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Nonspecific Orbital Inflammation

Robi N. Maamari, MD, Steven M. Couch, MD*

Department of Ophthalmology and Visual Sciences, Washington University School of Medicine in St Louis, 660 South Euclid Avenue, Box 8096, St Louis, MO 63110, USA

Keywords

• Nonspecific orbital inflammation • Pseudotumor • Dacryoadenitis • Myositis • Scleritis • Orbital apex syndrome • Orbitotomy

Key points

- Nonspecific orbital inflammation is a diagnosis of exclusion; systemic and pathologic evaluation is required to rule out specific causes of inflammation and other infiltrative diseases.
- Nonspecific orbital inflammation is anatomically characterized on orbital imaging into dacryoadenitis, myositis, anterior orbital inflammation, orbital apex/optic nerve, and diffuse orbital inflammation.
- Histologic evaluation shows a nonspecific polymorphous inflammation with leukocytes and mature lymphocytes, upregulation of inflammatory cytokines, with varying degrees of fibrosis.
- Immunoglobulin G4 (IgG4)–related disease should be considered in patients with plasma cell infiltration, elevated IgG4 ratio, and many times elevated serum IgG4 level.
- High-dose oral steroids remain the most common therapy, but steroid-sparing agents and specific targeted immunologic treatments have gained traction.

INTRODUCTION

Nonspecific orbital inflammation (NSOI) describes a benign orbital inflammation characterized by a polymorphous infiltrate with varying degrees of fibrosis, without a known local or systemic cause [1].

NSOI has a wide spectrum of clinical features, anatomic involvement, disease course, and response to therapy. Because of this tremendous clinical

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*Corresponding author. *E-mail address:* CouchS@wustl.edu

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variability, NSOI may be confused with other orbital diseases, including infectious orbital cellulitis, thyroid-associated orbitopathy, malignancy, and numerous other immunologic and vasculitic processes [2]. NSOI remains a diagnosis of exclusion, and all other specific causes must be ruled out [3].

Although NSOI is described as the most frequently observed type of orbital mass, clinical diagnostic guidance for NSOI remains deficient in the literature. Although proposed diagnostic criteria and classification schemes have attempted to categorize the wide spectrum of findings in NSOI, none of these classification systems have been widely adopted. These systems differentiated NSOI subtypes based on specific clinical characteristics, anatomic location of the inflammatory process, and histopathologic features of the biopsied orbital tissue [4–6]. More recent efforts investigating immunologic biomarkers and gene expression profiling will likely expand our understanding of NSOI and provide improved, more specific diagnostic criteria [7].

Historical description and terminology

In 1905, Birch-Hirschfeld [8] reported a disease process affecting 4 patients that initially presented with new-onset exophthalmos with suspicion for an orbital malignancy [9]. Because of the lack of an identifiable underlying pathologic cause and the absence of any detectable tumor during surgical exploration, these patients were given the diagnosis of orbital pseudotumor, reflecting the benign disease process masquerading as a neoplastic mass. However, microscopic evaluation by Birch-Hirschfeld as well as Benedict and Knight [10] identified regions of the biopsied orbital tissue that demonstrated a histologic pattern of infiltration by lymphocytes and other leukocytes, which they thought pointed toward an inflammatory cause for these cases of orbital pseudotumor [9,10].

Since the original report of orbital pseudotumor dating back more than one century ago, advances in imaging techniques, molecular diagnostics, immunohistologic analysis, and cytologic testing have furthered our understanding of this inflammatory disease process [11,12]. Accordingly, recent reports in the medical literature have instead adopted the term *NSOI*, which accurately reflects our incomplete understanding of the disease pathogenesis but also highlights the exclusion of other inflammatory causes through modern diagnostic techniques. Other terms that have been used to describe NSOI in the preceding literature include *orbital pseudotumor*, *idiopathic orbital inflammation*, *orbital inflammatory syndrome*, and *orbital inflammatory disease*.

SIGNIFICANCE

NSOI is the third most common noninfectious orbital disease, following thyroid orbitopathy and lymphoproliferative diseases [13]. It has been shown to account for up to 6.3% of orbital disorders in the adult population and 6% to 17% in the pediatric population [13–15]. Unilateral presentation is generally observed, but bilateral involvement, either simultaneously or sequentially, can occur.