Case report

IgG4-related disease presenting as a lung mass and weight loss: Case report and review of the literature

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ABSTRACT

We describe a case of IgG4-related lung disease presenting as a lung mass with associated weight loss. IgG4-related disease is a systemic sclerosing disorder that causes fibrotic, often tumor-like manifestations that variably effect different organ systems. The clinical presentation of IgG4-related disease is protean. Timely recognition and diagnosis requires awareness on the part of clinicians and pathologists to the variable manifestations of this newly recognized disorder. We offer a concise review of the pulmonary manifestations, diagnosis and treatment of IgG4-related lung disease.

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1. History

A 60-year-old woman presented with 3 weeks of left-sided chest pain and a cough. She had taken oral amoxicillin-clavulonate for suspected pneumonia, without relief. She reported unintentional weight loss of 35–40 pounds over a few months prior to admission. She noted chills and night sweats but denied fevers. Her cough produced a small volume of whitish sputum. She denied skin changes, muscle pains, dysphagia or joint abnormalities. She had no sick contacts. Her past history was significant for hypertension and hyperlipidemia. She was originally from Puerto Rico and migrated to Connecticut 17 years prior. She was a lifelong nonsmoker.

2. Physical examination

She was alert and had normal cognition. Vital signs and oxygen saturation were normal. Inspection of the mouth revealed no abnormalities. Palpation of the neck and clavicular region did not reveal enlarged lymph nodes. Inspection of the chest wall revealed normal movement. Chest auscultation was unremarkable. Examination of the muscles and joints was unremarkable. Digital clubbing was absent. There were no skin lesions.

3. Diagnostic studies

Contrast enhanced chest CT revealed a 5.0 × 3.5 cm mass in the left lower lobe and right hilar fullness (Fig. 1A). Laboratory analysis revealed an erythrocyte sedimentation rate of >130 mm/h. Blood count and serum chemistries were normal. Autoimmune serologies were non-reactive. Positron Emission Tomography (PET) showed increased uptake in the left lower lobe and the right hilum (Fig. 1B). Surgical lung biopsy revealed a rubbery mass. Histopathological examination revealed a mixed inflammatory infiltrate with abundant plasma cells associated with fibrosis in a patchy, nodular distribution (Fig. 2). Immunohistochemistry showed reactivity to IgG4 (Fig. 3) and thyroid transcription factor 1. The number of plasma cells that stained positive for IgG4 was greater than 50 per high power field (greater than 100 in some fields). Serum IgG levels were within normal limits.

4. Discussion

IgG4-related disease (IgG4-RD) is a recently described disorder that involves lymphocytplasmacytic infiltrates causing fibrotic and tumor-like lesions that can affect multiple organ systems [1]. Histopathologic examination of affected tissue shows infiltration with abundant IgG4-positive plasma cell and storiform fibrosis. Hematologic examination reveals elevated IgG levels [2]. Whether IgG4 plays a pathogenic role in the inflammation and fibrosis that characterize this disease remains uncertain. The incidence and prevalence of IgG4-RD are unknown, however, and many
conditions previously thought to be unrelated are now believed to belong to this newly recognized group of illnesses (e.g. autoimmune pancreatitis, Mikulicz’s syndrome, Riedel’s thyroiditis) [2].

Lung involvement in IgG4-RD is not rare although the exact prevalence is unknown. A cross-sectional study of 114 patients with IgG4-RD showed that 14% had lung or pleural lesions, and a separate study in 90 patients with autoimmune pancreatitis reported lung involvement in more than half [3]. Many with IgG4-RD affecting the lung will have no symptoms, and when symptoms are present, they are often non-specific (cough, dyspnea, fever, chest pain). Radiologic findings are variable. Parenchymal involvement can occur with a solitary large mass (pseudo-tumor), such as in our patient, or with multiple nodules [4]. Airway lesions (bronchiectatic changes), ground glass opacities, and interstitial abnormalities such as interlobular septal thickening or honeycombing have also been reported [4]. The most common thoracic manifestation of IgG4-RD is lymphadenopathy in the hila or mediastinum, found in up to 90% of cases [1]. Pleural involvement with thickening, nodules along the pleural surface, and effusions can also occur but are less frequent.

The diagnosis of IgG4-RD relies on radiologic imaging, serum IgG4 levels and histopathology. As mentioned above, the clinical and radiologic manifestations are nonspecific, and establishing the diagnosis of IgG4-RD lung involvement requires a high level of clinical suspicion. PET may show increased uptake but will not distinguish from other PET-avid lesions such as bronchogenic carcinoma or metastatic lung lesions. Increased serum levels of IgG4 can help establish a diagnosis of IgG4-related lung disease, but are not essential, since serum IgG4 levels can be normal in some affected individuals. In addition, elevated serum IgG4 levels may be found in as many as 5% of adults without evidence of IgG4-RD [4].

Histopathologic confirmation of IgG4-related lung disease is based on finding large numbers of plasmocytes in the affected tissue and immunohistochemical staining. Pathologic characteristics consist of dense lymphoplasmocytic infiltrates, fibrosis, and oblitative phlebitis [5]. Immunohistochemical staining of surgically-obtained lung biopsies that contain >40% of plasmocytes that are reactive with IgG4-specific antibody is highly suggestive of the diagnosis [6]. Alternatively, if either a surgical lung biopsy or transbronchial lung biopsy specimen contains 20–50 IgG4-positive plasma cells per high-powered field, the diagnosis is suggested.

Systemic corticosteroids are the mainstay of therapy for IgG4-RD, although spontaneous remission may occur. Since identifying
which patients may progress to fibrosis is not currently possible, experts recommend steroid treatment to lower the risk of irreversible fibrosis [6]. Recommended treatment for IgG4-related lung disease has been extrapolated from experience with autoimmune pancreatitis, and typically includes prednisone 30 mg (or higher) daily for 1–2 weeks. A gradual taper of the steroid dose over several months is recommended. It is not known if low-dose long-term steroid therapy is indicated to prevent relapse. It is also not known if non-steroid immunosuppressives are effective. Small case series have reported efficacious treatment with rituximab [6].

The long term prognosis of IgG4-related lung disease is uncertain. A favorable response to corticosteroid therapy is typical. However, relapse can occur months or years after initial treatment. Experts believe that patients with higher levels of serum IgG4 and more diffuse involvement have a greater risk of relapse.

5. Conclusion

IgG4-RD is a recently recognized systemic sclerosing disease that can affect almost any organ. Lung involvement appears to be common. Thoracic involvement may involve the parenchyma, airways, pleura, and mediastinum. IgG4-RD characterized on histopathology by tumor-like lesions with a dense lymphoplasmacytic infiltrate and abundant IgG4-positive plasma cells and storiform fibrosis. The diagnosis is established by a compatible clinical and radiologic presentation and histopathologic findings of increased IgG4-positive plasma cells in affected tissue. Systemic corticosteroid treatment is considered the mainstay of therapy to prevent fibrosis. The long-term prognosis of IgG4-related lung disease is uncertain.

Conflict of interest

Drs. Grewal, Cohen, Kwon and Kaufman do not report any conflict of interest.

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