Lung Cancer Complicated with IgG4-related Disease of the Lung

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Few have reported a concomitant malignant neoplasm with immunoglobulin G4 (IgG4)-related diseases. We describe a case of lung cancer and gastric cancer accompanied with IgG4-related disease. A 78-year-old man had an area of ground-glass opacity with central collapse in right upper lobe and a gastric cancer. The patient underwent a right upper lobectomy following a gastrectomy for the gastric cancer. Histological examination of the resected lung specimen revealed a lepidic pattern of an adenocarcinoma and a large amount of plasmacyte infiltration around the tumor. In immunohistochemical findings, the plasmacytes were stained for IgG4. Therefore, the lung tumor was considered to have associated with IgG4-related interstitial lesions.

Keywords: IgG4-related disease, lung cancer, gastric cancer

Introduction

Recently, much attention has been focused on immunoglobulin G4 (IgG4)-related diseases, which are clinically characterized by high serum IgG4 concentration and diffuse lymphoplasmacytic infiltration with marked interstitial fibrosis.1) However, few have reported a concomitant malignant neoplasm with this disease.2) Herein, we describe a case of lung cancer and gastric cancer accompanied with IgG4-related disease, which complicated clinical staging of the lung cancer.

Case

A 78-year-old man visited another clinic with epigastric discomfort. A gastrointestinal fiberscope examination revealed gastric cancer (multicentric IIa type), and he was referred to our hospital for further evaluation. Chest X-ray radiograph findings revealed a tumor in the right upper lung field. Chest computed-tomography (CT) scanning showed an area of ground-glass opacity (25 mm in diameter) with central collapse and pleural indentation in right segment-1 (S1), another consolidation in the periphery of the middle lobe (14 mm in diameter), and symmetric mediastinal and hilar lymphadenopathy (Fig. 1). A bronchofiberscopy examination of the S1 tumor resulted in a diagnosis of lung adenocarcinoma.

Biochemistry results indicated a high serum IgG4 concentration at 983 mg/dl (normal range, 4.8–105 mg/dl). Furthermore, abdominal CT scanning revealed a low-density tumor in the pancreatic tail, which indicated autoimmune pancreatitis due to IgG4-related disease. We performed 18-fluoro-deoxy-glucose positron emission tomography (FDG-PET), which showed an accumulation in the lung tumor, with a standardized uptake value
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(SUV) max of 2.9 in the early and 3.8 in the delayed phase, multi-focal accumulations in the mediastinal and hilar lymph nodes, accumulations in the stomach, with an SUV max of 5.2 and 6.8, respectively, and accumulations in the pancreatic tail, with an SUV max of 4.8 and 6.2, respectively. Since the lymphadenopathy was likely related to IgG4-related disease, we clinically diagnosed the lung cancer as T1BN0M0.

The patient underwent a right upper lobectomy and lymph node dissection following a gastrectomy for the gastric cancer which was not accompanied with an IgG4-related lesion. The right middle lobe was also partially resected in order to diagnose the consolidation. Recovery was uneventful. The patient was discharged on day 12 after lung surgery and was free from both cancers at 18 months after the operation.

A pathological examination of the S1 tumor demonstrated a lepidic pattern of an adenocarcinoma (Fig. 2A) with pleural indentation (Noguchi C) and a large amount of plasmacyte infiltration in the solid lesion of the tumor. In immunohistochemical findings, the plasmacytes were stained for IgG4 (Fig. 2B). Therefore, the tumor was considered to have associated with IgG4-related interstitial lesions. The consolidation in the middle lobe was diagnosed as an IgG4-related pseudo-inflammatory tumor as IgG4-positive plasmacytes had formed lymph follicles inside. All swollen lymph nodes from the hilus and mediastinum were without malignancy.

Discussion

The present case featured co-existence of lung cancer and an IgG4-related lung lesion, with the former likely originating from the latter. IgG4-related disease is an entity belonging to chronic inflammatory systemic disease and characterized by elevated IgG4 in serum, along with extensive infiltration of IgG4-positive plasmacytes and T-lymphocytes in various organs.1–4) It was first reported as an autoimmune type of pancreatitis.5)

IgG4 plays a major role in the pathogenesis of this disease, though the trigger for IgG4 elevation or its pathogenetic role has not been clearly established. A number of studies have presented findings that support the involvement of immunological mechanisms in this disease, whereas target antigens have not been detected. IgG4-related lesions similar to autoimmune pancreatitis have been identified in the bile duct (sclerosing cholangitis),4) salivary gland (chronic sclerosing sialadenitis),6) lacrimal gland (chronic sclerosing dacryoadenitis),7) retroperitoneum (retroperitoneal fibrosis),8) mediastinum (mediastinal fibrosis),9) and aorta (inflammatory aneurysm).10) In addition to an IgG4-related lung lesion, the present patient also had autoimmune pancreatitis, retroperitoneal fibrosis, and chronic prostatitis.

It was recently reported that 10% of patients with IgG4-related disease have a lung lesion.11) IgG4-related lung disease more commonly occurs in older men. Affected patients are usually asymptomatic, with an abnormal shadow first revealed by routine chest X-ray findings, though some present hemosputum. Reported radiological features vary, such as a solid nodule-like pseudo-inflammatory tumor, multiple round-shaped ground-glass opacity areas, thickening of bronchovascular bundles and
pleura, diffuse reticular shadow-like non-specific interstitial pneumonia, and bilateral hilar lymphadenopathy. 2) Few reports have documented the association between pulmonary lesions and malignancy in this disease. Zen, et al.2) reported 1 patient with lung cancer in a group of 21 with IgG4-related lung disease. That patient had a reticular shadow and was treated with corticosteroid therapy for 2 years, after which a nodular lesion was found within the reticular shadow. Surgical resection was performed, and the tumor was diagnosed as pT1N2M0 lung adenocarcinoma. Radiologic changes of IgG4-related lung disease make it difficult to distinguish lung cancer from these lesions. In the present case, chest CT findings showed central collapse (nodular lesion) and lymphadenopathy, whereas a pathological examination revealed that the lung cancer showed a lepidic pattern while the nodular lesion was an IgG4-related lesion and lymph nodes were without cancer cells. It is important to be aware of possible co-existence of IgG4-related disease and lung cancer, which might result in over-staging of the latter. The gastric cancer was not accompanied with an IgG4-related lesion in our case.

A few reports have documented the relationship between IgG4-related disease and malignancy, such as malignant lymphoma12) and pancreatic cancer.13,14) This is the second report of IgG4-related disease accompanied by lung cancer.

**Conclusion**

We experienced a very rare case of lung cancer accompanied by IgG4-related disease. IgG4-related disease sometimes involves the lung parenchyma and hilar lymph nodes and makes radiologic diagnosis of lung cancer difficult.

**Disclosure Statement**

No conflicts of interest are declared.

**References**

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