Development of Multi-Organ Involvement Including a Left Atrial Myxoma-like Lesion in a Patient with Granulomatosis with Polyangiitis

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Abstract

A 76-year-old woman suffering from granulomatosis with polyangiitis (GPA) developed organizing pneumonia with positive antineutrophil cytoplasmic antibodies and microscopic hematuria. Prednisolone improved the hematuria and radiological findings; however, after tapering the dose of prednisolone, a posterior left atrial wall mass was detected in association with a fever. Both regressed spontaneously, although secretory otitis media and sinusitis were noted; the resected sinusitis specimen exhibited vasculitis highly suggestive of GPA. The clinical picture of GPA with multi-organ involvement can vary. Recognizing the various manifestations of GPA is therefore necessary in order to provide an appropriate diagnosis and disease management.

Key words: granulomatosis with polyangiitis, Wegener’s granulomatosis, cardiac involvement, heart, organizing pneumonia


Introduction

Granulomatosis with polyangiitis (GPA), previously termed Wegener’s granulomatosis, is a necrotizing granulomatous vasculitis of small- to medium-sized vessels. Common target organs outside the lungs include the kidneys, skin, eyes, joints, muscles and nervous system (1), although other organs can also be affected. The clinical course of GPA can be severe or fatal; however, the spontaneous improvement or wandering of pulmonary and/or renal lesions has been reported at a low frequency. It is important to recognize the variety of clinical presentations of GPA in order to provide an appropriate diagnosis and disease management.

Recently, we experienced a woman with GPA that initially presented with lung involvement with a histologic pattern of organizing pneumonia (OP) who subsequently developed cardiac and otorhinolaryngologic complications regarded as wandering. We herein report this case, which offered diagnostic and therapeutic challenges, focusing on the patient’s cardiac involvement and clinical course in order to illustrate the varied clinical presentations of GPA.

Case Report

In September 2011, a 76-year-old woman developed appetite loss and a low-grade fever. A local physician found abnormal shadows on a chest X-ray (Fig. 1a) and referred the patient to our hospital. She had no history of smoking and had not been exposed to dust. In addition, she had no significant underlying diseases, past medical history, drug allergies or history of vaccination prior to the onset of symptoms. Her height and body weight were 146 cm and 36.5 kg, respectively. Laboratory tests showed a white blood cell count of 10,400/μL (neutrophils, 84.2%; lymphocytes, 8.5%; monocytes, 6.8%; eosinophils, 0.3%; and basophils, 0.2%), a hemoglobin level of 11.7 g/dL, a platelet count of 36.8×10⁴/μL and an erythrocyte sedimentation rate of 127 mm/h. Serum samples showed a total protein level of 6.0 g/dL (albumin, 40.8%; α₁, 6.5%; α₂, 16.8%; β, 11.1%; and γ, 45.8%).
24.8%), a creatinine level of 0.6 mg/dL, a lactate dehydrogenase level of 156 IU/L and a C-reactive protein level of 9.4 mg/dL. Autoantibodies were negative, except for an anti-neutrophilic cytoplasmic antibody against myeloperoxidase (MPO-ANCA), with a titer of 24.6 U/mL, and the fluoroenzyme immunoassay value of <3.5 U/mL was normal. Chest computed tomography (CT) showed bilateral subpleural consolidation (Fig. 1b) that did not improve with treatment with levofloxacin.

We performed bronchoscopy in October 2011. Transbronchial lung biopsy specimens obtained from the right lower lobe exhibited histologic changes consistent with a diagnosis of OP (Fig. 1c); however, no histologic evidence of GPA was found. Bronchoalveolar lavage fluid yielded methicillin-sensitive *Staphylococcus aureus*. A urinary sediment test detected microscopic hematuria (red blood cell count, 20-29 cells/high-power field without urinary casts). We therefore diagnosed the patient as having cryptogenic OP (2) and initiated treatment with prednisolone (30 mg daily), trimethoprim (80 mg daily) and sulfamethoxazole (400 mg daily). This therapy resulted in the resolution of the patient’s fever, with negative findings for red blood cells on a urinary sediment test and negative MPO-ANCA, as well as improvements in the chest CT findings (Fig. 1d). Treatment with trimethoprim and sulfamethoxazole was continued after the patient was discharged from the hospital, while the dose of prednisolone was gradually tapered. In July 2012, under treatment with prednisolone at a dose of 14 mg daily, the patient again developed chest discomfort, general fatigue, appetite loss and a low-grade fever. Microscopic hematuria also recurred (10 to 19 cells/high-power field), and the C-reactive protein level was elevated at 14.5 mg/dL. Chest CT revealed no recurrence of the lung lesions, and MPO-ANCA remained negative. Repeated cultures of the sputum, blood and urine were negative. Gallium-67 scintigraphy showed an abnormal uptake in the posterior wall of the left atrium (Fig. 2a). Transsthoracic echocardiography showed a low echoic mass lesion (26 mm long and 9 mm thick) on the posterior wall of the left atrium (Fig. 2b) that was also detected on transesophageal echocardiography (Fig. 2c). This sessile mass did not exhibit the usual polypoid anatomy of a left atrial myxoma; however, we considered it to most likely be a variant of myxoma. The patient rejected any further tests and has since been followed on an outpatient basis. The dose of prednisolone was gradually tapered to 11 mg daily.

In September 2012, the patient’s general fatigue and appetite loss improved spontaneously. However, she developed

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**Figure 1.** Chest X-ray, computed tomography and histologic findings. A chest X-ray showed right-sided consolidation (a). Chest computed tomography demonstrated subpleural consolidation (b) with a pathology of airspace organization and interstitial infiltration (×100, Hematoxylin and Eosin staining, c). The subpleural consolidation improved with steroid therapy (d).
hearing difficulty in January 2013. The serum levels of MPO-ANCA and PR-3 ANCA were negative. A local physician diagnosed her with secretory otitis media with sinusitis, and she underwent surgery for the sinusitis. The histology of the resected specimen showed vasculitis (Fig. 3), and we therefore diagnosed her with GPA. The mass located in the left atrium was obscured on transthoracic echocardiography, and gallium-67 scintigraphy showed the disappearance of the radioisotope uptake observed at the previously positive location in the left atrium. Chest CT showed no relapse of the pulmonary lesions. The dose of prednisolone was increased to 30 mg daily, and cyclophosphamide (500 mg/m²) was administered once a month starting in March 2013, which resulted in improvements in the patient’s hearing difficulty.
ability and CRP level. As of November 2013, the patient continues to be followed on an outpatient basis.

**Discussion**

The lung specimen obtained via a transbronchial lung biopsy in this case showed histologic findings compatible with a diagnosis of OP. Although OP is associated with a variety of etiologies, in some cases, the etiology is unknown (cryptogenic OP). We initially treated our patient as having cryptogenic OP, and her lung lesions improved following the administration of corticosteroids. Later, however, we diagnosed her with GPA, and because there are reported cases of GPA in which an OP pattern is predominant (3), we therefore regarded the OP to not be cryptogenic, but rather indicative of pulmonary involvement of GPA. Histologic variety of GPA in the lungs has been reported (3, 4), typically showing a combination of necrotizing granulomatous inflammation with extensive parenchymal necrosis and necrotizing vasculitis. However, GPA can also present with several other histologic variants and associated features, including bronchocentric inflammation, marked eosinophil infiltration, alveolar hemorrhage and capillaritis, interstitial fibrosis and an OP pattern (4). The OP pattern is a common nonspecific histologic manifestation of acute lung injury involving the peribronchial parenchyma. The pulmonary specimen obtained in this case was small, and it is possible that the typical histologic findings of GPA were simply not detected. Nevertheless, we should have suspected GPA based on the positive MPO-ANCA results and presence of hematuria, in addition to the histologic findings of OP.

The MPO-ANCA titer in our patient was not elevated during the course of either cardiac involvement or otorhinolaryngologic symptoms. MPO-ANCA is found in 5-20% of patients with GPA (5). It is assumed that, clinically, the ANCA titer is correlated with the disease activity (6); however, there is a report that only 40% of patients exhibit an increased ANCA level upon relapse of GPA (7). In the present patient, elevation of the CRP level was associated with the development of both cardiac and otorhinolaryngologic complications. Physicians should therefore realize that the ANCA values do not always reflect the disease activity of GPA, which should be evaluated comprehensively based on the findings of a physical examination, inflammatory markers and radiological examinations.

A low echoic mass was found in the left atrium in the present patient. The differential diagnosis included malignancy or cardiac infection; however, these diagnoses contradicted our findings, as the mass regressed without any additional drug treatment. We therefore considered the cardiac lesion to be a manifestation of cardiac involvement of GPA. Such cardiac involvement has been reported in 6% to 44% of cases of GPA (8). Pericarditis or coronary arteritis are the most common findings, with other manifestations including myocarditis, conduction system involvement and myocardial infarction (9). Cases of a mass in the left ventricle have also been reported (10), and severe manifestations include congestive cardiomyopathy (11) and pericardial tamponade (12). Furthermore, valvular/endothelial diseases that occasionally mimic left atrial myxoma or bacterial endocarditis have been reported to be manifestations of GPA (13, 14), similar to that observed in the present patient. Although the mass observed in this case was not assessed histologically, we assumed the presence of inflammatory cell infiltration with or without granulomas or myxomatous degeneration (13).

The clinical course of GPA can be severe or fatal; however, some cases of the spontaneous improvement or wandering of pulmonary and/or renal lesions have been reported (15-19). Although prednisolone and trimethoprim/sulfamethoxazole were administered in the present case, the cardiac involvement improved without additional treatment. Therefore, we regard this as spontaneous improvement or wandering. The detailed mechanisms underlying the regression of cardiac involvement during the tapering of prednisolone remain unclear. Interactions between extrinsic factors, genetic factors and the cellular and humoral immune systems may be involved (16); however, further studies are needed to clarify this issue.

Cases of the spontaneous improvement of cardiac involvement are usually not reported, possibly because the patients are treated aggressively with surgery or immunosuppressants. Unfortunately, we did not initially suspect the patient to have GPA, and she rejected further tests or surgery. Therefore, no histologic evidence was obtained, and we did not administer an immunosuppressant. This case shows that cardiac manifestations can resolve spontaneously. However, cardiac manifestations of GPA are often associated with increased morbidity and a poorer prognosis (20); therefore, simple observation is not recommended.

In conclusion, the clinical picture of GPA with multisystem involvement can vary, and recognizing the various manifestations of GPA is necessary in order to provide an appropriate diagnosis and carry out effective disease management.

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

**References**

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