REFERENCES


Key words: corticosteroids; usual interstitial pneumonitis; varicella pneumonia

Abbreviations: UIP=usual interstitial pneumonitis; VZV=varicella-zoster virus

Usual interstitial pneumonitis (UIP) or cryptogenic fibrosing alveolitis is presumed to be an immunologic response to some undetermined antigen in genetically predisposed people. No such antigen has been definitively identified; however, there are some reports of the association between UIP and viral infections. Pulmonary infection caused by varicella usually resolves or, in some cases, causes a severe acute illness that may develop into ARDS. Here an unusual case of varicella pneumonia is presented in which the development of UIP, which was responsive to corticosteroid therapy, followed the viral pneumonia.

CASE REPORT

A 33-year-old woman with cerebral palsy had a 6-week history of cough and chest pain. Three months earlier, she was seen in the clinic for evaluation of shortness of breath, and on examination, she had the characteristic rash of varicella. Two of her children had chickenpox at that time; however, she had never had varicella before. A chest x-ray film showed the reticulonodular infiltration of varicella pneumonia (Fig 1, a), and she was admitted to the hospital for treatment with 900 mg of acyclovir every 6 h intravenously. A preexisting chest film taken two months before her varicella infection showed clear lung fields (Fig 1, a). She had an uneventful recovery, and the roentgenogram of the chest showed improvement (Fig 1, c). The patient had remained well until this episode occurred. She denied any other respiratory symptoms, and she was not taking any drugs or medications. She smoked three cigarettes a day.

A physical examination showed that she had kyphoscoliosis and walked with a spastic gait. She had no signs of anemia or clubbing. The examination of the chest revealed only occasional basilar crepitations. On walking up one flight of stairs, the oxygen saturation level fell from 98% to 84% while she was breathing room air. Serum bicarbonate level was 27 mmol/L (normal, 23 to 33 mmol/L); antinuclear antibody titer was less than 1:140; angiotensin-converting enzyme level was 25 U/L (normal, 8 to 52 U/L); and pulmonary function tests (Table I) showed a moderate restrictive pattern, with a decrease in the corrected diffusion coefficient, which suggested interstitial disease.

Her chest x-ray film demonstrated a diffuse reticulonodular interstitial process involving both lung fields. A high-resolution CT scan confirmed this pattern of reticulonodular infiltrate and showed some patchy ground-glass attenuation, mostly affecting the bases. Comparison of this CT scan of the chest to the archival CT scan of the same area (performed 6 months previously during an episode of pneumonia) demonstrated that the interstitial process was a recent development. Consequently, an open-lung biopsy was performed before any empirical treatment for UIP was suggested. A biopsy specimen of the lower lobe of the right lung was done through a

Usual Interstitial Pneumonitis Responsive to Corticosteroids Following Varicella Pneumonia*

Joseph Keane, MD; Bernadette Gochuico, MD; John M. Kasznica, MD; and Hardy Kornfeld, MD

Varicella pneumonia usually resolves after treatment, and occasionally miliary calcification develops on the roentgenogram of the chest years afterward. A case of varicella pneumonia is presented that followed a previously unreported course. In this case, usual interstitial pneumonitis (UIP) developed. The pneumonitis responded well clinically and radiographically to corticosteroid treatment. The role of viral pneumonia in the cause of UIP is discussed. (CHEST 1998; 113:249-51)

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Manuscript received February 20, 1997; revision accepted June 11, 1997.

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The histopathologic findings of the specimen showed UIP with diffuse, primarily lymphocytic inflammation and patchy areas of increased fibrosis in the interstitium (Fig 2, a and b). Both reticulin and trichrome stains were positive for collagen even in many areas that appeared architecturally intact. The inflammatory activity was of moderate intensity (Fig 2, c). No viral inclusions were seen. No organisms were seen on specific stains (acid-fast bacilli stain, periodic acid-Schiff, and Gomori's methenamine-silver stain). A polymerase chain reaction analysis of DNA prepared from the biopsy specimen of the lung proved negative for varicella-zoster virus (VZV) DNA. (The polymerase chain reaction is based on a primer set which amplifies a 249-base pair product of a conserved region of the VZV glycoprotein H gene. This assay has the sensitivity to detect between 10 to 100 copies of the VZV genome. A positive control of diluted supernatant from a culture of VZV-infected human foreskin fibroblast cells was used in the assay.)

Consequently, therapy was begun with prednisone, 60 mg daily. Her symptoms of cough and chest pain improved, and she developed only minor side effects from the corticosteroid therapy. Results of pulmonary function tests performed after 7 weeks of treatment showed significant improvement (Table 1). After 32 weeks of corticosteroid therapy, the patient was asymptomatic, and the roentgenogram of the chest showed some resolution of the reticulonodular infiltrate. The steroid dosage was consequently tapered and then stopped, and the patient remains asymptomatic.

**DISCUSSION**

Varicella in adults is complicated by pneumonia in about 15% of cases. The clinical course of this pneumonia usually is complete resolution within days. Years after recovery, there may occasionally develop miliary calcifications, which represent calcified necrotic foci, that may be evidenced on roentgenograms of the chest. In some patients, particularly those receiving immuno-suppressant therapy, pneumonia can progress rapidly within a period of days into ARDS, and the associated respiratory failure may be fatal. Postmortem studies of some of the patients who have experienced these serious problems demonstrate viral involvement of other organs, such as the liver, the spleen, the pancreas, the lymph nodes, and the esophagus. One case of persistent pulmonary granulomas occurring after vari-

**Table 1—Pulmonary Function Tests on Presentation and After Steroid Therapy**

<table>
<thead>
<tr>
<th>Tests</th>
<th>Initial % Predicted</th>
<th>Follow-up % Predicted</th>
</tr>
</thead>
<tbody>
<tr>
<td>FVC, L</td>
<td>1.64</td>
<td>1.98</td>
</tr>
<tr>
<td>FEV1, L</td>
<td>1.57</td>
<td>1.55</td>
</tr>
<tr>
<td>FEV1/FVC, %</td>
<td>121%</td>
<td>95%</td>
</tr>
<tr>
<td>Dsb, mL/min/mm Hg</td>
<td>8.28</td>
<td>9.24</td>
</tr>
<tr>
<td>DVA</td>
<td>3.31</td>
<td>4.52</td>
</tr>
<tr>
<td>VC, L</td>
<td>1.49</td>
<td>1.87</td>
</tr>
<tr>
<td>TLC, L</td>
<td>2.66</td>
<td>2.72</td>
</tr>
</tbody>
</table>

*Abbreviations: Dsb=diffusing capacity for carbon monoxide expressed as milliliters of CO transferred per minute per millimeter of mercury (sb=single breath); DVA=CO diffusing capacity per liter of alveolar volume; VC=vital capacity; TLC=total lung capacity.

Thoracotomy. The histopathologic findings of the specimen showed UIP with diffuse, primarily lymphocytic inflammation and patchy areas of increased fibrosis in the interstitium (Fig 2, a and b). Both reticulin and trichrome stains were positive for collagen even in many areas that appeared architecturally intact. The inflammatory activity was of moderate intensity (Fig 2, c). No viral inclusions were seen. No organisms were seen on specific stains (acid-fast bacilli stain, periodic acid-Schiff, and Gomori's methenamine-silver stain). A polymerase chain reaction analysis of DNA prepared from the biopsy specimen of the lung proved negative for varicella-zoster virus (VZV) DNA. (The polymerase chain reaction is based on a primer set which amplifies a 249-base pair product of a conserved region of the VZV glycoprotein H gene. This assay has the sensitivity to detect between 10 to 100 copies of the VZV genome. A positive control of diluted supernatant from a culture of VZV-infected human foreskin fibroblast cells was used in the assay.) Consequently, therapy was begun with prednisone, 60 mg daily. Her symptoms of cough and chest pain improved, and she developed only minor side effects from the corticosteroid therapy. Results of pulmonary function tests performed after 7 weeks of treatment showed significant improvement (Table 1). After 32 weeks of corticosteroid therapy, the patient was asymptomatic, and the roentgenogram of the chest showed some resolution of the reticulonodular infiltrate. The steroid dosage was consequently tapered and then stopped, and the patient remains asymptomatic.

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**Figure 1. Roentgenograms of chest. a: a premorbid film with clear lung fields. b: bilateral reticulonodular infiltrates at the time of the varicella illness. c: resolution of infiltrates after treatment with acyclovir. Kyphoscoliosis also is noted. There was no mediastinal lymph node enlargement, and signs of cardiac failure were not evident.**

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cella pneumonia has been described. The disease in the patient described here followed a previously unreported course owing to the development of UIP after varicella infection.

This case is unusual in that it describes a new pathologic outcome for varicella pneumonia. Studies have shown an association between UIP and exposure to other viruses. Although a viral prodrome often precedes the development of UIP, there has been no success in culturing viruses from UIP bronchoalveolar fluid. UIP has been reported in two patients following influenza virus A2 infection, and cytomegalovirus infection has been identified in a patient with untreated UIP. An association has been drawn between UIP and high titers of antibodies for Epstein-Barr virus and anti-hepatitis C. UIP has also been described as an unexpected complication of Legionnaires' disease and following Mycoplasma pneumonia.

CONCLUSION

The development of UIP in the patient reported here following varicella pneumonia suggests, but does not prove, a causal relationship. This patient's case supports a role for viral infection in the cause of UIP. Because the polymerase chain reaction for varicella was negative 6 months after the varicella pneumonia, we suggest that the UIP continued even after the viral infection that initiated the pneumonitis was successfully cleared. This patient also demonstrated a response to steroids, which probably spared her the fibrotic consequences of progressive UIP.

ACKNOWLEDGMENT: Peter D. Clarke, MD, gave advice and assisted in preparing radiologic data in this report.

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