Giant Cell Arteritis Presenting as Interstitial Lung Disease

George H. Karam, M.D.; and Jack D. Fulmer, M.D., F.C.C.P.

A 58-year-old woman had a clinical history compatible with polymyalgia rheumatica but with an unexplained interstitial lung disease. Evaluation, including biopsy specimens of temporal artery, lung, and gastrocnemius muscle, was consistent with giant cell arteritis. This case identifies giant cell arteritis as a cause of interstitial lung disease.

Giant cell arteritis affecting temporal arteries was first described by Horton et al1 in 1932 as a "focal localization of some unknown systemic disease." Involvement of the aorta and its large branches with giant cell arteritis subsequently expanded the concept of the extent of vascular involvement of this disease. It is now evident that giant cell arteritis is a systemic disease, and many organ systems can be involved. Pulmonary involvement, however, is quite rare.

A patient is reported who presented with clinical features of temporal arteritis and also had interstitial lung disease. Biopsy specimen of temporal artery demonstrated giant cell arteritis and lung biopsy specimen showed peribronchial and interstitial granulomata. Gastrocnemius muscle biopsy specimen also showed an arteritis. In this report, the clinical and pathologic features of the case are presented, and the literature on lung involvement with giant cell arteritis is reviewed.

Case Report

A 58-year-old white woman was in her usual state of health until October 1980, when she noted the onset of a sore throat with nasal discharge, cough, and fatigue. She was treated with an antibiotic for one week with some resolution in her sore throat, but with continued fatigue. She subsequently developed myalgias and arthralgias and again was treated with an antibiotic for an additional five days without improvement. In early November 1980, she began to develop temperature elevations to 102°F (38.8°C) daily. She was again treated with ten days of antibiotics but continued to have daily temperature spikes up to 102°F (38.8°C). She was subsequently hospitalized in an outlying hospital where work-up revealed an abnormal chest roentgenogram (see right). Bronchoscopy was performed and was considered nondiagnostic. Multiple skin tests for tuberculosis were negative, and in early December 1980, she was transferred to the University Hospital at the University of Alabama in Birmingham (UAB).

Examination at the time of transfer revealed a healthy-appearing white female in no distress. She was normotensive and had a temperature of 99.8°F (37.6°C) orally. Eye examination revealed a left subconjunctival hemorrhage, but funduscopic examination was unremarkable. Temporal arteries were nontender and not prominent. Auscultation of the chest was pertinent for the presence of late harsh crackles over both bases posteriorly, most pronounced on the left side. No muscle tenderness, swelling, or weakness was demonstrable. The remainder of her examination was normal.

Positive laboratory findings included an anemia with a packed cell volume of 28 percent, a reticulocyte count of 1.4 percent, and an elevated WBC count of 12,000/cu mm. Erythrocyte sedimentation rate was 114 mm/hr (Wintrobe). Chest roentgenogram showed bibasilar reticular pattern with upper lobe fibrocystic disease (Fig 1).

Multiple cultures on admission were negative for bacteria, fungi, and mycobacterial organisms. Collagen vascular work-up was positive only for a latex RA of 1:1280. The patient was HLA B27 negative and hepatitis-B surface antigen negative. Pulmonary function studies revealed a restrictive ventilatory pattern with a vital capacity of 73 percent predicted, total lung capacity of 72 percent predicted, and a diffusing capacity of 70 percent predicted; the forced expiratory volume in one second/forced vital capacity was

Figure 1. Chest roentgenogram showing bibasilar reticular infiltrates and bilateral upper lobe fibrocystic disease.
79 percent observed. Because of suspected arteritis, multiple biopsy specimens from varied sites were obtained. Temporal artery biopsy specimen showed noncaseating granulomata in the tunica media with destruction of the internal elastic lamina (Fig 2). Transbronchial biopsy specimen from the right lower lobe demonstrated ill-defined granulomata within the bronchial wall and within the alveolar interstitium (Fig 3). Granuloma consisted of epithelioid histiocytes, occasional multinucleated giant cells, and a mantle of lymphocytes and plasma cells. Gastrocnemius muscle biopsy specimens showed diffuse infiltration of the gastrocnemius artery with inflammatory cells consisting of both neutrophils and eosinophils. The lumen was obliterated by inflammatory debris. Fibrinoid necrosis was not observed (Fig 4). Special stains of all biopsy material were negative for acid-fast organisms and for fungi. Subsequent cultures were negative.

**DISCUSSION**

Since the original description by Horton et al of giant
The classic histopathologic feature of giant cell arteritis is granulomatous arteritis with prominent Langhan's giant cells, with the major involvement in the tunica media. In some cases, there may be smooth muscle necrosis and deranged internal elastic membrane. While the prominent cell types are lymphocytes, plasma cell, and macrophages, the presence of eosinophils and neutrophils has been noted. The pathologic spectrum of giant cell arteritis may, however, include nonspecific inflammatory reactions of vessels with infiltration of the arterial wall with neutrophils, lymphocytes, and eosinophils without granulomata. Some vessels may have intimal fibrosis with severe obliteration of the media and the internal elastic membrane without an inflammatory process. This likely reflects the natural course of the disease process. Skip lesions, in which areas of active arteritis are interposed among seemingly normal sections of artery, are common in temporal arteritis and contribute to the difficulty in making the diagnosis.

This patient initially presented with nonspecific symptoms suggesting an upper respiratory tract infection. Her symptoms gradually progressed to include myalgias and fever. Chest roentgenogram showed a bibasilar reticular infiltrate with upper lobe fibrocystic disease, and pulmonary function studies showed a mild restrictive defect. Temporal artery biopsy specimen showed the features of classic giant cell arteritis. In contrast, transbronchial biopsy specimen failed to show any arteries but showed interstitial granulomata and peribronchial granulomata. Gastrocnemius muscle biopsy specimen showed an acute polymorphonuclear arteritis with the inflammatory cells being primarily neutrophils and eosinophils. Although a granulomatous arteritis was not demonstrated in transbronchial lung biopsy specimen, the presence of peribronchial granulomata and interstitial granulomata are consistent with disseminated giant cell arteritis involving lung.

Lung involvement in giant cell arteritis is extremely rare. In 1947, Anderson described a patient with temporal arteritis who presented with hemoptysis. Subsequent histologic studies of lung at the time of autopsy demonstrated giant cells in the interstitium. Cravioto and Feigin, in 1959, reported an 18-year-old male with temporal arteritis who also developed cerebral arteritis, which led to his death. At autopsy, his lungs showed small granulomata resembling those in brain. No specific mention was made of giant cells as the inflammatory component of the pulmonary infiltrate. In 1978, Lie described disseminated giant cell arteritis in four men who had no antemortem diagnosis of temporal arteritis. All had giant cell arteritis involving at least three of the following organs in some combination: heart, lungs, kidneys, liver, pancreas, and stomach. No involvement of temporal arteries could be demonstrated in any of these four individuals, and none had symptoms to suggest polymyalgia rheumatica; therefore, these patients were felt to have a newly recognized entity referred to as "disseminated giant cell arteritis." Very recently, Rotenstein et al have re-

**Table 1—Vessels Reported as Being Involved in Giant Cell Arteritis**

<table>
<thead>
<tr>
<th>Arteries</th>
<th>Branches of the aorta:</th>
<th>Intraparenchymal vessels</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal</td>
<td>Subclavian</td>
<td>Meningeal</td>
</tr>
<tr>
<td>Ophthalmic</td>
<td>Aorta</td>
<td>Intracerebral</td>
</tr>
<tr>
<td>Posterior ciliary</td>
<td>Axillary</td>
<td>Renal</td>
</tr>
<tr>
<td>Facial</td>
<td>Radial</td>
<td>Hepatic</td>
</tr>
<tr>
<td></td>
<td>Ulnar</td>
<td>Splenic</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>Mesenteric</td>
</tr>
<tr>
<td></td>
<td>Femoral</td>
<td>Myometrial</td>
</tr>
<tr>
<td></td>
<td>Iliac</td>
<td>Tubal</td>
</tr>
<tr>
<td></td>
<td>Renal</td>
<td>Lymph nodes</td>
</tr>
</tbody>
</table>

**Figure 4. Gastrocnemius muscle biopsy specimen showing a polymorphonuclear vasculitis.**

Cells in the temporal artery of a patient who clinically had giant cell arteritis, it has been recognized that there is a clear association between giant cell arteritis (temporal arteritis) and polymyalgia rheumatica. However, Cooke et al, in 1943, described two patients who had temporal arteritis and at postmortem examination had arteritis involving multiple medium and large-sized arteries. Since this time, multiple reports of involvement of other medium and large-sized arteries in many other organ systems, as well as arteriole and venous involvement, have been described (Table 1). Lung involvement has been extremely rare, and giant cell arteritis has not been referred to as a cause of interstitial lung disease. The clinical symptoms of arteritis were not always present at death.
ported granulomatous (giant cell) arteritis in a family with polyarthritis. Autopsy of one of the family members showed granulomata in lung.

Several theories on the etiology of temporal arteritis have been advanced; all are only speculative. The histopathologic findings in patients with temporal arteritis frequently show fragmentation of the internal elastic membrane with a surrounding inflammatory exudate containing giant cells with ingested bits of elastic membrane. The observations have led to the speculation that the collagenous structures of artery serve as an autoantigen. In certain other diseases, collagen has also been implicated in the pathogenesis of the disease. In the fibrotic lung diseases, it has been shown that collagen may be recognized as foreign. Similar pathogenic mechanisms have been suggested in progressive systemic sclerosis and rheumatoid arthritis. Further work to suggest the participation of the immune system in temporal arteritis has been the demonstration of anti-IgG antibodies in the temporal artery biopsy specimen. This led to the speculation that temporal arteritis can be caused by circulating immune complexes. This remains to be proven, however.

The clinical picture in giant cell arteritis may be varied, with the most common symptoms being headache, polymyalgia rheumatica, and jaw claudication, in association with nonspecific symptoms such as anorexia, malaise, and visual symptoms. Tenderness over the temporal artery, scalp tenderness, fever, and weight loss are the most frequently noted signs. Although our patient's clinical presentation was compatible with giant cell arteritis, her interstitial lung disease was not initially explainable on this basis.

Since 1943, it has been recognized that temporal arteritis may be part of a spectrum of a disease involving multiple organs. With the description of the entity of disseminated giant cell arteritis, it seems likely that temporal arteritis may be only part of the spectrum of giant cell arteritis that ranges from isolated arteritis involving extracranial vessels to a generalized arteritis involving a number of different organ systems. This patient demonstrates this type of multisystem involvement. The clinical significance of this interesting association remains to be proven, but there may be a growing recognition that the disorder that was once considered as a focal giant cell arteritis may be a form of disseminated disease that may present either in a limited or disseminated form.

REFERENCES

4 Huston KA, Hander GC. Giant cell (cranial) arteritis: a clinical review. Am Heart J 1980; 100:99-107
7 Eshaghi J. Controversies regarding giant cell (temporal, cranial) arteritis. Documenta Ophthalmol 1979; 47:43-67
10 Mumenthaler M. Giant cell arteritis (cranial arteritis, polymyalgia rheumatica). J Neurol 1978; 218:219-36