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CASE REPORT

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A case of Wegener's granulomatosis complicated with seropneumothorax

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Abstract We report the case of a 52-year-old man with Wegener's granulomatosis complicated with seropneumothorax. Pneumothorax or seropneumothorax has previously been reported as a rare complication of Wegener's granulomatosis. The patient was successfully treated with prednisolone and cyclophosphamide, and seropneumothorax was resolved without tube drainage. This case suggests that the pathogenesis of seropneumothorax may be associated with the disease activity of Wegener's granulomatosis because it developed spontaneously before treatment with immunosuppressive agents and without being complicated by infection.

Key words Cyclophosphamide · Prednisolone · Seropneumothorax · Wegener's granulomatosis

Introduction

Wegener's granulomatosis is a systemic disorder of unknown etiology characterized by the development of necrotizing granulomatous vasculitis resulting in organic involvement, which is mostly found in the upper and lower respiratory tracts and kidneys. Pneumothorax or seropneumothorax has been reported as a rare complication of Wegener's granulomatosis, although various clinical features can develop.[1,2] Here, we describe the case of a patient with Wegener's granulomatosis complicated with seropneumothorax who was successfully treated with prednisolone and cyclophosphamide.

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Case report

A 52-year-old man presented with a fever, general fatigue, and polyarthralgia on December 15, 2000. He had first visited a local hospital, where antimicrobial agents were prescribed. However, his symptoms did not improve, and multiple pulmonary nodules were observed on chest X-ray. He was then referred to Kariwagun General Hospital on December 31, 2000. A high fever continued after admission although meropenem, a broad-spectrum carbapenem antibiotic, was administered intravenously. In addition, epistaxis, proteinuria, hematuria, oliguria, serum creatinine elevation, and a swelling of the extremities developed. He was transferred to our hospital on January 9, 2001.

On examination, petechia was identified on the periphery of his upper and lower extremities and anasarca was observed. No abnormal neurological findings were noted. The results of hematological, biochemical, and immunological examinations were as follows: white blood cell (WBC) count 13800/μl (neutrophils, 86.2%; basophils, 0.4%; eosinophils, 0.6%; lymphocytes, 10.3%; monocytes, 2.5%); erythrocyte sedimentation rate (ESR) 24 mm/h; C-reactive protein (CRP) concentration 6.1 mg/dl. Serum total protein was 5.3 g/dl and serum albumin was 2.2 g/dl. Serum creatinine was 3.2 mg/dl and serum urea nitrogen was 81 mg/dl. Serum potassium concentration was 5.4 mEq/l. Antinuclear antibody, rheumatoid factor, myeloperoxidase-specific antineutrophil cytoplasmic antibodies (MPO-ANCA) and proteinase 3-ANCA (PR3-ANCA) were negative. Daily urinary protein was 1.4 g. Hematuria and sterile pyuria were found. An examination of resting arterial blood gases in room air showed pH 7.374, PaO_2 90.6 Torr, $PaCO_2$ 26.9 Torr, bicarbonate 15.3 mEq/l, and a base excess of −8.3 mEq/l. A chest radiograph and computed tomography

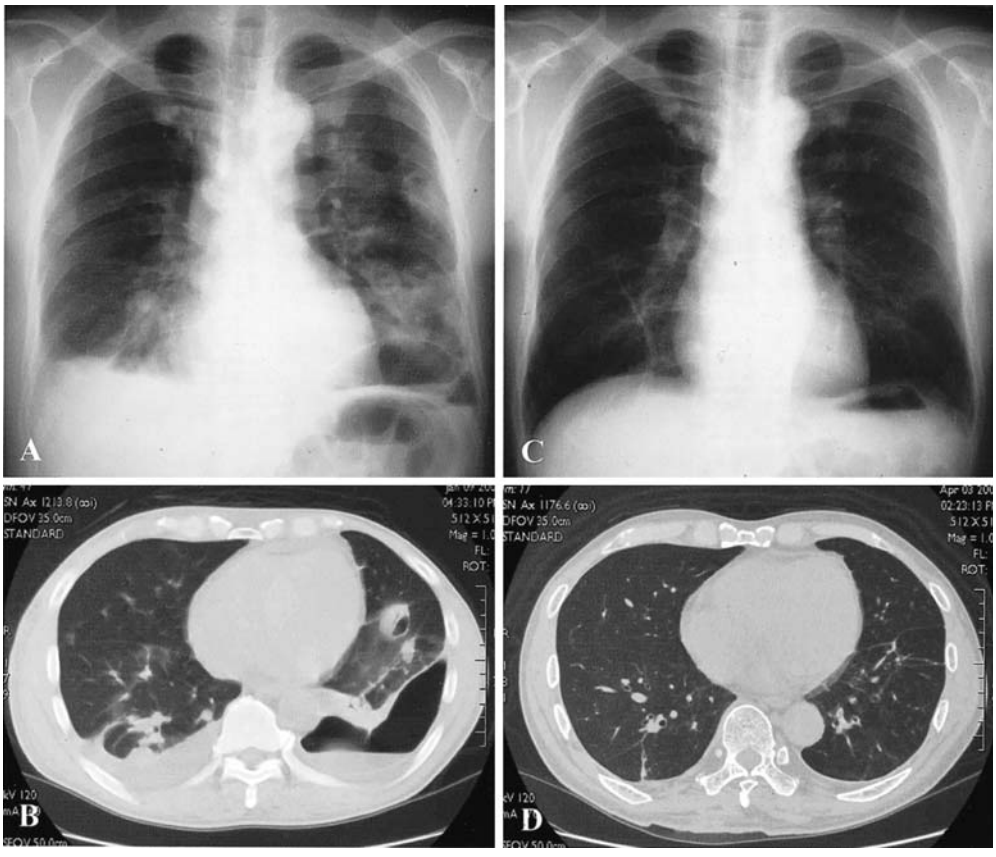

Fig. 1. Chest radiograph (**A**) and computed tomography (CT) scan (**B**) on admission showed bilateral multiple pulmonary nodules, some of which were complicated with cavity formation, left pneumothorax, and bilateral pleural effusion. After treatment with immunosuppressive agents for 4 months (**C**, **D**), the lesions had almost disappeared

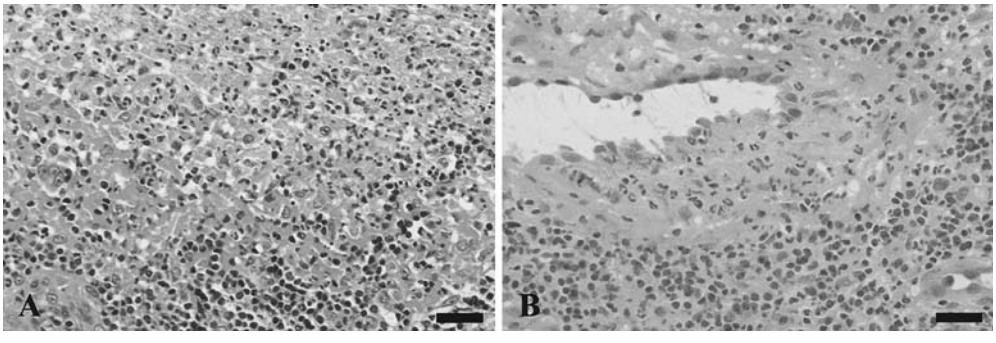

Fig. 2. **A** Low-power view of the nasal mucosa, showing marked infiltration of various inflammatory cells (HE stain; original magnification ×40). *Bar*, 100 μm. **B** High-power view of the nasal mucosa, showing necrosis of part of the vessel wall as well as cellular infiltration (HE stain; original magnification ×400). *Bar*, 10 μm

(CT) scan showed bilateral multiple pulmonary nodules, some of which were complicated with cavity formation, left pneumothorax, and bilateral pleural effusion (Fig. 1A,B). A nasal mucosal biopsy was performed because the patient had a history of epistaxis before admission to our hospital. A specimen showed infiltration of numerous inflammatory cells, such as neutrophils, lymphocytes, and plasma cells, in the nasal mucosa, and necrotizing vasculitis (Fig. 2). These findings were consistent with Wegener's granulomatosis, although there was no granulomatous formation within the specimen. Cytological examination of the sputum showed no fungi, acid-fast bacilli, or other pathogenic microorganisms. No malignant cells were seen. Bacteriological cultures yielded normal respiratory flora. Fungal cultures and mycobacterial cultures were negative. Bronchoalveolar lavage and diagnostic thoracentesis had been performed at Kariwagun General Hospital before his transfer to our hospital. Cytological examinations of the specimens had shown no microorganisms or malignant cells, and cultures of the specimens were negative. However, the pleural effusion was bloody and exudative. Various leukocytes, such as histiocytes, lymphocytes, and neutrophils, were seen. The results of biochemical examinations were as follows: lactate dehydrogenase (LDH) 770 IU/l, adenosine deaminase (ADA) 21.3 IU/l, and carcinoembryonic antigen (CEA) 1.9 ng/ml. We diagnosed Wegener's granulomatosis because of the clinical course, radiological findings, and pathological findings, according to the standard criteria.

Methylprednisolone at 1.0 g/day was administered for 3 days. The patient was then started on prednisolone at 60 mg/day (1 mg/kg/day) and cyclophosphamide at 50 mg/day (0.8 mg/kg/day). Left seropneumothorax was treated

conservatively without tube drainage owing to the lack of any respiratory symptoms or hypoxemia. Pleural adhesion was thought to prevent the left lung collapsing completely. After the medication, a gradual improvement in renal function and increased urine volume were noted. Serum creatinine, serum urea nitrogen, and daily urinary protein decreased to 1.1, 26 mg/dl, and 0.15 g, respectively. Pulmonary nodules and pleural effusion dwindled slowly, and left pneumothorax disappeared over the next 3 months (Fig. 1C,D). The dose of prednisolone was decreased to 35 mg/day, and the patient was discharged on April 27, 2001. He has been followed up in our out-patient department.

Discussion

We have described a patient with Wegener's granulomatosis complicated with seropneumothorax. Seropneumothorax or pneumothorax has previously been reported as a rare complication of Wegener's granulomatosis, although various pulmonary problems can develop.[1,2] To the best of our knowledge, Beidleman, in 1963,[3] reported the first case that developed pneumothorax after starting treatment for Wegener's granulomatosis. Several cases that developed seropneumothorax or pneumothorax in association with this treatment have since been reported.[4–7] Both the disease process and the treatment might cause unexpected pathological changes. A necrotic granulomatous lesion was thought to rupture into the pleural space. A bronchopleural fistula was found in a patient who presented with seropneumothorax.[8] Also, some cases were reported in which pulmonary infection might be associated with the occurrence of pneumothorax.[3–5] All these patients died. Jaspan et al.[4] described a case of a secondary infection in a cavitated nodule which possibly precipitated pneumothorax. That patient had a respiratory tract infection after immunosuppressive agents (prednisolone and cyclophosphamide) were administered, and then developed right pyopneumothorax. Despite intensive treatment, he died of septicemia caused by uncontrolled infection 6 weeks after admission. The existence of bronchopulmonary lesions as well as the use of immunosuppressants might compromise the host's defense against microbial pathogens. Inflammation due to secondary infection might easily cause the destruction of fragile tissue. Epstein et al.[9] reported that the occurrence of spontaneous pneumothorax was associated with the activity of the disease. They experienced two cases that spontaneously developed pneumothorax before treatment and showed no evidence of microbial infection. In addition, pneumothorax was the initial radiographic pulmonary manifestation of the disease in one case. Therefore, seropneumothorax or pneumothorax might not represent a complication, but be the primary disease, although this is a very rare manifestation. Although the frequency of pleural lesions complicated by Wegener's granulomatosis is unknown, Farrelly[2] reported that two of 91 cases had developed pleural effusion. Gohel et al.[10] reported that pleural effusion was present in one of 20 cases and pneumothorax in one of 20 cases. Couthaliac et al.[11] reported that two of 10 cases of Wegener's granulomatosis developed pneumothorax, and these two had excavated subplueral nodules. The rupture of subpleural lesions occurring incidentally in a patient with pleural effusion may cause seropneumothorax. Vasculitis of the disease might cause both pneumothorax and pleuritis. There have been an insufficient number of cases reported for the mechanism of development of seropneumothorax complicated by Wegener's granulomatosis to be ascertained.

Our patient had clinical features characteristic of Wegener's granulomatosis and his nasal mucosal biopsy showed infiltration of numerous inflammatory cells and necrotizing vasculitis which are compatible with Wegener's granulomatosis. He was therefore diagnosed with Wegener's granulomatosis, although PR3-ANCA specific to the disease was negative. He developed seropneumothorax at the incipient stage of the disease before starting specific treatment. Since all culture specimens were negative, there was no evidence of bacterial infection. It is suggested that seropneumothorax in this case might have been associated with the disease process of Wegener's granulomatosis as reported by Epstein et al.[9] The finding of exudative pleural fluid suggested pleuritis, probably associated with vasculitis of the disease. A severe inflammatory reaction of the pleura might be a factor in the development of seropneumothorax or pneumothorax, but it is not clear why only a few cases of Wegener's granulomatosis developed these pleural diseases.

At present, patients with Wegener's granulomatosis should be treated with both corticosteroid and an immunosuppressive cytotoxic agent, such as cyclophosphamide.[12] Because our patient had systemic organ involvement at the onset of disease, strong immunosuppressive therapy was thought to be necessary. Most cases of Wegener's granulomatosis complicated with pneumothorax are treated with tube drainage. However, the use of catheters might increase the risk of bacterial infection in a compromised host receiving immunosuppressive therapy. Conservative therapy for seropneumothorax or pneumothorax without tube drainage may be tried if the patient lacks respiratory symptoms and hypoxemia, as in our patient. Minimizing the risk of infection may have facilitated a successful outcome in this case.

This case indicates that the occurrence of pneumothorax or seropneumothorax as a rare complication of Wegener's granulomatosis can be associated with the pathogenesis of the disease. Also, pulmonary infection by microbial pathogens should be avoided because of possible lethal complications caused by infection when a patient with Wegener's granulomatosis develops pneumothorax or seropneumothorax either before or after starting treatment.

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