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CASE REPORT

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IgG4-related disease of the lung: a rare differential diagnosis to lung cancer after positive positron emission tomography and biopsy

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Abstract

Immunoglobulin G4-related disease is a rare immune-mediated condition that often causes serious diagnostic problems. Symptoms are unspecific, and several organs can be involved. To date, IgG4-related lung disease has seldom been reported in literature. Nevertheless, a variety of pulmonary involvement has been described, which can mimic malignancy. The gold standard for the diagnosis is the identification of typical histopathological features, even if diagnostic biomarker such as serum IgG4 concentration can be an indicator for a more aggressive course of the disease.

Keywords: IgG4-related lung disease • Mimicking malignancy • Lobectomy

INTRODUCTION

Immunoglobulin G4 (IgG4)-related disease (IgG4-RD) is a poorly understood immune-mediated condition consisting of a group of disorders that share specific pathological, serological and clinical features. Lung involvement has seldom been reported in this disease [1]. On imaging, a variety of pulmonary involvement have been demonstrated including mass-like lesions, bronchovascular nodular pattern or even round areas of ground-glass opacification that may mimic adenocarcinoma *in situ*. Enlargement of hilar or mediastinal lymph nodes is also common in patients with IgG4-related lung disease. Diagnosis of IgG4-RD requires characteristic findings upon biopsy/resection of the affected tissue [2]. Therapy mainly consists of glucocorticoids (GCs) as the first-line agent for active disease.

CASE PRESENTATION

In the following, we present the case of a 55-year-old woman who was referred to our tertiary care centre with the suspicion of a malignant tumour of the right lower lobe. The patient had been suffering from a dry cough, fever, night sweat and weight loss since 3 months.

Chest computed tomography (CT) showed a subpleural mass of $3 \times 4 \times 5$ cm with ill-defined margins and multiple satellite lesions in the right lower lobe. Positron emission tomography–computed tomography (PET-CT) confirmed a metabolically active mass compatible with a centrally necrotic malignancy and hilar and mediastinal lymph nodes with high-fluorodeoxyglucose (FDG) uptake (Fig. 1). A bronchoscopy and endobronchial ultrasound (EBUS) with fine-needle biopsy was subsequently performed, which resulted in the suspected diagnosis of an adenocarcinoma in the right lower lobe. In assumption of a sampling error, a mediastinoscopy and a pleural biopsy via thoracoscopy (video-assisted thoracoscopic surgery - VATS) were done to rule out mediastinal lymph node and pleural tumour involvement. Because only the initial tumour biopsy showed malignancy, the patient was scheduled for a lobectomy.

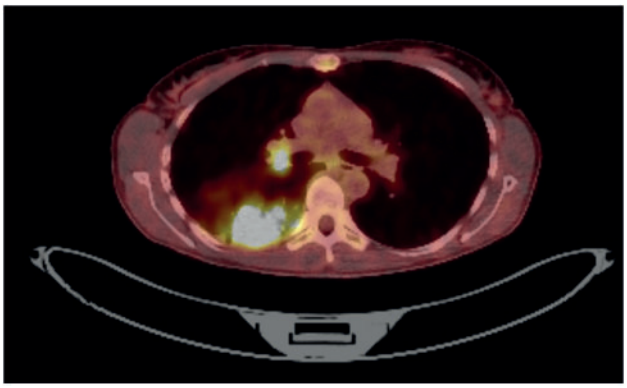

Figure 1: Positron emission tomography–computed tomography (PET-CT) scan with high-FDG uptake mimicking bronchial carcinoma.

On histopathological examination, a small neuroendocrine tumorlet of 0.2 cm was found within the vast nodular lymphoid tissue with associated pneumonia, typical for IgG4-RD (Fig. 2). No other malignancy was found. Shortly after, treatment with peroral GCs (0.5 mg/kg) was initiated, which resulted in a

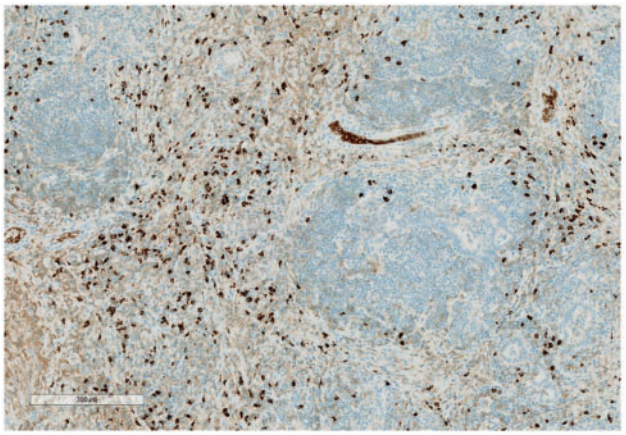

Figure 2: Histopathology picture: typical immunoglobulin G4 + plasma cell infiltrate (immunohistochemical staining for immunoglobulin G4 and haematoxylin–eosin staining; scale bar 300 μm).

significant improvement of the patient's condition. Unfortunately, the patient subsequently developed ocular vasculitis and microhaematuria, which prompted us to begin with Imurek (100 mg/day) and reducing the GC dose (25 mg/day). Finally, rituximab was added to the treatment regimen (2 × 1 g with 14 days break). Two months after initiating the therapy with rituximab, we could further reduce the GCs to 15 mg/day, and the course of the disease remained stable.

DISCUSSION

Recently, a study of 125 patients with IgG4-RD, including clinical and laboratory features, was published [1]. It has emerged as a unique immune-mediated condition that links multiple fibroinflammatory disorders previously considered as separate entities. It has now been discovered that IgG4-RD can affect nearly every other organ system, even the lung.

The gold standard for the diagnosis of IgG4-RD, regardless of the organ systems involved, is the identification of typical histopathological features (e.g. a rich lymphoplasmacytic infiltrate, storiform fibrosis and obliterative phlebitis) in the context of a significant IgG4 + plasma cell infiltrate [2, 3]. Nearly 50% of all patients with biopsy-proven, clinically active IgG4-RD have normal serum IgG4 concentrations. Nevertheless, an elevation in serum IgG4 concentration, as seen in our case, can be an indicator for a more aggressive disease [4]. Lung involvement in IgG4-RD is reported in about 17.6% of all the cases [1]. Because of the rarity of the disease and the difficulty of diagnosis, a considerable number of patients undergo surgery during the evaluation of their illness. Isolated pulmonary involvement is only seen very rarely, because the disease usually affects other organ systems first (e.g. autoimmune pancreatitis) [1, 2, 5].

Most of the patients showed improvement following treatment with GC, but in around 77%, a stable remission could be achieved with GC alone. In addition, methotrexate, azathioprine and rituximab can be effectively used for patients in whom GC treatment alone is insufficient.

The presented case demonstrated a very rare case of IgG4-RD with primary lung involvement. Especially the PET-CT finding of a highly metabolically active tumour mass in the lung, very well compatible with malignancy, led to the further diagnostic workup with an EBUS-fine-needle biopsy, which again resulted in the suspected diagnosis of primary lung cancer. Therefore, this case is a good example of why IgG4-RD can be considered a diagnostic conundrum.

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Conflict of interest: none declared.

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