Enlargement of the Infraorbital Nerve

An Important Sign Associated with Orbital Reactive Lymphoid Hyperplasia or Immunoglobulin G4–Related Disease

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Objective: To describe the clinical, histopathologic, and radiologic features of a recently identified cause for enlargement of the infraorbital canal.

Design: Retrospective, noncomparative case series.

Participants: Consecutive patients were identified from the orbital databases at Moorfields Eye Hospital, London, England, and the Royal Victorian Eye and Ear Hospital, Melbourne, Australia.

Methods: A retrospective, noncomparative review of the clinical case notes, radiology, and histopathology was performed. The English-language medical literature was reviewed for reports of enlargement of the infraorbital canal or nerve.

Main Outcome Measures: Extent of clinical and radiologic changes in patients with enlargement of the infraorbital canal.

Results: A total of 14 patients (10 male) presented between the ages of 29 and 76 years with proptosis, eyelid swelling or a mass (10/14 cases), and periocular ache (5/14 cases). Clinical evidence of bilateral involvement was present in 6 of 14 patients. None had impairment of visual functions or facial sensation, but 4 of 14 patients had some reduction in ocular motility. Imaging showed a focal orbital mass in 10 of 14 patients (16/28 orbits), and all patients (22/28 orbits) had enlargement of some extraocular muscles. The infraorbital canal was enlarged in 20 of the 28 orbits, with associated ipsilateral orbital changes in 19 of 20 (all 14 patients) and ipsilateral maxillary sinus changes in 12 of 20 (11 patients). Biopsy-proven chronic orbital inflammation was present in all patients; this resembled reactive lymphoid hyperplasia (RLH) in 7 patients and immunoglobulin (Ig) G4–related sclerosing inflammation in 7 patients. When tested, serum IgG4 was elevated in 6 of 7 patients. Clinical or histologically proven enlargement of cervical lymph nodes was present in 7 of 14 patients. All patients responded well to systemic corticosteroid therapy, although some had a relapse upon withdrawal. One patient developed diffuse large B-cell lymphoma and subsequently leukemia, of which he later died 20 years after presentation.

Conclusions: Enlargement of the infraorbital nerve and canal is rare and strongly suggests a diagnosis of RLH or IgG4-related disease, especially in the presence of ipsilateral extraocular muscle enlargement, sinus disease, or focal orbital disease. *Ophthalmology 2014;■:1–7 © 2014 by the American Academy of Ophthalmology.*

Periocular adnexal lymphoproliferative lesions comprise a spectrum of disease, from benign reactive lymphoid hyperplasia (RLH) to lymphoma, although the clinical presentation and radiologic findings for these conditions may be similar. Histopathologic examination, including immunohistochemistry, and occasionally gene rearrangement studies are required to distinguish polyclonal from monoclonal infiltrates. Ocular adnexal RLH is uncommon,[1–3] can be associated with systemic disease,[4] and might have potential for subsequent development of lymphoma.[5–7] Immunoglobulin (Ig) G4–related disease (IgG4-RD)[8] has many similarities to RLH and clinically might represent a newly recognized variant of the latter.

Expansion of the infraorbital nerve (ION) canal is rare, but epineural disease is increasingly recognized as a marker for IgG4-RD.[9] We present 14 cases of patients with chronic orbital inflammation who display this distinct clinico-radiologic manifestation.

Methods

Consecutive patients with expansion of the ION or canal were identified from 2 orbital databases (Moorfields Eye Hospital, London, England, and the Royal Victorian Eye and Ear Hospital, Melbourne, Australia), and a retrospective review of the clinical case notes, radiology, and histopathology was performed. The nerve or canal was regarded as expanded where the diameter on coronal imaging exceeded that of the optic nerve.[10] Institutional review board/ethics committee approval was obtained for this study.

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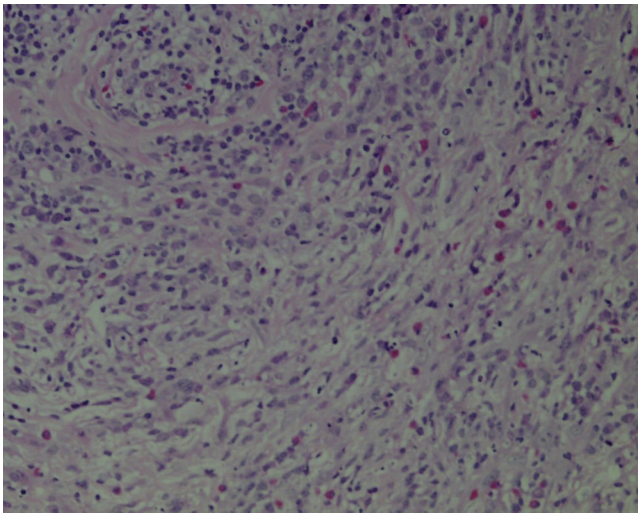

Figure 1. Case 1. Low-power hematoxylin–eosin photomicrograph of infraorbital nerve tissue showing lymphoplasmacytic cell infiltrate with scattered follicle formation and moderately elevated eosinophil counts (×400).

Immunohistochemistry was performed on orbital biopsies from all patients, together with Ig heavy-chain gene rearrangements in 1 patient (case 3; Table 1, available at www.aaojournal.org). Tissues were stained for IgG4 in 13 of 14 cases, and serum IgG4 levels were available in 7 cases. The histologic criterion for IgG4-RD was based on typical morphologic features and a mean of >10 IgG4-positive cells per high-power field,[11,12] and any patients assigned this diagnosis were also in accord with the criteria published recently by the international IgG4-RD working group.[8]

The English-language medical literature was reviewed for publications regarding enlargement of the infraorbital canal or nerve, ocular adnexal RLH, and IgG4-RD. The PubMed database was searched using the keywords *infraorbital nerve, reactive lymphoid hyperplasia* AND (*orbit* OR *ocular adnexa*), and *IgG4*, and selected references from articles found by this search were obtained.

Results

Fourteen consecutive patients with ION enlargement were identified from the authors' databases: 5 from Moorfields Eye Hospital and 9 from the Royal Victorian Eye and Ear Hospital. Their initial presentations ranged from 1991 to 2005. We describe the details of 3 of these patients and summarize the findings.

Case Reports

Case 1. A 37-year-old white man with chronic asthma had a limited right orbital decompression at another institution for a diagnosis of euthyroid thyroid eye disease with compressive optic neuropathy. Five years later, he was referred to Moorfields Eye Hospital with severe orbital inflammation, bilateral proptosis of 30 mm, no optic neuropathy, and good ocular motility. Systemic blood test and thyroid function test results were normal, thyroid

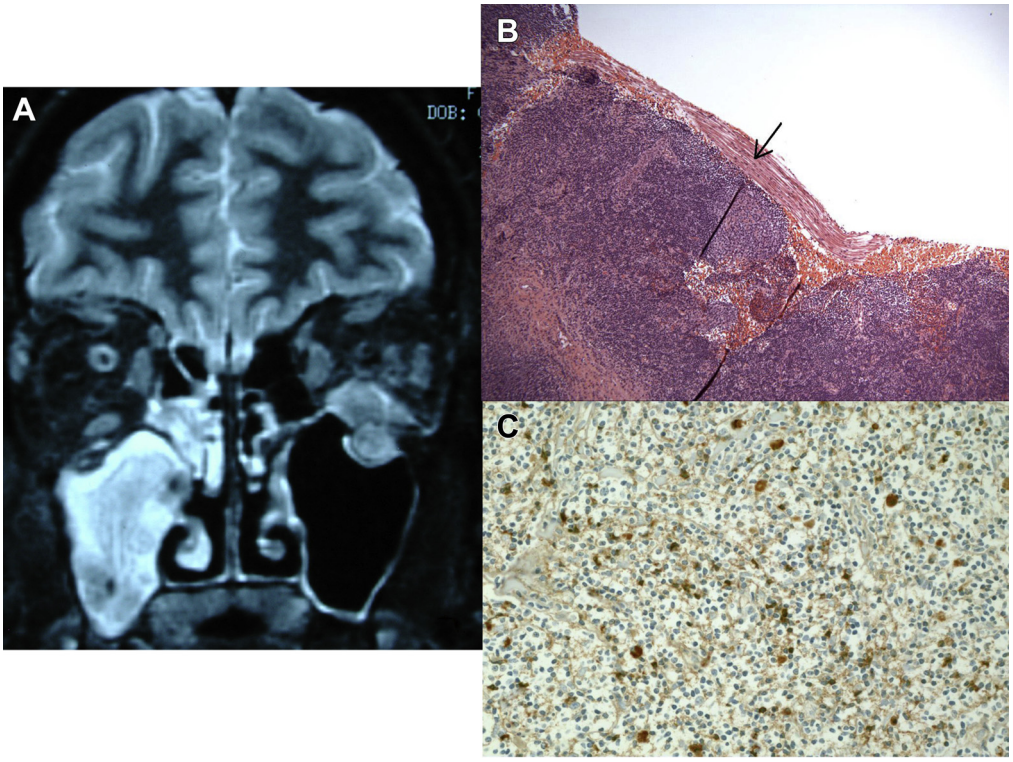

Figure 2. Case 2. **A,** Coronal magnetic resonance imaging showing enlarged left infraorbital canal, extraocular muscle enlargement, paranasal sinus mucosal thickening, and right maxillary and ethmoid sinus opacification. **B,** Low-power hematoxylin–eosin photomicrograph of infraorbital canal biopsy showing diffuse lymphoplasmacytic infiltrate and occasional reactive follicles within the epineurium; *arrow* shows uninvolved endoneurium (×40). **C,** Infraorbital nerve biopsy. Immunohistochemistry stain for immunoglobulin (Ig) G4–positive plasma cells, along with histopathologic and clinical features, fulfilling diagnostic criteria for IgG4–related disease (×400).