4°C), pharyngitis, arthralgia of the wrists, shoulders, and knees, and pleuritic chest pain. Hepatomegaly, a right knee effusion, but no oropharyngeal abnormalities were noted. Erythrocyte sedimentation rate was 54 mm/h, and leukocyte count ranged between 11,000 and 20,000/cu mm. Blood, urine, and oropharyngeal cultures were negative. Chest x-ray film was normal, as were results from a bone marrow biopsy. Serum transaminase values were persistently elevated; liver biopsy revealed interstitial inflammation and fatty metamorphosis. The patient was treated with aspirin and indomethacin with resolution of his symptoms.

Thirteen years later, the patient presented to the Dallas Veterans Administration Medical Center with pharyngitis, pleuritic chest pain, fever (38.5°C), and bilateral knee, ankle, shoulder, and wrist arthralgia. Oropharyngeal examination was unremarkable. The lungs were clear to auscultation. A pericardial friction rub was heard. Splenomegaly was present without hepatomegaly or adenopathy. A right knee effusion and tenderness of the knees, shoulders, wrists, and metacarpophalangeal joints were noted. Extension of the wrists was reduced. Peripheral edema and ascites were absent, and there was no jugular venous distention or gallop rhythm. The initial chest x-ray film revealed a patchy lower lobe infiltrate. An ECG showed diffuse ST segment elevation consistent with pericarditis. The patient's white blood cell count was 26,500/cu mm (79 percent neutrophils, 2 percent band forms, 14 percent lymphocytes, 5 percent monocytes). The alkaline phosphatase, lactate dehydrogenase, aspartate aminotransferase, and alanine aminotransferase were all mildly elevated. The creatine phosphokinase was 46 units/L (nl <195). Arterial blood gas values while breathing room air were as follows: pH, 7.55; P O2, 53 mm Hg; and P CO2, 37 mm Hg. Thyroid function test results were normal. Serologic tests for rheumatoid factor, antinuclear antibody, syphilis, tularemia, and Brucella were negative. Cold agglutinins were absent and febrile agglutinins were nondiagnostic. The hepatitis B surface antigen was nonreactive. The erythrocyte sedimentation rate was 35 mm/h. Multiple blood, urine, and oropharyngeal cultures were negative. The right knee synovial fluid contained 4.4 g/L of protein, 216 mg/dL of glucose, 5,400 red blood cells and 56,400 white cells/cu mm (96 percent neutrophils and 4 percent mononuclear cells); Gram stain and culture results were negative. Roentgenograms of the hands, knees, ankles, and shoulders revealed degenerative changes out of proportion to the patient's age. Wrist films showed fusion of carpal bones.

During hospitalization, an evanescent macular rash developed over the trunk and upper extremities. Additionally, the patient experienced several episodes of dyspnea, worse in the supine position, associated with pulmonary rales and always accompanied by fever. Fleeting patchy infiltrates and small bibasilar pleural effusions were noted on daily chest x-ray films. A regimen of high dose aspirin was begun with initial resolution of all symptoms. Several days later, despite continuing aspirin therapy, fever, arthralgias, and episodic dyspnea returned. An echocardiogram showed no pericardial effusion. At cardiac catheterization, ventricular function and chamber sizes were normal and cardiac index was 3.7 L/min·m2. Pulmonary capillary wedge pressure, pulmonary arterial pressure, and pulmonary vascular resistance were normal. Endomyocardial biopsy revealed normal myocardium with no cellular infiltrate. Prednisone, 40 mg twice a day, was prescribed with gradual improvement of his symptoms, but complete resolution occurred only with the addition of high dose aspirin.

Table 1—Pulmonary Function Before and After Five Weeks of Therapy with Prednisone and Aspirin

<table>
<thead>
<tr>
<th></th>
<th>Before Therapy</th>
<th>%</th>
<th>Actual</th>
<th>Predicted</th>
<th>After Therapy</th>
<th>%</th>
<th>Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC (L)</td>
<td>2.01</td>
<td>45</td>
<td>2.84</td>
<td>64</td>
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<tr>
<td>FEV₁ (L)</td>
<td>1.68</td>
<td>46</td>
<td>2.19</td>
<td>60</td>
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<tr>
<td>FEV₁/FVC (%)</td>
<td>83</td>
<td></td>
<td>77</td>
<td></td>
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<tr>
<td>TLC (L)</td>
<td>3.55</td>
<td>49</td>
<td>4.27</td>
<td>58</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>FRC (L)</td>
<td>1.30</td>
<td>35</td>
<td>1.84</td>
<td>49</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>RV (L)</td>
<td>1.09</td>
<td>47</td>
<td>1.56</td>
<td>68</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Do (ml/min·mm Hg)</td>
<td>24.95</td>
<td>84</td>
<td>25.36</td>
<td>86</td>
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<td>DLVA</td>
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<td></td>
<td>7.88</td>
<td></td>
<td></td>
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<td></td>
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<tr>
<td>MIP (cm H₂O)</td>
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<td>120</td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>MEP (cm H₂O)</td>
<td>40</td>
<td></td>
<td>132</td>
<td></td>
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</tr>
</tbody>
</table>

*FVC is forced vital capacity; FEV₁, forced expiratory volume in one second; TLC, total lung capacity; FRC, functional residual capacity; RV, residual volume; Do, single breath carbon monoxide diffusion capacity; DLVA, carbon monoxide diffusion capacity corrected for alveolar volume; MIP, maximal inspiratory pressure at residual volume; and MEP, maximal expiratory pressure at total lung capacity.
Table 1 depicts the patient's pulmonary function before and five weeks after combination prednisone and aspirin therapy. Initially, they revealed a severe restrictive defect. Lung volumes determined by helium dilution were consistent with severe restriction. Maximum inspiratory and expiratory pressures measured at residual volume and total lung capacity respectively were also far below normal. These tests were performed in the absence of pain and with good patient cooperation. After three weeks of therapy, repeat pulmonary function tests indicated considerable improvement. Maximum inspiratory and expiratory pressures had completely normalized and the forced vital capacity and forced expiratory volume in one second had increased to near normal. There was also improvement in the residual volume and functional residual capacity. Single breath carbon monoxide diffusing capacity was normal on both occasions. At follow-up three weeks after discharge, the patient was nearly symptom free with no dyspnea at rest or with exertion and only mild shoulder arthralgias. He has been maintained on gradually tapering doses of prednisone and aspirin and has continued to do well.

**Discussion**

With the exception of the patient's restrictive pulmonary defect, this case represents a classic presentation of adult-onset Still's disease. At some time during the course of his illness, our patient demonstrated fever, rash, pharyngitis, and arthralgias. Splenomegaly, pericarditis, abnormal liver function tests, leukocytosis, and characteristic ankylosis of the carpal bones were also present.

A review of the literature reveals approximately 105 patients reported with characteristic features of adult-onset Still's disease. Of these patients, 30 (29 percent) are reported to have pulmonary manifestations. The majority was found to have pleuritis or pneumonitis. Chest x-ray films revealed pleural thickening, pleural effusions, pulmonary infiltrates, or atelectasis.

Until recently, there have been no reports of restrictive pulmonary defects associated with adult-onset Still's disease. In 1983, Corbett et al. reported a case with pleural effusions, left lower lobe infiltrate, and a severe restrictive pulmonary defect. Forced vital capacity was 0.94 L (26 percent predicted), FEV₁ was 0.92 L (30 percent predicted), and a carbon monoxide diffusing capacity was 5.9 ml/m/mm Hg (30 percent predicted). Transbronchial biopsy revealed mild nonspecific chronic interstitial inflammation and patchy interstitial fibrosis. There was no significant improvement in pulmonary function after five months of therapy with prednisone.

Troun et al. reported that nine of 12 patients with adult-onset Still's disease had pulmonary manifestations. These included pleurisy, pleural effusions, lung infiltrates, and dyspnea. Restrictive disease was demonstrated in seven of eight patients tested by measurement of lung volumes and vital capacity maneuvers. Carbon monoxide diffusing capacities were also low. A lung biopsy specimen from one patient showed acute alveolitis.

Our patient represents the third report of restrictive ventilatory impairment associated with adult-onset Still's disease. As with the two prior reports, our patient had evidence of fleeting pulmonary infiltrates, widening of the A-a oxygen gradient, as well as a decreased RV and FRC. This suggests that at least one component of the observed ventilatory restriction might be explained by direct lung involve-ment. Unlike previous reports, however, our patient had normal diffusing capacity and improved with therapy.

The decreased maximum inspiratory and expiratory pressures during our patient's acute illness suggest an abnormality in respiratory muscle function as well. This could have also partially contributed to the observed restrictive ventilatory pattern. Diaphragmatic dysfunction has been described in patients with systemic lupus erythematosus. These patients had normal diffusing capacities despite severe restrictive pulmonary function and maximum transdiaphragmatic pressures were low. It is possible that a similar mechanism might contribute to the respiratory dysfunction in some patients with adult-onset Still's disease.

**Conclusions**

A patient had adult-onset Still's disease associated with severe ventilatory restriction which responded to combined steroid and aspirin therapy. As in prior reports, our patient appeared to have evidence of parenchymal lung involvement. Unlike previous reports, our patient had the additional finding of profoundly low maximum inspiratory and expiratory pressures, indicating that respiratory muscle involvement may occur in this disease as well. As is the case in other rheumatologic diseases, the pulmonary manifestations of adult-onset Still's disease may take diverse and coexisting forms. Furthermore, this report suggests that the respiratory abnormalities in some patients with this disease may respond to therapy.

**References**


Severe Restrictive Pulmonary Defect in Still's Disease (Cantor, Pitcher, Hurd)