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Case Report

A case of simultaneously diagnosed microscopic polyangiitis and lung adenocarcinoma

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An octogenarian female who developed edema in the lower extremities and exertional dyspnea was admitted to our hospital. A diagnosis of lung carcinoma was made from radiographic images and lung biopsy findings. Along with abnormal lung shadows, persistent pyrexia, elevated serum C-reactive protein levels, and progressive kidney dysfunction were also observed. The findings of the myeloperoxidase-antineutrophil cytoplasmic antibody led to a diagnosis of microscopic polyangiitis together with lung and kidney symptoms. Physicians should be aware that microscopic polyangiitis and lung adenocarcinoma may develop concomitantly.

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Key words: lung adenocarcinoma, microscopic polyangiitis, myeloperoxidase-antineutrophil cytoplasmic antibody

Introduction

Microscopic polyangiitis (MPA) is a form of antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) that affects many organ systems such as the lungs, kidneys, and peripheral nerves. To date, there are many studies investigating associations between AAV and malignancy. For example, Pankhurst et al reported that AAV increased the risk of concurrent or preceding malignancy1. However, there has been a debate about whether AAV itself increases malignancy, and the common etiology between AAV and malignancy is yet to be clarified. Whereas several forms of malignancy such as lymphoma are presumed to be associated with AAV2, cases of MPA with complicating lung adenocarcinoma, especially simultaneously diagnosed cases, have rarely been reported1.

We herein describe an octogenarian female diagnosed with having MPA and lung adenocarcinoma simultaneously.

Case

An octogenarian female developed cold symptoms and general malaise, which was followed by decreased urination and exertional dyspnea. She reported a family history of...
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lung cancer in her brother, but she herself had never smoked. She had not undergone health checkups for the past 20 years. About 1 month after the emergence of these symptoms, the edema in both lower extremities and exertional dyspnea worsened, and she visited a neighborhood clinic on the next day. A chest X-ray at the clinic revealed cardiomegaly, pleural effusion, and a mass lesion in the upper lung field. She was then admitted to our hospital for further examination.

Upon admission, her body temperature was 37.1°C, pulse rate was regular (85 beats per minute), and blood pressure was 114/75 mmHg. No crackle was audible on either lower lung fields. However, the oxygen saturation level from a finger probe was low (94% while receiving 1 L/min of oxygen via a nasal cannula). Pitting edema recovering soon after the release of pressure was found in both of her legs to the dorsa of the feet. The results of laboratory tests upon admission were as follows: white blood cell count, 8,900/µL; hemoglobin, 7.6 g/dL; platelet count, 415,000/µL; total protein, 6.2 g/dL; serum albumin, 2.1 g/dL; lactate dehydrogenase, 169 IU/L; total bilirubin, 0.3 mg/dL; aspartate aminotransferase, 24 IU/L; alanine aminotransferase, 18 IU/L; prothrombin time international normalized ratio, 1.25; activated partial thromboplastin time, 36.3 s; fibrinogen degenerative product, 22.6 µg/dL; D-dimer, 13.4 ng/mL; blood urea nitrogen, 22.5 mg/dL; serum creatinine, 0.98 mg/dL; Na 137 mEq/L; K, 5.0 mEq/L; Cl 106 mEq/L; C-reactive protein, 10.53 mg/dL; brain natriuretic peptide, 61.5 pg/mL, squamous cell carcinoma antigen, 0.8 ng/mL, cytokeratin 19 fragment, 4.3 ng/mL; carcinoembryonic antigen, 13.6 ng/mL. Tests for protein and occult blood in urine were both positive, and the microscopic examination of the urine sediment demonstrated red blood cells and white blood cells (20–29/high-power field, respectively). Hyaline and epithelial casts were found in urine. Chest X-ray showed a mass lesion in the upper right lung field and cardiomegaly (Figure 1). Chest computed tomography showed a tumorous lesion in the upper lobe of the right lung, and faint reticular shadows in lower lobes. A small nodular shadow in the right lower lobe, another small nodular shadow in the left lower lobe and mild subcarinal lymph node swelling were also suspected (Figure 2). Bronchoscopic examination revealed the presence of atypical cells in bronchoalveolar lavage fluid and bronchial brushing cytology, which led to the diagnosis of adenocarcinoma (Figure 3). Her stage of lung cancer was considered as cT4N2M1a, stage IVA.

The elevated inflammation levels and chest image findings suggested the coexistence of bacterial pneumonia. We started intravenous administration of piperacillin/tazobactam, which did not improve her inflammation symptoms. Even after the switch from piperacillin/tazobactam to ceftriaxone and clindamycin, her pyrexia persisted and her renal function gradually worsened (estimated glomerular filtration rate was 41.4 mL/min/1.73m² on admission, which was worsened to 29.1 mL/min/1.73m² within 2 week from the start of treatment).

We suspected a possible autoimmune disease, especially AAV. The results of tests to detect autoantibodies were as follows: rheumatoid factor was negative, antinuclear antibody was negative, and myeloperoxidase (MPO)-ANCA was positive (178 U/mL), which led to the diagnosis of MPA together with chest CT findings, progressive kidney dysfunction, and inflammatory symptoms. Considering the positive finding of MPO-ANCA, we considered reticular shadows in lower lobes as a manifestation of MPA despite they were mild and might be non-specific. After the start of 50 mg/day of prednisone (PSL), her pyrexia improved. The dose of PSL was gradually decreased, and a titer of MPO-ANCA was confirmed negative under administration of 10 mg/day of PSL. Following that, administration of gefitinib for the treatment of adenocarcinoma was initiated. Despite administration of gefitinib, her lung cancer was observed progressive disease. She was then transferred to another hospital for supportive care.
Discussion

MPA is a form of AAV, in which granulomatosis with polyangiitis and eosinophilic granulomatosis with polyangiitis are also included. Although several studies have suggested that AAV enhances the risk of developing a malignancy\(^1\), the precise association between AAV and malignancy has not been established. There is a debate whether AAV enhances a risk of malignancy: van Daalen et al analyzed 203 AAV cases and found occurrences of malignancy preceding AAV, such as renal cell carcinoma, bladder cancer, and non-melanoma skin cancer, although the risk of malignancy prior to AAV was comparable with that of the general population\(^4\). On the other hand, risks of several forms of malignancy have been reported to be increased by drugs used for AAV: bladder cancer by cyclophosphamide (CYC)\(^5\), skin squamous cell...
carcinoma by azathioprine, and solid cancer by etanercept. CYC is widely known to increase the risk of cancer such as bladder carcinoma. However, use of CYC less than 1 year did not increase the risk of malignancy, suggesting the possibility that drugs used to treat AAV, rather than AAV itself, increase malignancy.

As mentioned above, patients with AAV may complicate several forms of malignancy at a certain rate. However, among various forms of malignancy, cases of lung cancer related to AAV have rarely been reported. To date, 11 cases of AAV with complicating lung carcinoma have been reported. They were diagnosed as either squamous cell carcinoma or adenocarcinoma. Cumulative doses of CYC varied from 1 to 16 g. In four of the 11 cases, titers of ANCA were decreased after treatment for cancer. Moreover, re-positivation of ANCA upon recurrence of lung carcinoma was found in one case, which suggested the possibility of an ANCA production mechanism related to lung carcinoma. Huugen et al. reported that the administration of bacterial lipopolysaccharide induced MPO-ANCA, neutrophil accumulation, glomerular necrosis, and tumor necrosis factor-α (TNF-α) in a mouse model. These changes were inhibited by an anti-TNF-α treatment, which suggested that inflammatory cytokines such as TNF-α took part in the pathogenesis of AAV. TNF-α is reported to be upregulated in surgically removed lung adenocarcinoma; therefore, a shared pathogenic mechanism through TNF-α may exist.

In this paper, we reported a case of simultaneously diagnosed MPA and lung adenocarcinoma. Whether MPA preceded adenocarcinoma or followed was unknown in this case. The patient had no smoking history and never received CYC. Although the precise relationship between AAV and malignancy has not been established, several cases of AAV with complicating malignancy have been reported. Therefore, further investigation with large sample numbers is required. Conflict of interests: The authors declare that they have no conflicts of interest.

References