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Case Report

Wegener's granulomatosis simulates pulmonary adenocarcinoma

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ABSTRACT

Wegener's granulomatosis is a rare systemic granulomatous necrotizing vasculitis that characteristically involves the upper airways, lungs, and kidneys. Pulmonary Wegener's granulomatosis can present with multifocal lung involvement or solitary lung lesions. Diagnosing Wegener's granulomatosis on the basis of cytological material from sputum may be challenging for pathologists. A wrong diagnosis may lead to inappropriate treatment. We report a case of Wegener's granulomatosis in a patient who first presented with hemoptysis, poor appetite, and weight loss. Multifocal pulmonary nodules were seen on a chest radiograph and the features seen on sputum cytology were similar to those of lung adenocarcinoma. A lung biopsy sample proved granulomatous inflammation. Wegener's granulomatosis was diagnosed based on the biopsy sample and a positive cytoplasmic antineutrophil cytoplasmic antibody titer (1:1280). After treatment with prednisone and cyclophosphamide, the lung lesions resolved. We recommend measuring the cytoplasmic antineutrophil cytoplasmic antibody titer in patients with bilateral pulmonary lesions. A lung biopsy sample should always be obtained, even when the cytology findings suggest a malignancy.

1. Introduction

Wegener's granulomatosis is a rare systemic granulomatous inflammatory process. The classic triad of Wegener's granulomatosis consists of upper respiratory tract, lower respiratory tract, and kidney involvement [1]. Patients with Wegener's granulomatosis can present with multifocal lung nodules. A diagnosis from sputum cytology may be a challenge for pathologists. We present the case of a patient with Wegener's granulomatosis who was originally diagnosed with an adenocarcinoma based on sputum cytology.

2. Case report

A 71-year-old woman presented with a 4-week history of a productive cough with blood-tinged sputum, general malaise, poor appetite, and weight loss. The patient did not smoke and had no nasal symptoms nor hematuria. The patient's general appearance showed cachexia, but the remainder of her physical examination showed no other abnormality. A chest radiograph showed bilateral multiple pulmonary nodules, as confirmed by a computed tomography (CT) scan of her chest (Fig. 1A and B). No hilar lymphadenopathy was evident. Her urinalysis was normal without hematuria or proteinuria. Sputum acid-fast stains and polymerase chain reaction for *Mycobacterium tuberculosis* were negative. Tumor markers, including carcinoembryonic antigen, CA-125, CA19-9, and squamous cell carcinoma antigen were not increased. Sputum cytology showed a three-dimensional cluster of cells with intracytoplasmic vacuoles, an increased nucleus to cytoplasmic ratio, and prominent nucleoli, favoring a diagnosis of adenocarcinoma (Fig. 2A). Positron emission tomography showed bilateral, multiple lung nodules without extrapulmonary involvement. Metastatic pulmonary adenocarcinoma was provisionally diagnosed and hospice care was planned. To our surprise, a lung biopsy guided by CT showed noncaseous granulomatous vasculitis (Fig. 2B). The cytoplasmic antineutrophil cytoplasmic antibody (c-ANCA) titer showed a strong positive (1:1280) result, and Wegener's granulomatosis was finally confirmed. The patient was treated with prednisone and cyclophosphamide and responded well. Follow-up chest radiography 2 weeks after treatment showed resolving pulmonary lesions (Fig. 3) and the c-ANCA titer decreased to 1:80. Unfortunately, the patient was later lost to follow-up.

Conflicts of interest: none.

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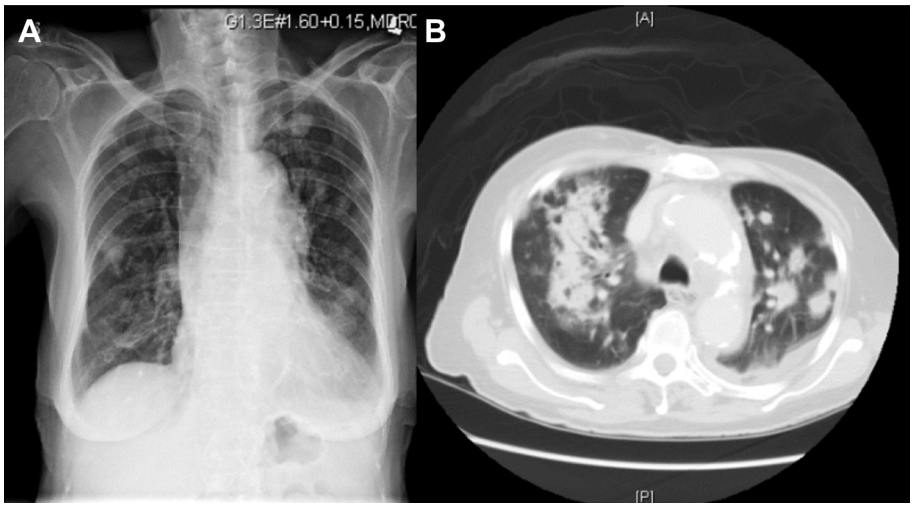

Fig. 1. (A) Chest radiograph on admission showing multiple nodular lesions in both lungs. (B) Computed tomography scan with contrast medium enhancement showing multiple nodular lesions scattered in both lungs without definite enhancement and patchy consolidation.

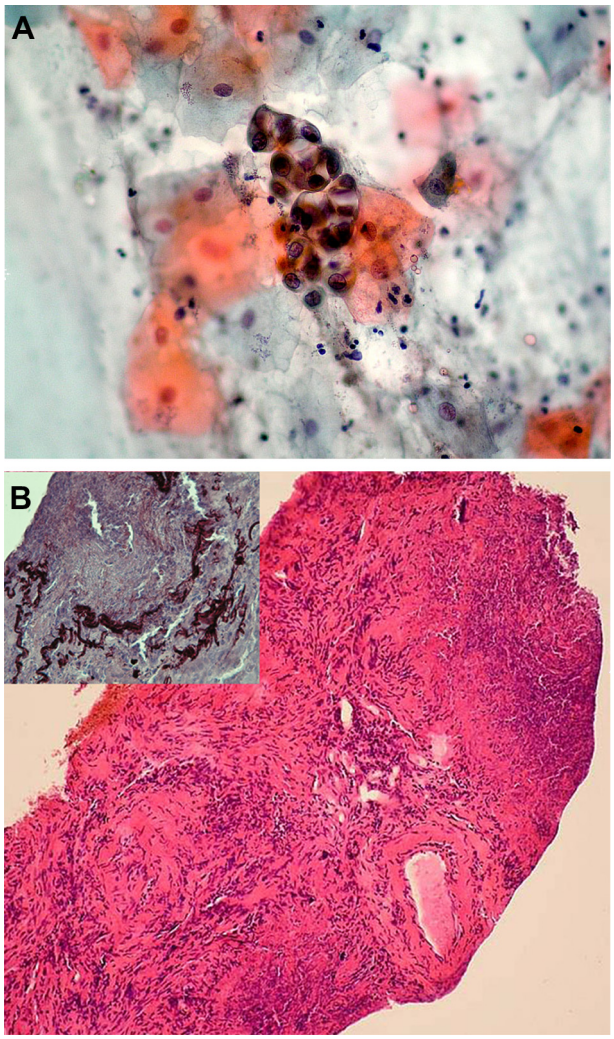

Fig. 2. (A) Sputum cytology showing a three-dimensional cluster of cells with intracytoplasmic vacuoles, an increased nucleus to cytoplasmic ratio, and prominent nucleoli, mimicking adenocarcinoma. (B) Histopathology showing noncaseous granuloma (HEX 40) and focal angioinvasion. (Inset: Orcein stain, ×400).

3. Discussion

Wegener's granulomatosis is a rare systemic granulomatous inflammatory process. The classic triad of Wegener's granulomatosis consists of upper respiratory tract, lower respiratory tract, and kidney involvement [1]. The peak incidence of Wegener's granulomatosis is in the 4th to 6th decades of life [2]. In addition to specific symptoms, nonspecific constitutional symptoms such as fever, fatigue, weight loss, and poor appetite are also frequently noted. c-ANCA, which shows a positive reaction in 90% of patients with Wegener's granulomatosis, is an important diagnostic test [3]. Chest radiography typically shows bilateral pulmonary nodules with or without cavitation. Histology shows necrotizing granulomatous inflammation with geographical necrosis and associated vasculitis [2], but may only show noncaseous granuloma. A combination of clinical manifestations, c-ANCA, and histological

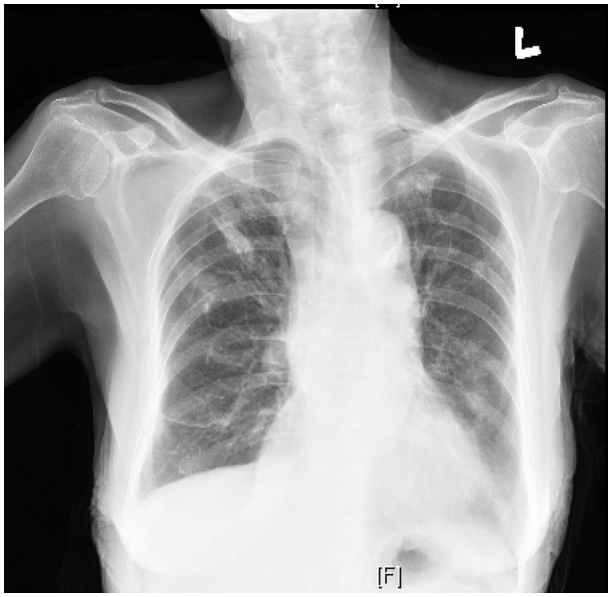

Fig. 3. Follow-up chest radiograph 2 weeks after treatment showing multiple resolving pulmonary lesions.

findings are important in making a correct diagnosis. If untreated, 90% of the patients with Wegener's granulomatosis die within 1 year. Immunosuppressive treatment with cyclophosphamide and prednisone results in a 85–90% response rate and up to 75% of patients achieve complete remission [4]. As a result, early diagnosis and treatment are necessary to prevent morbidity and mortality.

The accurate diagnosis of vasculitis can be difficult. Approximately 50% of patients with vasculitis severe enough to warrant admission to the intensive care unit remain undiagnosed [5]. The classic triad of symptoms is found in only 21% of patients [6]. Pulmonary-limited Wegener's granulomatosis has been reported [7]. Moreover, although multinucleated giant cells and epithelioid histiocytes are considered relatively more specific on cytology, acute inflammation and necrosis are the most common cytopathological findings in Wegener's granulomatosis [8].

In our patient with Wegener's granulomatosis, the sputum cytology findings simulated adenocarcinoma. Uppal et al [9] reported two patients with Wegener's granulomatosis which was originally diagnosed as adenocarcinoma, one case via fine needle aspiration and the other by sputum cytology. They assumed that bronchial epithelial cells are often atypical in patients with Wegener's granulomatosis. The cells may have enlarged eccentric and slightly hyperchromatic nuclei with prominent nucleoli, resembling a well-differentiated adenocarcinoma. They concluded that reactive alveolar cells seen on fine needle aspirates of the lung may lead to a false positive result or false suspicion of adenocarcinoma.

Wegener's granulomatosis mimicking squamous cell carcinoma on cytology has also been reported [10,11]. These workers suggested that features such as nuclear rim abnormalities, large nucleoli, and loss of cellular polarity in the aspirate may have been over-interpreted as malignancy in view of the clinicoradiological background which suggested a malignant process. As a result, the cytological features were suggestive, but not diagnostic, of malignancy. In patients with suspected malignancy, a biopsy sample should always be taken to confirm the diagnosis. They also suggested that the c-ANCA titer should be checked in patients with multiple pulmonary lesions, even in the absence of other clinical symptoms and signs.

In conclusion, Wegener's granulomatosis is a systemic vasculitis which is a significant diagnostic challenge for clinicians and pathologists. The results of sputum cytology and fine needle aspiration are unreliable and may further mislead pathologists to a diagnosis of malignancy. We suggest that the c-ANCA titer is checked in patients with bilateral pulmonary lesions, especially those with abrupt or new-onset multifocal pulmonary lesions. A lung biopsy sample should always be taken, even when the cytology findings suggest a malignancy.

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