Microscopic Polyangiitis Associated with Sinobronchial Syndrome
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Abstract

A woman with a long history of chronic bronchitis and chronic sinusitis, i.e., sinobronchial syndrome, was admitted with a fever. Radiologically, there were areas of long-standing consolidation in both lungs, with areas of active inflammation demonstrated by gallium-67 scintigraphy. Antineutrophil cytoplasmic antibody specific for myeloperoxidase was highly positive. Pulmonary hemorrhage and hematuria occurred 2 weeks after admission and responded to steroid therapy. However, the patient died of pneumonia. An autopsy revealed systemic necrotizing vasculitis affecting multiple organs, consistent with microscopic polyangiitis. The vasculitis might have been caused by the chronic inflammation in the lungs associated with sinobronchial syndrome.

Key words: systemic vasculitis, antineutrophil cytoplasmic antibody, myeloperoxidase, chronic bronchitis, chronic sinusitis, pulmonary consolidation

Introduction

Systemic vasculitis associated with chronic suppurrative lung disease has been reported in some cases of bronchiectasis, diffuse panbronchiolitis, and cystic fibrosis (1-5). Chronic inflammation may play a role in the pathogenesis of the vasculitis. We report a case of microscopic polyangiitis with a long history of sinobronchial syndrome, a chronic suppurrative lung disease. The patient had long-standing areas of consolidation in both lungs, thought to represent organized pneumonia. These areas of consolidation might have been the source of the chronic inflammation associated with the pathogenesis of the systemic vasculitis in this case.

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Dyspnea, slight hemoptysis, and gross hematuria developed for the first time. A chest radiograph and CT scan showed bilateral infiltration, suggesting pulmonary hemorrhage. The CT scan also showed bleeding within the capsule of the left kidney. The hemoglobin level decreased from 9.3 to 6.5 g/dl over 24 hours. Respiratory failure developed, requiring mechanical ventilation. Disseminated intravascular coagulation also developed: platelet count decreased to 111×10^9/L, prothrombin time was prolonged to 12.8 seconds (INR 1.38), fibrinogen concentration decreased to 76 mg/dl, and D-dimer test was 46.8 μg/ml (normal <1.2 μg/ml).

We suspected a diagnosis of ANCA-related vasculitis, and started pulse therapy with 1 g of methylprednisolone for 3 days followed by 60 mg (1.5 mg/kg body weight) of prednisolone per day. On the 20th hospital day, a needle biopsy specimen from the lingual consolidation showed scarred lung tissue and some focal irregularly shaped areas of necrosis. The scar was compatible with a long-standing organized pneumonia. Although the etiology of the necrosis could not be clarified, it might have been due to vasculitis. No microorganisms were cultured from this sample, and neither Mycobacterium tuberculosis nor Mycobacterium avium-intracellulare complex was detected by the polymerase chain reaction technique.

After the steroid therapy, the respiratory failure and infiltration in both lungs improved. The disseminated intravascular coagulation also was resolved. Although the leukocytosis was not resolved, the C-reactive protein level decreased to <0.3 mg/dl. The MPO-ANCA titer decreased to 150 EU, and the circulating immune complex decreased to the normal range. However, granulocytopenia, probably caused by antibiotics or famotidine, progressed from the 31st hospital day, and the patient died of severe pneumonia on the 37th hospital day.

An autopsy revealed systemic necrotizing vasculitis involving small and medium-sized arteries. Vasculitis was seen in the lungs, kidneys, heart, liver, spleen, uterus, small intestine, gallbladder, right adrenal gland, and thyroid gland (Fig. 3). Although there was no glomerulonephritis, capillaritis was seen in the lungs. There were no apparent epithelioid cell granulomata. This case was diagnosed as microscopic polyangiitis according to the nomenclature advocated by an International Consensus Conference in 1994 (6–8). All the areas of pulmonary...
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Nary consolidation consisted of fibrosis and focal necrosis, which was the same as seen in the lingual segment biopsy (Fig. 3). The autopsy did not reveal the etiology of the necrosis in these areas.

Discussion

“Microscopic polyangiitis”, formerly called “hypersensitivity vasculitis” or “microscopic polyarteritis”, is one of the small vessel vasculitides associated with ANCA (6–8). Pathologically, the absence of granulomata distinguishes it from Wegener’s granulomatosis and Churg-Strauss syndrome, the other two ANCA-associated vasculitides (6–8). Therefore, we diagnosed this case as microscopic polyangiitis from the high MPO-ANCA titer, systemic necrotizing vasculitis including capillaritis, and the absence of granulomata, although glomerulonephritis, which usually accompanies microscopic polyangiitis, was not seen.

There have been three case reports of microscopic polyangiitis associated with chronic suppurative lung disease (2, 3, 5), and our case is the fourth. Interestingly, three of the four cases are Japanese. The first case was a 57-year-old woman with “microscopic polyarteritis” and bronchiectasis (2). The second was a 53-year-old man with “hypersensitivity vasculitis” and bronchiectasis (3). The third was a 46-year-old woman with “MPO-ANCA-related vasculitis” and sinobronchial syndrome (diffuse panbronchiolitis and chronic sinusitis) (5). These variously named vasculitides should be classified as “microscopic polyangiitis” according to the present nomenclature (6–8).

Although the etiology of systemic vasculitides, including microscopic polyangiitis, is not known, it has been suggested that immune complexes are important in the pathogenesis (1–4). Moreover, in cases with chronic suppurative lung disease, the bacterial flora may be the antigen source (1–4). In addition, MPO-ANCA may play some role in the pathogenesis of cases of microscopic polyangiitis. Although it is uncertain whether MPO-ANCA is pathogenic or merely a serological marker, MPO-ANCA is known to stimulate neutrophils to produce oxygen radicals and to damage human endothelial cells in vitro (9–11). Therefore, the chronic inflammation in suppurative lung disease may cause microscopic polyangiitis by inducing MPO-ANCA production. Indeed, an interesting case was recently reported (12). A 56-year-old Japanese woman with bronchiectasis had areas of dilated bronchi with pulmonary fibrosis localized to the lingual segment and left lower lobe, which were similar to the findings of the present case. Although vasculitis was not seen, she had a high titer of MPO-ANCA. Furthermore, the titer decreased to the normal range after surgical resection of these areas. This report strongly suggests that

Figure 3. Microscopic findings of an autopsy. Top: pulmonary artery in the lingual segment showing vasculitis with disruption of the elastic lamina (arrows) (Elastica-van Gieson stain, x64). Middle: arcuate artery in the left kidney showing vasculitis with disruption of the elastic lamina (arrows) (Elastica-van Gieson stain, x64). Bottom: lingual consolidation of the lung showing organized pneumonia with irregularly shaped areas of necrosis (HE stain, x64).
chronic inflammation of the lung can cause MPO-ANCA production. In this case, a titer of ANCA specific for bactericidal/permeability-increasing protein (BPI) (BPI-ANCA) was also high before surgery, and decreased to normal after surgery (12). BPI-ANCA recently has been recognized to be associated with vasculitides including microscopic polyangiitis (13) and chronic suppurative lung disease with Pseudomonas aeruginosa infection (12, 14, 15). Therefore, it is also possible that chronic suppurative lung disease causes microscopic polyangiitis by inducing BPI-ANCA production.

The present patient had an extremely high titer of MPO-ANCA and a slightly increased circulating immune complex on admission, when she had a fever, but no other signs of vasculitis, such as hemoptysis or microhematuria. Perhaps the production of MPO-ANCA and immune complex was induced by the chronic inflammation in her lungs. It is also possible that MPO-ANCA or immune complex, especially the former, played some role in the pathogenesis of her systemic vasculitis. Although the titer of BPI-ANCA was not measured in this case, BPI-ANCA might have played some role in the pathogenesis, because she had a long history of recurrent infections with Pseudomonas aeruginosa.

In our case, minocycline was used from the 5th to 14th hospital day, before the development of her hemoptysis and hematuria on the 15th hospital day. And minocycline rarely induces autoimmune syndromes such as lupus and vasculitis, which are associated with ANCA including MPO-ANCA (16, 17). However, it is unlikely that minocycline caused her systemic vasculitis, because long-term use (mean, 30 months; range, 24–36 months) is necessary for the development of vasculitis in the reported cases (16). Furthermore, she had an extremely high titer of MPO-ANCA before the use of minocycline.

The present patient’s fever started five weeks before the appearance of hemoptysis and microhematuria. Furthermore, the inflammatory foci seen on the gallium-67 scintigram were localized to the areas of chronic pulmonary consolidation, consisting of fibrosis and irregularly shaped areas of necrosis. Therefore, her fever likely represented inflammation in these areas, especially in those with necrosis. Her fever did not seem to be caused by respiratory tract infection alone, because her sputum was not purulent, no microorganisms were detected in her samples, and her fever was not resolved with antibiotics. Although neither biopsy nor autopsy clarified the etiology of the necrosis, it might have been due to vasculitis, and these areas of pulmonary consolidation might have been the initial sites of her systemic vasculitis. However, we could not completely deny the possibility of infection, such as a micro- abscess, as the main etiology of the inflammation, because the biopsy was performed after many antibiotics had been administered. Even if infection was the main cause of her fever, it is likely that the chronic inflammation in the pulmonary consolidations played some role in the production of MPO-ANCA and the development of her systemic vasculitis.

In conclusion, we report a case of microscopic polyangiitis that might have originated from chronic inflammation of the lungs in association with sinobronchial syndrome. In addition, we emphasize that vasculitis must be included in the differential diagnosis when a patient with chronic suppurative lung disease has a fever, especially without purulent sputum.

**References**