IgG4-related Sclerosing Disease of the Lung without Pancreas Involvement: Presentation on 18F-FDG PET/CT

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ABSTRACT

IgG4-related sclerosing disease is a rare disease which received attention only recently. We present a case of IgG4-related sclerosing disease of lung without signs of pancreas involvement and report the unusual image findings that have not been reported. It presented as a pulmonary nodule having low 18Fluorine-fluorodeoxyglucose (FDG) uptake on PET/CT.

IgG4-related sclerosing disease is an emerging systemic disease [1]. The disease has most commonly been associated with autoimmune pancreatitis, but may have synchronous or solely extrapancreatic involvement [2, 3]. The IgG4-related sclerosing disease of lung can mimic lung cancer radiographically, especially when no other organ is involved. There were only three reports about the PET/CT finding for the IgG4-related sclerosing lung disease [4-6], all with synchronous pancreas involvement. In this article, we report the image findings of a 47-year-old woman with pathologically proven IgG4 related sclerosing disease of lung. To the best of our knowledge, this is the first report of the PET/CT findings in IgG4-related sclerosing disease of lung without signs of pancreas involvement. In addition, the multidetector CT (MDCT) finding of a dilated vessel adjacent to the lung nodule is described.

CASE REPORT

A 47-year-old woman with a medical history of hypertension and a carrier of the hepatitis B virus was incidentally found to have a left lung mass on chest X-ray during a routine health check-up. (Fig. 1) The patient

Figure 1

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Figure 2. a. High resolution CT and b. unenhanced CT images show a nodule at the left upper lobe of the lung (arrows), with a density of 13 Hounsfield units (H.U.) c. Close-up axial CT images show that the nodule (arrow) is 48 H.U. in density and that there is a large dilated vessel (arrowhead) measuring 5mm in diameter adjacent to the lesion. d. Contrast enhanced abdominal axial CT image shows normal appearance of pancreas (arrow) without pancreas enlargement or pancreatic duct dilatation.

Figure 3. a. axial and b. coronal PET/CT images show a hypometabolic nodule (arrow) with low FDG uptake; the SUVmax is measured 2.02.
denied symptoms such as cough, hemoptysis, blood-stained sputum, dyspnea, or chest discomfort. Physical examination revealed end-expiration crackle-like sounds in the left upper lung field. She had normal pulmonary function test results, as well as normal carcinoembryonic antigen and squamous cell carcinoma antigen. A chest CT incidentally revealed a left renal mass that was consistent with renal cell carcinoma. The appearance of the pancreas was unremarkable. The bronchoscopy, with endobronchial ultrasound, showed an eccentric consolidation at the bronchus of the superior segment of the left lingual lobe; the biopsy showed no sign of a malignancy. The patient underwent a left nephrectomy under the impression of renal tumor. The pathological diagnosis was renal cell carcinoma, stage pT1N0M0.

Seven months later, the lung nodule was still present without change in size on chest radiograph when compared to the initial radiograph. The multidetector CT (MDCT) examination showed a 2.5-cm solitary mildly enhancing nodule at the left upper lung field (Fig. 2a, 2b), without evidence of mediastinal lymphadenopathy. A markedly dilated vessel, about 5mm in diameter, with an irregular luminal surface, abutting the nodule, was noted (Fig. 2c).

**Figure 4.** a. Photomicrograph shows that the lung nodule had fibro-inflammatory changes with a characteristic distribution along the interlobular septa; while in the central part of the nodule, there was prominent irregular storiform fibrosis (hematoxylin and eosin stain, x 100). b. The Elastica van Gieson stain shows obliterative phlebitis (arrow) in the nodule (Elastica van Gieson stain, x 200). c. The IgG4 immunostaining shows numerous IgG4+ plasma cells characteristic of IgG4-related sclerosing disease. The IgG4 positive plasma cell count was 121 per high power field, and the IgG4 positive-IgG positive plasma cell ratio was 50.6%. The pathological diagnosis was IgG4-related sclerosing disease of the lung. The postoperative serum IgG and IgG4 level was 1140 and 43.2 mg/dl, respectively (IgG4 immunostaining, x 400). d. A large dilated vessel (arrowheads) measuring 5mm in diameter is adjacent to the lesion (hematoxylin and eosin stain, x 20).
The upper abdominal organs appeared normal (Fig. 2d). Lung cancer was suspected at the time, and \textsuperscript{18}F-FDG PET/CT (Discovery VCT, GE healthcare, Waukesha, WI, USA) was performed. The nodule had a low FDG uptake with the maximum standardized uptake value (SUVmax) being 2.02 (Fig. 3a, 3b); there was no abnormal FDG uptake throughout the body including the pancreas.

The patient underwent left upper lobectomy since lung cancer was still a concern. A soft grey nodule was found. The histopathology of the nodule showed fibro-inflammatory changes along the interlobular septa and the bronchovascular bundle, irregular storiform fibrosis, and obliterative phlebitis. The inflammatory cells were predominantly composed of lymphocytes and plasma cells that were positive for IgG and IgG4. There was a large dilated vessel, measuring 5mm in diameter, noted adjacent to the lesion (Fig. 4a-4d). IgG4-related sclerosing disease of the lung was diagnosed. The patient had no clinical evidence recurrence at lung or other organ involvement associated with the IgG4-related sclerosing disease after the operation.

**DISCUSSION**

IgG4-related sclerosing disease is the term used to describe a disorder with inflammatory, fibrosing, and vascular abnormalities characterized by prominent and extensive IgG4-positive plasma cells and T-lymphocyte Infiltration that may affect one or more organs [7]. While most IgG4-related sclerosing disease involve pancreas [8], it is not uncommon for the disease to involve other organs including bile ducts, gallbladder, salivary glands, lacrimal glands, retroperitoneum, kidneys, and prostates. However, IgG4-related sclerosing disease, without involvement of the pancreas, is not uncommon [9].

The lung is an organ that has recognized to be involved in IgG4-related sclerosing disease only recently [10]. The histopathological diagnosis of IgG4-related sclerosing lung disease was described by Zen et al. in a case series as having IgG4 positive plasma cell infiltration and an IgG4-positive to IgG-positive cell ratio of more than 30% at the site of the lesion [2]. Microscopic features include diffuse lymphoplasmacytic infiltration, fibrosis, obliterative arteritis and phlebitis of the lung segments. The location of involvement is often close to the pulmonary lymphatic system, including the alveolar interstitium, interlobular septa, and bronchovascular bundles and may extend to the pleura. IgG4-related lung disease has variable radiological characteristics sub-classified into several subtypes including: solitary nodular, bronchovascular, alveolar interstitial or round-shaped ground-glass opacities (GGO) [2]. The disease is often initially suspected as lung cancer on the basis of imaging studies with differential diagnoses of interstitial lung disease, sarcoidosis, and multicentric Castleman disease [11]. Recognition of this disease entity is particularly important since the clinical and radiological features may mimic a malignancy as in our case.

IgG4-related disease may involves the arteries and results in aneurysms or periarterial masses, with diffuse inflammatory cell infiltration in the adventitia [12]. There was a markedly dilated vessel adjacent to the lung lesion, confirmed by the histopathology. These finding reflect the aneurysmal change effect by the IgG4-related sclerosing disease. Differential diagnosis of focal dilated pulmonary vessels includes arteriovenous malformation, pulmonary metastases, and septic emboli. While arteriovenous malformation has both enhancing nidus and large drainage vein, the nodule in our case showed no enhancement. Septic emboli and some metastases can have “feeding vessel sign” as a feature on imaging [13], and may resemble the finding of our case.

Extra-pancreatic abnormal FDG uptake has been reported in several cases of systemic IgG4 sclerosing disease, including one with lung involvement [4]. The follow up PET or PET/CT usually shows resolution of the abnormal uptake after steroid treatment in both pancreatic and extra-pancreatic foci. The FDG uptake is reported to correlate with disease activity, probably due to the activated lymphocytes present during the acute inflammatory stage [14]. Our case has low PET/CT uptake which we speculate could be due to that the disease was in the relatively lower activity status with less inflammation. However, since there were very few cases reported for IgG4-related sclerosing disease of the lung, and thus there was no large scale research about the FDG uptake of the IgG4-related sclerosing disease, further study focusing on functional uptake of the disease is needed.

IgG4-related sclerosing disease is an underdiagnosed systemic disease. IgG4-related lung disease may present with a solid nodule that might have features similar to a malignancy on imaging. An accurate diagnosis on imaging can help choosing treatment.
REFERENCES