Case Report

IgG4-Related Disease Presenting as a Neck Mass

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Keywords
IgG4-related disease, lymphadenopathy

Received March 11, 2015; revised June 5, 2015; accepted June 12, 2015.

Introduction
IgG4-related disease (IgG4-RD) is now understood to be an immune-mediated condition affecting multiple anatomic sites. Disorders that were previously considered unrelated are now classified as IgG4-RD and share pathologic, serologic, and clinical features. Lacrimal and salivary gland swelling (formerly Mikulicz disease), bilateral submandibular gland enlargement (formerly Kuttner’s tumor), as well as extraocular muscle swelling and associated proptosis are common manifestations of IgG4-RD. Reidel’s thyroiditis is also considered to be one manifestation of IgG4-RD.¹ Patients with IgG4-RD often present with swelling of lymph nodes or other organs that are enriched with IgG4-positive plasma cells; most patients have elevated serum IgG4 concentrations. Here we discuss the case of a patient with IgG4-RD presenting with a neck mass.

Case Presentation
A 62-year-old man presented from his primary physician with a 1-week history of a mobile, nontender, relatively soft 4- × 3-cm left submandibular mass, consistent with lymphadenopathy on clinical examination. He had a history of myelodysplastic syndrome (MDS), the insufficient but often-asymptomatic production of 1 or more blood cell types. The patient was initially treated with oral antibiotics and observation because of a recent respiratory illness. The patient did not report “B” symptoms suggestive of lymphoma, such as fevers, night sweats, or unintended weight loss. However, the lymphadenopathy persisted for 3 weeks. Ultrasound-guided fine-needle aspiration (FNA) and computed tomography imaging were thus performed because of his MDS history and concerns for conversion to lymphoma (Figure 1). Pathology was consistent with normal lymph node tissue. After 3 additional months of observation, the patient developed 2 additional enlarged lymph nodes in the same area with no change in the original lymph node. Excisional biopsy of the original node was subsequently performed. Pathology diagnosed IgG4-related disease (Figure 2). He was started on prednisone 40 mg/d for 3 weeks, and the lymphadenopathy resolved within a week of initiation of the medication. At 12 months’ follow-up, the patient exhibited no lymphadenopathy or systemic clinical signs indicating relapse of IgG4-RD. Single case reports are exempt from institutional review board review at the University of Kentucky.

Figure 1. Axial computed tomography image of the neck with contrast showing left neck cervical lymphadenopathy in relation to the submandibular gland.

Figure 2. Pathology diagnosis of IgG4-related disease.

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Discussion

This case illustrates the importance of including IgG4-RD in the differential diagnosis of a cervical mass. IgG4-RD is a relatively newly described entity that consolidates what were previously thought to be unrelated systemic disorders. Increased levels of serum IgG4 occur in ~60% to 70% of affected patients. Signs of IgG4-RD include swelling of organs and lymph nodes due to IgG4-positive plasma cells, with sequelae based on the affected organ system. Pathology of organs affected with IgG4-RD will show significant IgG4-positive plasma cells with fibrosis of structures. Both clinical signs and histopathology are required to make the diagnosis of IgG4-RD. Radiology studies may be ordered as indicated based on signs or symptoms. Elevated serum IgG4 levels are considered adjunctive but not necessary for diagnosis—elevated serum IgG4 is sensitive for IgG4-RD, but not specific. The disease is more common in middle-aged or older men, and the exact etiology is unknown. Some research suggests that the plasmablast, a B-cell precursor to plasma cells, may proliferate in response to a particular antigen, and thus IgG4-RD may be autoimmune. In addition to the head and neck manifestations listed above, cervical lymphadenopathy due to IgG4-RD can present with synchronous or metachronous inflammatory fibrosclerosing lesions elsewhere in the body. Autoimmune pancreatitis, sclerosing cholangitis, retroperitoneal fibrosis, or fibrosis of several other tissue types have been described in the literature. There is no reported association of MDS with IgG4-RD, although studies have shown a higher rate of lymphoma in IgG4-RD patients.

The long-term natural history of IgG4-RD is not well understood. Many patients initially respond to oral steroids, but recurrences are common. For patients who cannot tolerate steroids, rituximab is another option. Medical management, especially with antimitabolites such as rituximab, is typically performed under the guidance of rheumatologists or hematologists. In retrospect, an empiric course of oral steroids for this patient after the initial (normal) FNA may have resolved the lymphadenopathy, but absence of subsequent excisional biopsy tissue for pathology may have delayed diagnosis of IgG4-RD.

Conclusion

During the course of evaluation and management of neck masses, consideration for IgG4-RD should be given. Diagnosis requires both clinical signs combined with pathologic verification. Otolaryngologists should be particularly aware of head and neck manifestations of IgG4-RD, because proper diagnosis may aid in diagnosis of other, seemingly unrelated systemic manifestations.

Author Contributions

Allyson L. Hughes, manuscript drafting, data analysis, drafting, final approval, accountability for all aspects of the work; Brett T. Comer, conception of idea, data analysis, drafting, final approval, accountability for all aspects of the work.

Disclosures

Competing interests: None.
Sponsorships: None.
Funding source: None.

References


Figure 2. Hematoxylin and eosin staining (a) and immunohistochemical staining (b) of lymph node tissue showing numerous IgG4-positive plasma cells (200× and 400× magnification, respectively).