

## Management of IgG4-related Sclerosing Disease

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### Abstract

*IgG4-related sclerosing disease is a systemic syndrome that is distinguished by high levels of both IgG4 and IgG4-positive lymphoplasmocytic infiltrative lesions in the body. We report an occurrence of orbital IgG4-related disease in a 62-year-old Hispanic male. IgG4 related sclerosing disease involving the orbit affects patients ranged from ages 30 to 86 with a 1:1 male to female ratio (1,2). The patient presented with bilateral painless, progressive nodular lesions of the lacrimal glands. Pathologic evaluation from the biopsy of the orbital mass showed an increase in IgG4 positive plasma cells, fibrosclerosis, and lymphoid hyperplasia. The patient was treated with a high dose of oral prednisone for a period of 3 months and was then placed on a maintenance dose with rapid resolution of both orbital masses. The work-up, diagnostic tools, and treatment of IgG4 disease are discussed. It is important to note that IgG4 can affect all orbital structures and physical findings, lab results, and biopsy results are required for appropriate diagnosis and management.*

### Introduction

IgG4-related disease (IgG4-RD) is a systemic syndrome characterized by the elevated levels of IgG4 and IgG4-positive lymphoplasmocytic lesions in the affected areas of the body (3-5). Pathologic evaluation from these lesions show lymphoplasmocytic infiltrate enriched in IgG4-positive plasma cells, and a variable degree of fibrosis that has a “storiform,” or whirling pattern, of fibroblasts and inflammatory cells. IgG4 disease of the orbit can affect several ocular adnexal tissues including the lacrimal gland and the eyelids (6,7). Manifestations of IgG4-RD of the orbit include inflammation, edema, and myositis (8). Diagnosis of IgG4-related disease is made by both an elevated serum IgG4 and histopathological features including lymphocyte and IgG4 positive plasma cell infiltration (1,9). The differential diagnosis for IgG4-related disease includes sarcoidosis, Wegener's granulomatosis, lymphoma, and other neoplasms(10). In this report, we present a case of IgG4-related disease of the orbit and discuss the work-up and management.

### Case Report

A 62 year-old Hispanic male presented to our Ophthalmology Clinic with a six month history of a left-sided proptosis with an associated orbital mass easily palpable under the eyelid that progressively increased in size,. A similar lesion then appeared on the right side. He endorsed minimally decreased vision on the left, but denied eye pain, diplopia, scotoma, or any other ophthalmic symptoms. He denied systemic symptoms including night sweats, weight loss, fever, or abdominal pain.

During physical examination, the patient was well-appearing with normal vital signs and a normal review of systems. External exam was significant for bilateral nontender, dense,

lobular masses involving the lacrimal glands. The remainder of the ophthalmic exam was normal. A battery of laboratory tests including complete metabolic panel, complete blood count, lipid panel, erythrocyte sedimentation rate, C reactive protein, rheumatoid factor, thyroid stimulating hormone, lactate dehydrogenase, blood culture, and urinalysis were obtained, all of which were within normal limits. Excisional biopsy of the left orbital mass was performed which showed an increased IgG4-positive plasma cells, fibrosclerosis, and lymphoid hyperplasia, with no evidence of lymphoma. The IgG4 positive cells were kappa cells and lambda cells (polytype pattern) with CD 3+ and CD 45+ T cells, CD 20+ B cells, and CD 21+ CD 138+ follicular and interfollicular plasma cells.

Based on physical findings, lab results, and biopsy results, the patient was given a diagnosis of IgG4-related sclerosing disease with bilateral orbital involvement. He was started on 60mg of prednisone orally daily for four weeks. During this period, the patient showed a significant response with rapid decrease in the nodular orbital masses. After four weeks, prednisone was tapered and, the nodules continued to improve, resolving completely within 4 months. The patient was also referred to the rheumatology service, which ruled out other organ involvement by the IgG4 disease.

### Discussion

Orbital IgG4-related disease classically presents with lid swelling and proptosis, and is often painless. Ocular motility may be restricted if there is involvement of the extraocular muscles. There are generally no visual disturbances with these orbital lesions (11).

The lacrimal gland is the most commonly affected structure in orbital IgG4-related disease (69%), and this may be

unilateral or bilateral (12,13). Patients with orbital IgG4-related disease may have other, non-orbital lesions, which are most frequently encountered in the submandibular glands (29%), lymph nodes (14%), pancreas (5%), or bile ducts (5%) (12,13). IgG4-related lesions in the thyroid and pituitary may also be present (14,15). Patients with orbital IgG4-related disease often show bilateral involvement (62%) (7,12,13).

The differential diagnosis for orbital IgG4-related disease is broad. Mimickers include marginal zone B-cell lymphoma, idiopathic orbital inflammation, idiopathic orbital myositis, antineutrophil cytoplasmic antibody (ANCA)-mediated systemic vasculitis (such as Churg-Strauss syndrome and granulomatosis with polyangiitis), and reactive lymphoid hyperplasia without IgG4-positive plasma cells (16).

Treatments for orbital IgG4-related disease may include systemic steroids, radiotherapy, or rituximab (12,13). Oral glucocorticoids are typically first line treatment for IgG4-related disease. Improvement, and often resolution, of symptoms is typically seen with this therapy. With the discontinuation of steroids, however, relapse is common. As a result, chronic immunosuppression is often required, which may be with low dose prednisone, or with steroid-sparing agents such as azathioprine, mycophenolate mofetil, and methotrexate (1). The efficacy of these drugs at preventing relapse is a topic for further investigation. In cases where prednisone is ineffective, Rituximab has also shown improvement both clinically and serologically (17), although recurrences have also been observed (13).

Given the success associated with treatment, early initiation is recommended. Further, prompt diagnosis and treatment is critical as, left untreated, patients with IgG4-related sclerosing may, in rare cases, develop secondary malignancies including cholangiocarcinoma (18) and malignant lymphoma (19).

### Conclusion

In conclusion, we describe a case of IgG4 related sclerosing disease involving the orbit bilaterally. It is important to note that IgG4 can affect all orbital structures. Physical findings, lab results, and biopsy results are required for appropriate diagnosis and management.

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