Mod Rheumatol (2008) 18:76-80
DOI 10.1007/s10165-007-0007-y

CASE REPORT

Spontaneous pneumothorax in Wegener's granulomatosis: a case report

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Received: 1 May 2007 / Accepted: 7 September 2007 / Published online: 27 December 2007

Abstract Wegener's granulomatosis (WG) is a multiorgan system disease of unknown etiology characterized by granulomatous inflammation, tissue necrosis, and variable degrees of vasculitis in small- and medium-sized blood vessels. In patients with WG, the musculoskeletal system can be involved before other typical symptoms of the disease. Also in WG, pneumothorax can develop as a rare complication. In this paper, we report a case with WG who had early articular involvement in the absence of classic features of illness and had pneumothorax which resulted from the rupture of the sub-pleural nodule. The aim of this work is to increase the awareness of early articular involvement in WG and the pneumothorax possibility especially in cases with cavitated nodules closure to pleura. This case emphasizes that early diagnosis and treatment is very important in avoiding further complications.

Keywords Wegener's granulomatosis · Pneumothorax · Musculoskeletal involvement

Introduction

Wegener's granulomatosis (WG) is a multisystem disease characterized by necrotizing granuloma of the upper and lower respiratory tracts, disseminated vasculitis, and glomerulonephritis. Respiratory system involvement varies from pulmonary nodules to fulminant alveolar hemorrhage. Arthritis or arthralgia symptoms are seen more frequently. In this literature, we report a case that had articular symptoms for years and where the patient later died from spontaneous pneumothorax, which is a rare complication of WG.

Case report

A 62-year-old man admitted to our department with complaints of left knee and bilateral ankle swelling, purpuric rash at lower legs, cough, high fever, and hemorrhagic sputum. His complaints began with upper respiratory system symptoms such as sneezing, nasal flux, sore throat, and constitutional symptoms one month earlier. Ten kilograms of weight loss, necrotizing bullous purpuric rash at the lower legs and over the right third metacarpophalangeal (MCP) joint, palpable purpura on the calf, oral ulceration, fever, cough, and hemorrhagic sputum were added within 3 weeks. His medical history began with shoulder pain that developed 6 years earlier as a first complaint when he was living in a European country. In the following 4 years he had migratory arthralgias that occurred for few days and then recovered. Arthritis at the knees also occurred 2 years ago. The characterization of the arthritis was similar. He then began treatment with 20 mg/day prednisolone and the treatment was continued with low-dose steroids for 6 years due to a diagnosis of undifferentiated migratory joint disease.

Systemic examination revealed multiple oral necrotizing ulcerations, submandibular lymphadenopathies sized approximately 0.5 cm in diameter, rales over both lower lung fields, and splenomegaly. Arthritis in left knee and

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both ankles, left third metacarpophalangeal and proximal interphalangeal joints and necrotizing bullous purpuric rash and palpable purpura were determined in the examination of extremities. Laboratory tests demonstrated proteinuria of 667 mg/day. Mid-stream urine analysis showed proteinuria and hematuria, in the urine microscope no red cell casts, but a few hyaline casts were seen. White blood cell count was 16,000 mm^{-3}, erythrocyte sedimentation rate (ESR) was 106 mm/h, and C-reactive protein (CRP) was 23.5 mg/L. Blood urea, creatinine, and transaminases were high. Rheumatoid factor and antinuclear antibodies were negative. C-antineutrophilic cytoplasmic antibody was positive at a titer of 1:100. Chest radiography showed a cavitary nodule at the right sub-pleural localization and another nodule at the left lower lobe. Reticulonodular opacities, cavitated nodules in bilateral lobes and ground glass attenuation in the left lobes were determined in thorax computerized tomography (CT) scan (Fig. 1). A biopsy specimen from the right lung revealed necrotizing granulomatous vasculitis that is concordant with WG (Fig. 2a, b). Histopathologic evaluation of a skin biopsy taken from palpable purpura in the left lower extremity showed leukocytoclastic vasculitis.

The patient was diagnosed with WG according to the 1990 American College of Rheumatology [1] and the Chapel Hill criteria [2]. One mg/kg intravenous prednisolone and 4 mg/kg oral cyclophosphamide per day administration were ordered. Marked improvement in clinical and laboratory findings (ESR was 35 mm/h, and CRP was 1.14 mg/L) were seen due to treatment. At the ninth day of treatment, the patient's fever rose to 38.8°C. *Pseudomonas aeruginosa* was determined in the cultures of blood of the patient. Sensitive antibiotherapy was started and his fever began to fall, but suddenly his general state worsened and dyspnea developed. He was referred to the intensive care unit but his oxygen saturation decreased rapidly and he did not respond to the resuscitation. Unfortunately we lost the patient due to respiratory arrest. Chest X-ray demonstrated pneumothorax resulting from the rupture of the sub-pleural nodule which had collapsed into the pleural space (Fig. 3).

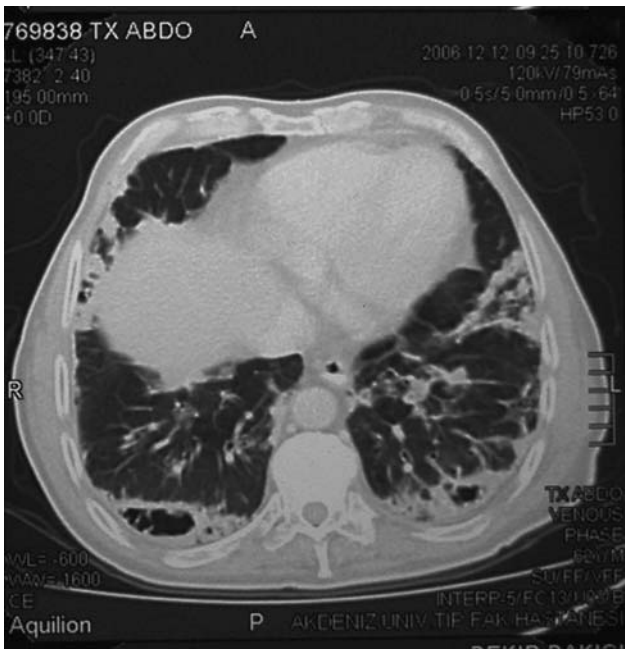

Fig. 1 Axial CT image of chest shows bilateral reticulonodular opacities and pleural adhesive cavitations at the right lobe with surrounding inflammatory changes and basal of the left lobe reveals randomly distributed ground-glass opacities

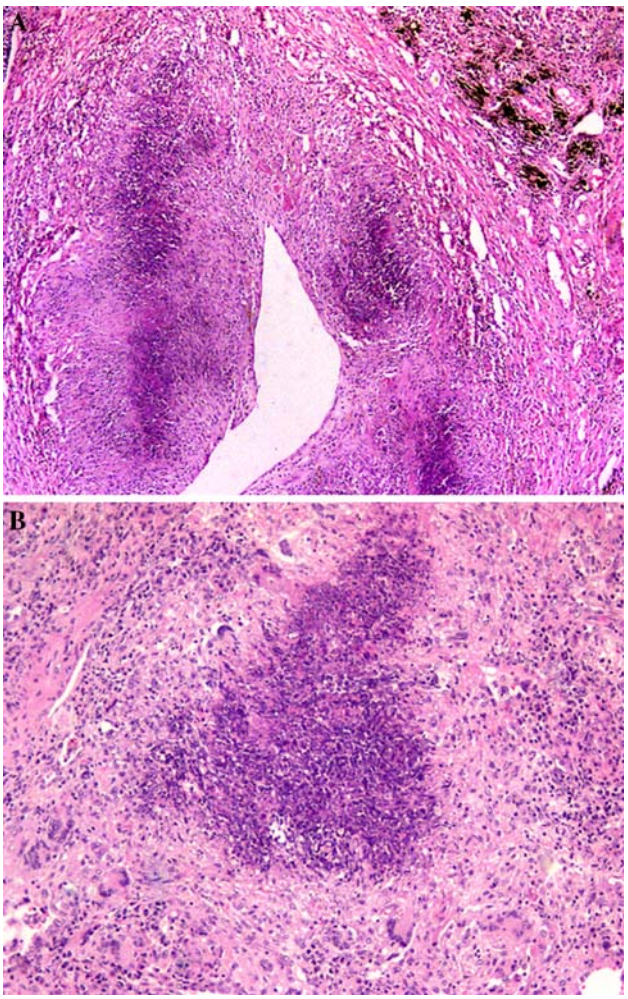

Fig. 2 The typical pulmonary lesions of Wegener's granulomatosis consist of vasculitis, parenchymal necrosis, and granulomatous inflammation. **a** The artery shows foci of eccentric, transmural inflammatory infiltrate destroying the vessel wall and basophilic necrosis (H&E ×40). **b** There is a large zone of geographic necrosis with an irregular, serpiginous border and the central necrotic zone is surrounded by a dense mixture of acute and chronic inflammation, palisading histiocytes, and several multinucleated giant cells (H&E ×100)

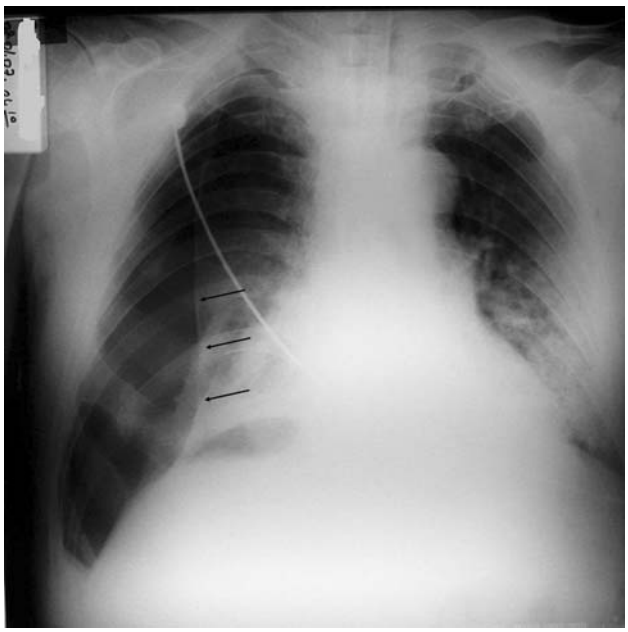

Fig. 3 Chest X-ray showing a curvilinear shadow possibly representing pneumothorax in the right lung and multiple, irregular reticulonodular opacities in the left lung

Discussion

WG is a multiorgan system disease of unknown etiology characterized by granulomatous inflammation, tissue necrosis, and variable degrees of vasculitis in small- and medium-sized blood vessels. Although WG may affect virtually any organ system, the disease has a predilection to the upper respiratory tract, lungs, and kidneys [3]. Except for these classical symptoms, articular complaints are the most encountered finding [4–7]. Pulmonary involvement incidence was reported 61–94% in different series [4–7]. Although 70% of the pulmonary lesions are nodules, pleural involvement is under 10% [8]. The occurrence of a pneumothorax as a complication of WG is very rare. Currently, ten WG cases that had pneumothorax have been reported [8–14] (Table 1). The mechanism by which this complication occurs in the disease is not clear. Some authors reported that the cavitated nodules tend to develop pneumothorax [8, 14]. Seven of the 11 presented cases have cavitated lesions that may support this idea. The lesions' closure to pleura could be another possible mechanism. In our patient, pneumothorax developed in the right lobe from which the biopsy was taken so administration of corticosteroid and immunosuppressive agents could cause pneumothorax due to delayed wound recovery in spite of a month-long period after the open biopsy. Most presented WG cases with pneumothorax had high dose corticosteroid and cyclophosphamide. With our case, the presented four cases resulting in death were accompanied by infection, which could be another reason. Therefore, under immunosuppressive therapy, pneumothorax should be suspected as a complication in WG cases with unexpected dyspnea and fever.

As musculoskeletal system involvement, arthralgia can be seen in a high ratio in 80% of the cases with WG, but active arthritis is not frequent. Myalgias are common in most patients with joint symptoms and may occur alone. When joint complaints are persistent, recurrent, and are the dominant abnormality, the differential diagnosis may be difficult. If small and large joints involve symmetrically and rheumatoid factor is positive in laboratory findings (60%), the patient may be misdiagnosed with having rheumatoid arthritis. Other patients may have monoarticular, pauciarticular, or migratory polyarthritis [3]. Although articular involvement in WG has been described in detail, data regarding onset time of articular complaint is not clear. In some patients in whom musculoskeletal

Table 1 Reported WG cases with pneumothorax

Source	Age/sex	WG duration	Radiologic feature	Pleural drainage	Pneumothorax or pyopneumothorax	Disease course
Epstein et al. [9]	48, male	4 years	No lesion	Yes	Pneumothorax	Improvement
	58, male		Multiple cavities	No	Pneumothorax	Death
Jaspan et al. [10]	33, male	A few weeks	Nodules cavities	Yes	Pyopneumothorax	Death
Wolffebbuttel et al. [11]	63, male	3 weeks	Bilateral multiple nodules	Yes	Pyopneumothorax	Death
Ogawa et al. [12]	16, female	9 months	Bilateral multiple cavities	Yes	Pneumothorax	Improvement
Bulbul et al. [13]	45, male	1 month	Bilateral cavities	Yes	Pneumothorax and empyema	Death
Delèvaux et al. [8]	46, male	6 weeks	Cavitery nodules	Lobectomy	Pyopneumothorax	Improvement
	25, male		Bilateral nodules	No	Pneumothorax	Improvement
	70, male		Pulmonary hemorrhage	No	Pneumothorax	Improvement
Ates et al. [14]	29, female	15 months	Cavitery nodules	Yes		Improvement
Our patient	65, male	6 years	Cavitery nodules	No	Pneumothorax	Death

symptoms are the major initial feature of disease, the diagnosis of WG may not be made until other, more classic features of illness occur. The duration between the onset of complaints and diagnosis time has been reported as 6–12 months in a study containing 701 cases with WG [5]. This period reflects the diagnosis time in WG cases with typical systemic symptoms of the disease and the duration may be longer in cases with milder or atypical symptoms. The complaints of arthralgia and arthritis of our patient began 6 years previously before classical features of active disease occurred; which was the longest articular involvement period that we encountered in the literature without other components of the disease. The long time between the beginning of articular complaints and active disease in our case can be attributed to mild pattern of the disease or corticosteroid administration for a long time. Although his articular complaints could have been caused by either the inception of WG or any other disease, it was considered as the precursor of WG because of the relapsing and remission periods with no deformity development and migratory characteristics of arthritis.

Migratory arthritis is characterized by a rapid onset of swelling in one or two joints, with resolution over a few days. As the symptoms resolve, similar symptoms emerge in another joint, usually in an asymmetric location. This symptom pattern can also occur in gonococcal arthritis, rheumatic fever, sarcoidosis, systemic lupus erythematosus, Lyme disease, bacterial endocarditis, and Whipple's disease [15]. Although it is rare, patients with WG may also have migratory arthralgias and/or arthritis [3, 16]. Viruses (e.g., human parvovirus B19, hepatitis viruses), crystals, and serum sickness reactions are known causes of acute, self-limited polyarthritis [17]. Our patient had migratory arthralgias 6 years and arthritis 2 years before the classical symptoms of the disease began.

Cutaneous lesions (papules, nodules, purpuric patches, palpable purpura or ulcers) due to cutaneous leukocytoclastic vasculitis have been observed in 30–50% of patients during the course of the disease, while they are presenting sign in 8.6–13% of patients [18]. Usually, the presence of cutaneous lesions in WG can be correlated with a higher severity of systemic disease, as was seen in our patient [19]. Our patient had palpable purpura on both calves that appeared 1 month before arriving at our department and his illness was rapidly progressive.

Infection with a range of common and opportunistic pathogens like *pseudomonas*, *Escherichia coli*, *Klebsiella*, *Staphylococcus aureus*, is a frequent complication in patients using cyclophosphamide. The reported frequency of cyclophosphamide-associated infection varies, probably as a function of the stage and severity of the underlying disease, the degree of cyclophosphamide-induced immunosuppression, and variations concomitant glucocorticoid regimens. Despite differences in clinical experience, infections are a common and potentially serious complication of all cyclophosphamide-based regimens [20]. In a previous study it was suggested that oral cyclophosphamide regimens generally pose a greater risk of infection than IV pulse regimens [21]. Furthermore, some clinicians believe that IV cyclophosphamide is less effective than oral cyclophosphamide for the treatment of Wegener's granulomatosis [22]. In the light of this knowledge, and because our patient's disease was severe, we started oral cyclophosphamide therapy. At the ninth day of the treatment, *Pseudomonas aeruginosa* infection also developed in our patient. The patient immediately responded to the sensitive antibiotheraphy and his fever fell. Therefore we do not believe that infection was the cause of death. The patient's respiratory reserve was already impaired due to his disease and respiratory arrest developed very swiftly. The patient died without the opportunity to place a chest tube.

In patients with WG, the musculoskeletal system can indicate disease before other typical symptoms arise, and these factors can be observed several years prior to diagnosis of WG, as occurred in the present case. Also in WG, especially in patients with cavitated nodules close to pleura, an increased awareness of the possibility of pneumothorax as a complication may contribute to more accurate diagnosis and patients may benefit from early intervention. In conclusion, when a clinician meets with a patient with arthritis and/or arthralgia, remembrance of vasculitides in differential diagnosis may be very important in terms of complications which may arise in the future.

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