Available online at www.sciencedirect.com

ScienceDirect

journal homepage: www.elsevier.com/locate/survophthal

Viewpoint

Orbital inflammation: Corticosteroids first

*Lora R. Dagi Glass, MD, Suzanne K. Freitag, MD**

Ophthalmic Plastic Surgery Service, Massachusetts Eye and Ear Infirmary, Harvard Medical School, Boston, Massachusetts, USA

ARTICLE INFO

Article history:
Received 27 September 2015
Received in revised form 14 January 2016
Accepted 15 January 2016
Available online 10 March 2016
L. Jay Katz and **Hermann D. Schubert**, Editors

Keywords:
orbital inflammation
corticosteroid
ancillary testing
biopsy
targeted therapy

ABSTRACT

Orbital inflammation is common, and may affect all ages and both genders. By combining a thorough history and physical examination, targeted ancillary laboratory testing and imaging, a presumptive diagnosis can often be made. Nearly all orbital inflammatory pathology can be empirically treated with corticosteroids, thus obviating the need for histopathologic diagnosis prior to initiation of therapy. In addition, corticosteroids may be effective in treating concurrent systemic disease. Unless orbital inflammation responds atypically or incompletely, patients can be spared biopsy.

1. Introduction

Orbital inflammatory processes comprise up to 11% of orbital pathologies and affect all ages and both genders.[15,37] Patients may present with a variety of signs and symptoms, including periorbital pain, proptosis or globe dystopia, a palpable periorbital mass, eyelid ptosis or edema, reduced ocular motility causing diplopia, afferent pupillary defect, decreased vision, dyschromatopsia, or a visual field deficit. Imaging with contrast enhancement may demonstrate diffuse or discrete orbital abnormalities affecting the periorbita, lacrimal gland, muscles, fat, sclera, or nerves. Even with extensive ancillary testing, it may not be possible to identify a specific etiology. Patients with clinical presentations most consistent with inflammatory orbital disease are often empirically treated with corticosteroids, which may be both diagnostic and rapidly curative.

A review of the diagnostic breakdown of orbital inflammation helps to validate the recommendation for corticosteroids as a first-line diagnostic and therapeutic intervention. There are several series reporting the results of orbital biopsy. Shields et al published a review of 1264 patients,[37] and the Newcastle Eye Center reviewed 162 patients[42] with biopsied orbital lesions; 167 (13%) and 71 (44%), respectively, had nonneoplastic, noninfectious inflammatory conditions. Idiopathic orbital inflammation comprised 81% to 87% of orbital

* Corresponding author: Suzanne K. Freitag, MD, Ophthalmic Plastic Surgery Service, Massachusetts Eye and Ear Infirmary, Harvard Medical School, 243 Charles Street, Boston, MA 02114, USA. Tel.: 617-573-5529; fax: 617-573-5525.
E-mail address: suzanne_freitag@meei.harvard.edu (S.K. Freitag).
0039-6257/$ – see front matter
http://dx.doi.org/10.1016/j.survophthal.2016.01.005

inflammatory conditions.[37,42] This incidence may be an overestimate, given retrospective reviews of histopathology relabeling certain samples as IgG4-related disease. Although older IgG4 histopathologic definitions were more inclusive, allowing for up to 40% of reviewed specimens to be recategorized, better understanding of normative lacrimal gland IgG4 staining reduced the number of recategorized cases to as low as 5%.[3,11,32,36,41] Other biopsy-proven specific inflammatory conditions demonstrated similarly low incidences. Sarcoidosis was diagnosed in 1.5 to 5.5% of biopsied inflammatory orbital lesions in the Shields et al and Newcastle series, respectively.[37,42] Similarly, Shields et al found 2%, and the Newcastle group 3%, of biopsied lesions consistent with granulomatosis with polyangiitis.[37,42] Four percent of patients in the Newcastle series showed another cause of vasculitis.[3] Up to 10% of inflammatory lesions were consistent with histiocytosis in the Shields et al series, and there was 1 such patient in the Newcastle series.[37,42] Because biopsy has classically been reserved for atypical and poorly responsive cases, reports subdividing orbital processes according to histopathologic diagnosis were likely biased toward those that were atypical or did not respond rapidly or fully to corticosteroid therapy. Furthermore, thyroid eye disease (TED) is rarely biopsied given its characteristic findings, but accounts for approximately 60% of orbital inflammation in young to middle-aged adults and up to 40% after the seventh decade.[24] Hence, most cases of orbital inflammation that undergo biopsy are classified as idiopathic, which does not allow for the determination of a more selective treatment regimen.

In the sections that follow, the rationale regarding the empiric initiation of steroid therapy for diagnostic and therapeutic management of patients with orbital inflammatory disease will be elucidated through the sequence of patient care, from the initial evaluation and examination to ancillary testing and initiation of treatment.

2. The importance of performing a thorough history and physical examination

Despite a multitude of technological advances, the practice of medicine today still relies on the basic tenants of tailored, in-depth history taking and clinical examination. Clues regarding the possibility of a systemic inflammatory process may be elicited with a review of systems addressing symptoms such as fever, malaise, weight loss, poor appetite, and fatigue. A history of prior malignancy should make the clinician more suspicious of a neoplastic orbital process. Patients with TED may have a history of hyperthyroidism or hypothyroidism, or symptoms consistent with either.[5,45] Patients with IgG4-related disease may have abdominal discomfort or a history of non-neoplastic masses in the chest, abdomen, pelvis, or meninges.[9,22,26] Patients with sarcoidosis may have pulmonary or cardiovascular symptoms, skin lesions, or a history of adult-onset respiratory problems.[35] Patients with granulomatosis with polyangiitis may have sinus, pulmonary, or renal symptoms.[1] Patients with histiocytosis may have asthma or yellow discoloration of the affected areas.[21] General physical examination may demonstrate diagnostically helpful findings, including enlarged lymph nodes, skin nodules, thyroid enlargement or tenderness, wheezing, heart murmurs, abdominal masses or enlargement of abdominal organs. These findings may then allow for tailored ancillary testing or may suggest a diagnosis. Conferring with appropriate consultants may complete the clinical picture, often allowing for the "bladeless" presumptive diagnosis of an inflammatory orbital process with appropriate corticosteroid treatment and monitoring thereafter.

3. Ancillary testing: imaging and laboratory studies help identify or rule-out diagnoses

Thoughtful ancillary testing is good practice when confronted with a patient with suspected orbital inflammation and can point to or exclude a causative etiology. Although comprehensive testing may be low yield, selective testing predicated on a careful review of systems, history, and physical examination may provide helpful positive results. Antinuclear antibody, erythrocyte sedimentation rate, and C-reactive protein may be elevated in systemic inflammation or demonstrate proclivity to autoimmune orbital disease.[14] A thyroid function panel and thyroid antibody testing can help diagnose thyroid disease or risk for TED. When appropriate, diagnostic imaging of the thyroid may demonstrate changes consistent with various forms of thyrotoxicosis.[2,44] Liver function testing may show evidence of pancreatic dysfunction in autoimmune pancreatitis associated with IgG4-related disease. Although serum IgG4 is not always elevated in IgG4-related disease, the finding of elevated serum levels is one of the diagnostic criteria and may be somewhat helpful in monitoring disease.[26,27] On imaging, patients with IgG4-related disease may demonstrate involvement of tissues ranging from the salivary and thyroid glands to the pancreas, aorta, retroperitoneum, lungs, mediastinum, and pituitary, among others.[9,22,26] Elevated angiotensin-converting enzyme, lysozyme, or calcium levels may point to sarcoidosis. Chest imaging may show hilar lymphadenopathy.[35] Antineutrophil cytoplasmic antibody testing and urinalysis may be consistent with granulomatosis with polyangiitis, and imaging may show involvement of the sinuses or lungs.[1] A paraproteinemia may be evident in histiocytosis, and a skeletal survey may demonstrate lytic bone lesions.[21] Serum testing to exclude infections that could be worsened by corticosteroid therapy, such as tuberculosis, is also important to consider in this patient population.[40] Furthermore, positive serologies for infectious diseases such as Lyme borreliosis, syphilis, and tuberculosis may allow for targeted antimicrobial treatment of a specific orbital infection.

4. Surgical morbidity

By initiating empiric corticosteroid therapy, patients receive a treatment that is likely to improve or resolve their orbital and systemic inflammatory disease while allowing most patients to forgo a surgical biopsy. Even in experienced hands, orbitotomy with biopsy may result in significant morbidity, including loss of vision, diplopia, and ptosis. This risk is greater in lesions of the orbital apex or intricately surrounding