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Case report

IgG4-related lung disease mimicking lung cancer

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Introduction

IgG4-related disease (IgG4-RD) is an autoimmune, systemic fibroinflammatory process involving IgG4-positive plasma cells infiltrating multiple organs, with or without elevation of plasma IgG4 levels [1]. Histologically, IgG4-RD is characterized by a lymphoplasmacytic infiltrate, storiform fibrosis and obliterative phlebitis, with mild to moderate eosinophilia [2]. The disease was first reported by Hamano et al in 2001, who described an infiltration of IgG4-positive plasma cells in a patient with autoimmune pancreatitis [3]. Since then, IgG4-RD has been reported in virtually every organ, including the lungs, first by Duvic et al in 2004, who reported a case of retroperitoneal fibrosis, sclerosing pancreatitis, and bronchiolitis obliterans with organizing pneumonia that was successfully treated with a course of steroids [4].

IgG4-related lung disease (IgG4-RLD) can be classified clinically as either an inflammatory pseudotumor, interstitial pneumonitis, organizing pneumonia, or lymphomatoid granulomatosis. Three-quarters of patients are identified incidentally on chest imaging, but some can present with a dry cough, chest pain, or exertional dyspnea [5]. Radiologically, CT findings can be divided into four categories: 1. Solid nodular type, 2. Round-shaped ground-glass opacities, 3. Alveolar interstitial type, and 4. Bronchovascular type [6]. Evidently, both the clinical and radiological findings of IgG4-RLD are varied, and therefore overlap with other diagnoses, leading to a long list of differentials including lung cancer, Castleman disease, lymphomatoid granulomatosis, interstitial pneumonia and sarcoidosis [7]. Here, we present a case of IgG4-RLD in a patient suspected of having lung cancer.

Case presentation

A 70-year-old man presented to the ENT clinic, with a bilateral parotid gland swelling that had been present for five years and had not changed in size according to the patient. He had a past medical history of diabetes mellitus, atrial fibrillation, and severe ischemic cardiomyopathy with an ejection fraction of only 15% on echocardiogram for which a CRTD was placed, memory deficit, chronic kidney disease, and a positive family history for lung cancer. The patient was a former heavy smoker (more than 40 pack years) and had quit smok-

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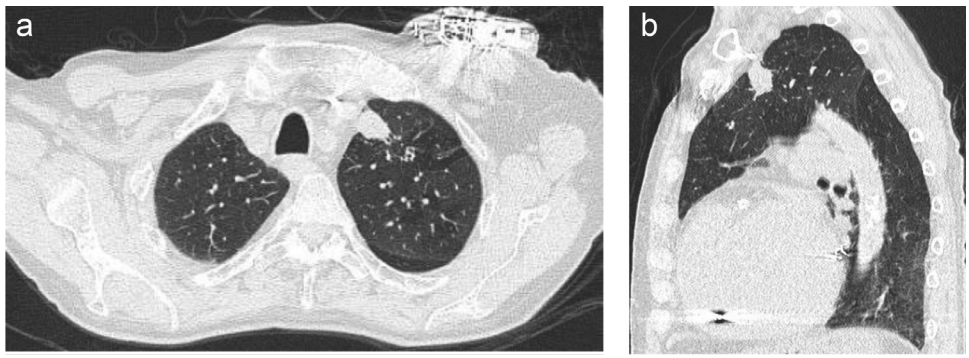

Fig. 1 – .Initial CT chest showing a 16 x 13mm soft tissue nodule in the anterior medial aspect of the left upper lobe.

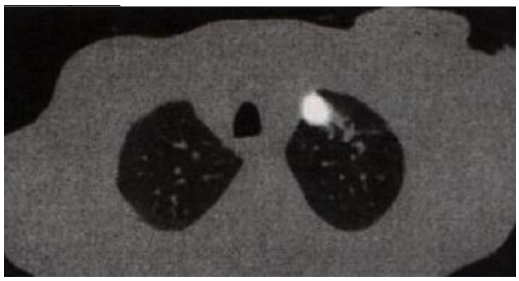

Fig. 2 – .PETCT showing the left upper lobe nodule to be FDG avid (SUV mas 11.8).

ing more than 10 years ago. Physical examination was unremarkable. A neck CT scan was performed, which revealed a large enhancing mass (28 × 27 × 37 mm) in the left superficial parotid gland with associated necrosis, and six enhancing lesions in the right superficial parotid gland, the largest measuring 39 × 30 × 23 mm. Incidentally, the scan also showed a nodular density in the left lung apex with retraction of the pleura. Subsequently, a chest CT scan showed a 16 × 13 mm soft tissue nodule in the anterior medial aspect of the left apex (Figs. 1A and B). A positron emission tomography (PET) scan was performed, which showed that the lung nodule exhibited intense hypermetabolic activity (SUV max 11.8), highly suspicious for malignancy (Fig. 2). Hypermetabolic activity was also present bilaterally in the parotid glands and cervical lymph nodes, and in the pancreas. A repeat chest CT scan at 3 months interval showed that the lung nodule had increased in size to 35 × 18 mm and was in broad contact with the anterior and mediastinal pleural surface (Figs. 3A and B). A bronchoscopy with bronchoalveolar lavage and endobronchial ultrasound was performed but no malignant cells were seen on either bronchoalveolar lavage or endobronchial ultrasound cytology. The patient was not a candidate for surgical resection of the nodule due to his cardiovascular risk factors, so a CT-guided core needle lung biopsy was performed, which revealed storiform fibrosis of the lung parenchyma, infiltrated by numerous plasma cells and few eosinophils, with no evidence of malignancy or granuloma formation. In-situ hybridization studies showed that the plasma cells were not monoclonal and were negative for CD56. Patient also had significantly elevated levels of IgG4 (1645 mg/dL, normal range 6-130 mg/dL). Based on his clinical history, physical examination and histological and serological findings, he was diagnosed with IgG4-RLD. As the patient was asymptomatic, he was treated conservatively, with regular 3-month follow-up visits. His subsequent clinical course was unremarkable, barring two episodes of pneumonia and low volume hemoptysis, which were successfully treated with antibiotics and oral steroids. He remained stable and has continued clinical and radiological follow up in clinic over the last 4 years with most recent CT showing reductions in size of the left upper lobe nodule to 11 mm at the greatest dimension (Figs. 4A and B).

Discussion

We present a case of an enlarging and strongly FDG avid lung nodule in a heavy ex-smoker which was strongly suspected to be a lung cancer but was eventually diagnosed as IgG4-RLD. Although IgG4-RLD is a benign process in its own, it has been associated with lung cancer. A study of 21 patients with IgG4-RLD revealed that one case had concomitant lung cancer [8]. Another study involving 126 patients reported that 10% developed malignant lesions, some of which were pulmonary. Nodular lesions, similar to the one seen in our patient, are the second most common manifestation in IgG4-RLD, accounting for 30.8% in one study [6,8]. Other types of manifestations include round shaped ground-glass opacities, alveolar interstitial involvement, and bronchovascular involvement [6]. Such manifestations overlap with primary pulmonary malignancies, which therefore must be excluded. Another common feature between IgG4-RLD and lung cancer is elevated standardized uptake values (SUV) on PET scans [9]. However, SUV levels in IgG4-RLD are reportedly lower than in lung cancer and decline as the inflammatory process subsides [10,11].

In addition to his pulmonary findings, our patient had parotid gland involvement, presenting as bilateral neck swelling, which was his initial primary complaint. Salivary gland involvement in IgG4-RLD has been previously reported; one study found that 25% of IgG4-RLD patients had some form of salivary gland involvement. Furthermore, the pancreas was also affected in our patient, in the form of hypermetabolic ac-

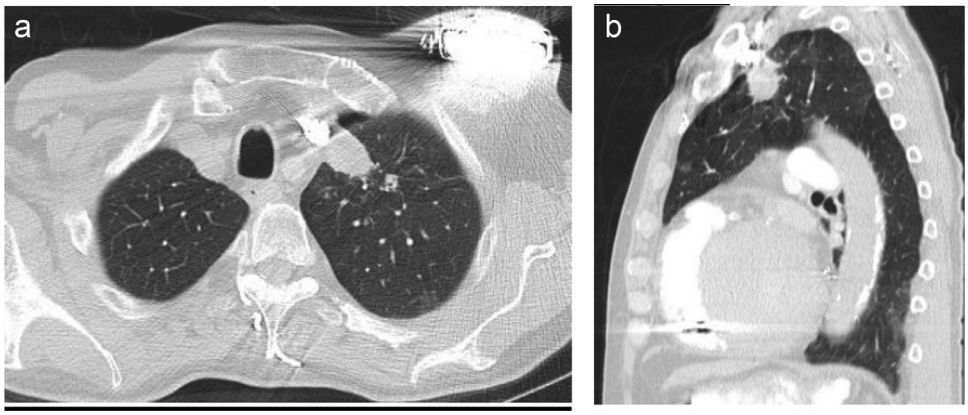

Fig. 3 – .3 months interval chest CT scan showed increase in size to 35 x 18mm

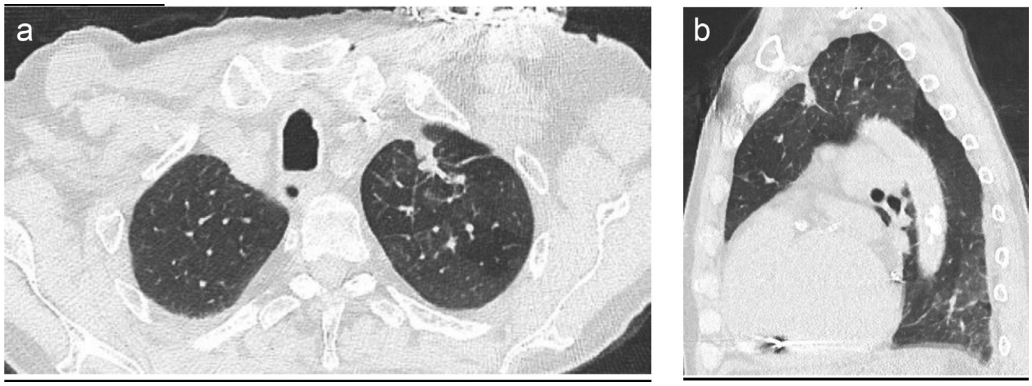

Fig. 4 – .Most recent CT showing reduction in size of the left upper lobe nodule to 11mm at the greatest dimension.

tivity on PET scan. The most common manifestation of IgG4-RD is type 1 autoimmune pancreatitis affecting 13% of patients [12]. In addition to salivary gland and pancreatic involvement, other associations of IgG4-RLD that have been reported, include autoimmune hepatitis, constrictive pericarditis, asthma, Sjogren syndrome, psoriasis, and lymphomas [13–15].

The current mainstay of treatment of IgG4-RLD is corticosteroid therapy. A consensus guideline published in 2015 revealed that most experts viewed corticosteroids as the first-line induction treatment in IgG4-RLD, and that some patients may need maintenance therapy [16]. Moreover, the majority of experts believed that in addition to symptomatic patients, some asymptomatic patients may also require treatment. Other experts suggested that dual therapy with steroids and immunosuppressive agents are required in the case that steroids alone fail to achieve remission.

Conclusion

In conclusion, the radiological findings of IgG4-RLD can be similar to those of primary pulmonary malignancies, and therefore a biopsy is always recommended to confirm the diagnosis.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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