

Idiopathic sclerosing inflammation presenting as sinusitis

Henry P. Barham, M.D.,¹ Megan K. Dishop, M.D.,² and Jeremy D. Prager, M.D.¹

ABSTRACT

Idiopathic sclerosing orbital inflammation is a rare finding that is poorly delineated, immune mediated, and causes severe symptoms and disability. It has been described affecting the orbit in addition to other sites within the head and neck, but has rarely been described presenting as sinusitis. A case report and literature review were performed. A 14-year-old girl with right-sided face and eye pain and pressure for >1 month presented 3 days after endoscopic sinus surgery for presumed acute sinusitis. She subsequently developed ipsilateral vision loss and hypesthesia of the infraorbital nerve. MRI revealed a mildly enhancing soft tissue intensity lesion extending from the right maxillary sinus into the pterygopalatine fossa and orbital apex through the inferior orbital fissure. Biopsy specimens of the lesion were consistent with a sclerosing inflammatory lesion. High-dose steroids led to rapid improvement in vision and pain; however, the patient was unable to tolerate steroid weaning because of recurrence of eye pain and headache. Repeat imaging showed progression of the lesion. Rheumatology was consulted and the patient's steroid therapy was altered and her medications were expanded to include azathioprine. The patient's symptoms improved and subsequent imaging showed a reduction in the size and extent of the lesion. Idiopathic sclerosing inflammation is characterized by primary, chronic, and immunologically mediated fibrosis. Patients typically have a poor response to corticosteroid treatment or radiotherapy. Immunosuppressive therapy in addition to corticosteroids is the recommended treatment.

(Allergy Rhinol 3:e101–e104, 2012; doi: 10.2500/ar.2012.3.0031)

Orbital inflammation has been shown to result from a large variety of entities and is classified by the site of origin or underlying pathology.¹ Idiopathic sclerosing orbital inflammation (ISOI) is a rare finding that is characterized by primary, chronic, and immunologically mediated fibrosis. It typically presents as a chronic but aggressive process with fewer inflammatory signs than typical nonspecific orbital inflammation (NSOI). The anatomic location of inflammation dictates the associated signs and symptoms, with the most common symptoms being blurry vision, orbital pain, and diplopia. It typically shows a poor response to corticosteroids or radiotherapy. It typically causes severe symptoms and disability. The recommended therapy frequently involves immunosuppressive treatment to help slow progression.^{2,3}

CASE PRESENTATION

A 14-year-old girl presented to her primary care provider with right cheek pain, pressure, and nasal congestion and was treated for acute sinusitis with antibiotics. When her pain worsened and began to involve her right eye she underwent CT and MRI studies that were interpreted as consistent with sinus-

itis. She subsequently underwent bilateral inferior turbinate reduction and bilateral maxillary, sphenoid, ethmoid, and right frontal functional endoscopic sinus surgery. With no improvement in her symptoms and the addition of diplopia, photophobia, and nausea with vomiting and 10-lb weight loss, she presented to the Emergency Department at our institution. On admission, her erythrocyte sedimentation rate and c-reactive protein were found to be 85 mm/hr and 6.7 mg/L, respectively. CT with contrast of sinuses and brain were consistent with postoperative situation; however, on an overread by an ear/nose/throat specialist she was found to have a soft tissue mass in the maxillary sinus in addition to a bony defect of the posterior maxillary wall (Fig. 1, A and B). She was initially treated by the Neurology Department for presumed migraine and myofascial pain. Three days after admission, she experienced sudden, painful vision loss and developed an afferent pupillary defect. She was started on steroids with a presumed diagnosis of optic neuritis. The following day, she noted progression of her vision loss with light perception and movement only. High-dose steroids were continued. Emergent MRI revealed a soft tissue intensity extending likely from the right maxillary sinus into the pterygopalatine fossa and into the orbital apex through the inferior orbital fissure (Fig. 1 C). Mild enhancement was seen after gadolinium. There was suggestion of posterior maxillary wall destruction. There was abnormal enhancement at the right cavernous sinus as well as dural enhancement of the right medial temporal lobe and at the level of the inferior frontal gyrus. Abnormal enhancement was also seen at the cribriform plate,

Departments of Otolaryngology¹ and Pathology,² University of Colorado School of Medicine, Aurora, Colorado

The authors have no conflicts of interest to declare pertaining to this article
Address correspondence and reprint requests to Jeremy D. Prager, M.D., Department of Pediatric Otolaryngology, Children's Hospital Colorado, 13123 E. 16th Avenue B455, Aurora, CO 80045

E-mail address: jeremy.prager@childrenscolorado.org

Published online September 18, 2012

Copyright © 2012, OceanSide Publications, Inc., U.S.A.

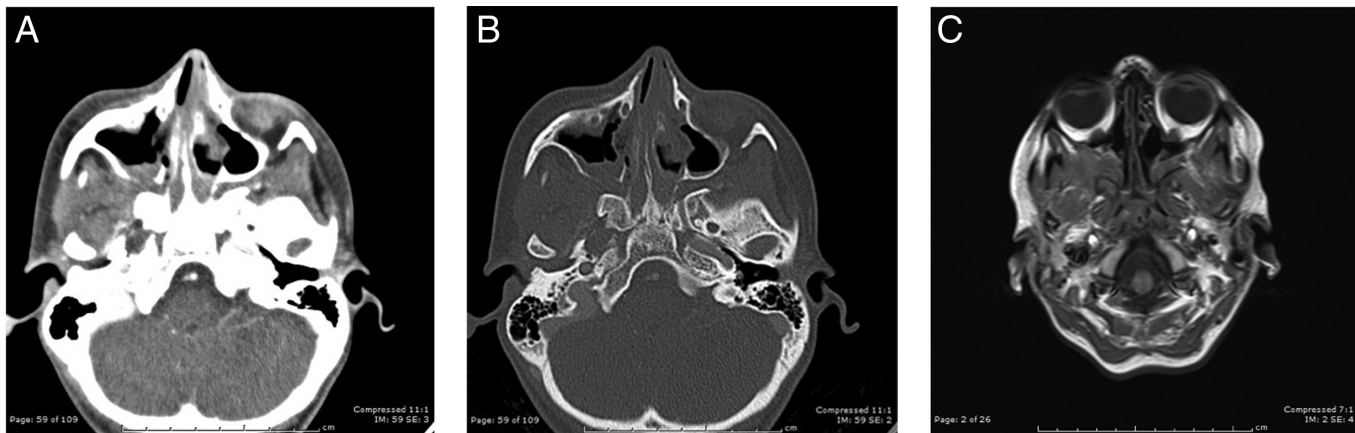


Figure 1. (A) A soft tissue window CT showing a soft tissue mass in the maxillary sinus in addition to a bony defect in the posterior maxillary wall. (B) A bone window CT showing the mass and bone defect in the posterior maxillary wall. (C) A MRI showing a soft tissue intensity extending from the right maxillary sinus into the pterygopalatine fossa and into the orbital apex.

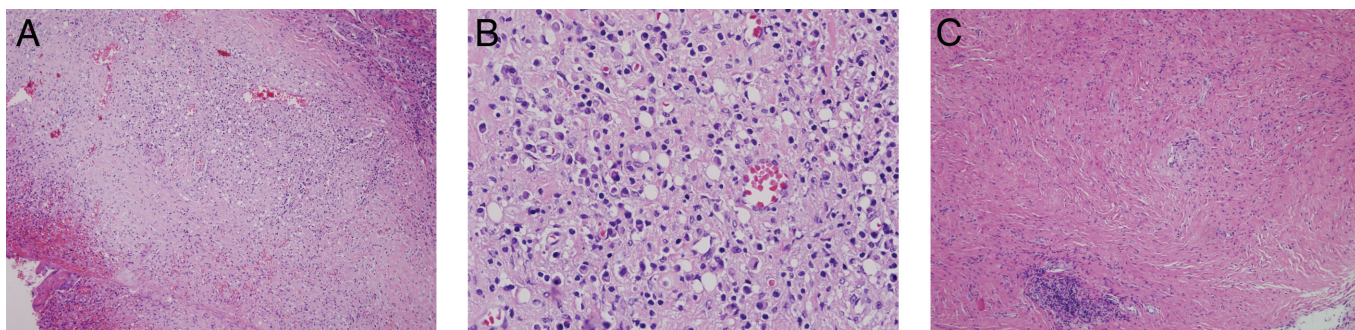


Figure 2. (A) A H&E stain at 25× multiplication, showing focal necrosis and lymphoplasmacytic inflammation. (B) A H&E stain at 100× multiplication, showing the chronic inflammatory component of predominant lymphocytes and plasma cells. (C) A H&E stain at 25× multiplication, showing the tissue was more densely sclerotic with less inflammation.

greater on the right. Otolaryngology and ophthalmology specialists were consulted for further evaluation. The patient was taken to the operating room for endoscopic biopsy of the lesion through the right posterior wall of the maxillary sinus into the pterygopalatine fossa. Pathological evaluation showed no evidence of neoplasm or malignancy, but instead showed fibrosis and lymphoplasmacytic inflammation (Fig. 2 A), as well as focal necrosis and rare neutrophils. There was no evidence of granulomas or infectious organisms. Only rare coagulase-negative *Staphylococcus* species were identified in culture, not considered to be pathogenic.

The patient was given the diagnosis of idiopathic orbital inflammation with extraorbital disease. Her inflammatory markers returned to normal and her Wegener's and sarcoid workup were negative as well. Her pain and vision improved rapidly on high-dose steroids and she was discharged from the hospital on a steroid taper with follow-up arranged with otolaryngology and ophthalmology specialists. Three months after discharge her MRI revealed a decreased lesion size and the patient was doing well off steroids. How-

ever, 3 months later she again developed headache and eye pain. She was restarted on steroids and MRI revealed progression of the lesion with extension through the inferior orbital fissure and soft tissue mass now present in the inferior lateral aspect of the right orbit. Symptoms resolved but the patient was unable to wean from oral steroids. A rheumatology specialist, who had seen the patient while admitted, was reconsulted and based on the inability to wean steroids, orbital involvement, and the pathological findings dominated by chronic fibrotic changes rather than inflammatory infiltrate, the patient's diagnosis was altered to ISOI and her medical therapy was changed. Initially, the lesion showed a fibroinflammatory process with focal necrosis (Fig. 2 A). The chronic inflammatory component included predominant lymphocytes and plasma cells (Fig. 2 B). On follow-up, the tissue was more densely sclerotic with less inflammation, consistent with idiopathic sclerosing inflammation. (Fig. 2 C). Azathioprine (Roxane, Columbus, OH) was initiated and steroid therapy was changed to high-dose (30 mg b.i.d.) oral prednisone and Solu-Medrol (Pfizer, New York, New York) infusions. The

patient has experienced resolution of face pain, headaches, and diplopia and she is currently managed on 3 mg of prednisone and 125 mg of azathioprine daily.

DISCUSSION

ISOI comprises 5–7.8% of all inflammatory lesions that involve the orbit.^{1–3} It typically presents as a more chronic onset process with fewer inflammatory signs at presentation than typical NSOI, but patients with ISOI tend to have more aggressive disease than those with NSOI, as reflected by extraorbital disease and less successful response rate to steroids.^{1,4–6}

Affected patients' signs and symptoms are dictated by the anatomic location of the inflammation. The most common symptoms are orbital pain, diplopia, and blurry vision.¹ Proptosis and extraocular muscle restriction are the most common signs. Anterior disease often shows more of inflammatory signs including eyelid swelling and chemosis and posterior disease may present with optic nerve compromise.^{2,3,7}

The associated inflammation is typically diffuse but does involve at least part of the orbit.³ The lacrimal gland is often involved because it normally contains lymphoid tissue.⁸ Lymphocytes have been studied in this process and are felt to play a crucial role in fibrosis.⁹

ISOI has been studied as a primary fibrosing disorder, similar to retroperitoneal fibrosis based on the marked fibrosis early in the disease course and similarity of cell populations.^{3,10,11} The histological picture shows significant fibrosis associated with a sparse mixed chronic inflammatory cell infiltrate.

The mean duration of disease before biopsy has been found to be 18–24 months,^{1,3} which leads one to consider the diagnosis of chronic NSOI. This presentation can be frustrating when determining a diagnosis but the treatment plan should not change. The severity of disease is what dictates management because posterior orbital disease may lack inflammatory signs but have extensive disease.¹

The majority of previous studies are case reports or small case series. Hsuan *et al.* studied this process in 31 patients and found prednisolone to have a more than partial response in 35% of patients; however, they did note improved results in patients with a shorter duration of disease. The duration of symptoms in patients after starting treatment was been found to range from 14 to 90 weeks.¹

Corticosteroids have a moderate role in treatment success and are the recommended as first line treatment because they have a broad immunosuppressive effect and are more successful if given early in the disease process. Immunosuppression needs to be maintained for the duration of active disease. Steroid-sparing immunosuppressive treatments have been at-

tempted including azathioprine with some success, as some patients will have an initial response to corticosteroids followed by recurrence of disease.^{3,12,13} Azathioprine, in addition to other agents, can help in the long-term control of disease with sparing or reduction in corticosteroid use. Hsuan *et al.* concluded that when corticosteroids have been ineffective, other immunosuppressants or radiotherapy have also been ineffective.¹ Cruz *et al.* studied ISOI in the orbit and nearby structures with successful treatment including radiotherapy.¹⁴

Our case shows a rare presentation as sinusitis with facial pain and pressure and nasal congestion, followed by rapid vision loss. Based on a search of the American literature,^{15–20} this is a rare presentation and should help alert clinicians to be mindful of ISOI with an abnormal sinusitis presentation. To date, there is still little known as to what causes this disease to affect patients or what causes it to become inactive.^{15,16,20} This disease process should be further studied including randomized and clinical trials to help increase information on its pathogenesis and resolution. Although there is an overall lack of information regarding the details of this process,^{17,18} we recommend high-dose corticosteroids in addition to azathioprine to help control the disease process by immunosuppression.

CONCLUSION

ISOI is considered by some a rare pathological subgroup of idiopathic NSOI. Extraorbital disease or presentation as sinusitis is even rarer. It is a clinical entity characterized in the majority of patients by chronic pain and vision changes as well as signs of orbital involvement. Pathologically, the lesion is characterized by fibrosis with sparse mixed chronic inflammatory cellular infiltrate. Successful treatment consists of early recognition of associated signs and symptoms and biopsy for pathological diagnosis. As indicated by our patient, immunosuppression consisting of corticosteroids and consideration of corticosteroid-sparing agents may control the disease.

REFERENCES

1. Hsuan JD, Selva D, McNab AA, et al. Idiopathic sclerosing orbital inflammation. *Arch Ophthalmol* 124:1244–1250, 2006.
2. Rootman J. Inflammatory diseases. In *Diseases of the Orbit: A Multidisciplinary Approach*, 2nd ed. Rootman J (Ed). Philadelphia, PA: Lippincott Williams & Wilkins, 455–506, 2003.
3. Rootman J, McCarthy M, White V, et al. Idiopathic sclerosing inflammation of the orbit: A distinct clinicopathologic entity. *Ophthalmology* 101:570–584, 1994.
4. Blodi FC, and Gass JDM. Inflammatory pseudotumor of the orbit. *Trans Am Acad Ophthalmol Otolaryngol* 71:303–322, 1967.
5. Kaye AH, Hahn JF, Craciun A, et al. Intracranial extension of inflammatory pseudotumor of the orbit. *J Neurosurg* 60:625–629, 1984.

6. Weissler MC, Miller E, and Fortune MA. Sclerosing orbital pseudotumor: A unique clinicopathologic entity. *Ann Otol Rhinol Laryngol* 98:496–501, 1989.
7. Fujii H, Fujisada H, Kondo T, et al. Orbital pseudotumor: Histopathological classification and treatment. *Ophthalmologica* 190:230–242, 1985.
8. Garner A. Orbital lymphoproliferative disorders. *Br J Ophthalmol* 76:47–48, 1992.
9. Charles NC, and Turbin RE. Bilateral sclerosing orbital pseudotumor with intracranial spread. *Arch Ophthalmol* 121:412–413, 2003.
10. McCarthy JM, White VA, Harris G, et al. Idiopathic sclerosing inflammation of the orbit: Immunohistologic analysis and comparison with retroperitoneal fibrosis. *Mod Pathol* 6:581–587, 1993.
11. Abramovitz JN, Kasdon DL, Sutula F, et al. Sclerosing orbital pseudotumor. *Neurosurgery* 12:463–468, 1983.
12. Kennerdell JS. The management of sclerosing nonspecific orbital inflammation. *Ophthalmic Surg* 22:512–518, 1991.
13. Levine MR, Kaye L, Mair S, and Bates J. Multifocal fibrosclerosis: Report of a case of bilateral idiopathic sclerosing pseudotumor and retroperitoneal fibrosis. *Arch Ophthalmol* 111:841–843, 1993.
14. Cruz AA, Akaishi PM, Chahud F, and Elias JJ. Sclerosing inflammation in the orbit and in the pterygopalatine and infratemporal fossae. *Ophthal Plast Reconstr Surg* 19:201–206, 2003.
15. Cervellini P, Volpin L, Curri D, et al. Sclerosing orbital pseudotumor. *Ophthalmologica* 193:39–44, 1986.
16. Frohman LP, Kupersmith MJ, Lang J, et al. Intracranial extension and bone destruction in orbital pseudotumor. *Arch Ophthalmol* 104:380–384, 1986.
17. Garner A. Pathology of “pseudotumours” of the orbit: A review. *J Clin Pathol* 26:639–648, 1973.
18. Mombaerts I, Schlingemann RO, Goldschmeding R, and Koornneef L. Are systemic corticosteroids useful in the management of orbital pseudotumors? *Ophthalmology* 103:521–528, 1996.
19. Noble SC, Chandler WF, and Lloyd RV. Intracranial extension of orbital pseudotumor: A case report. *Neurosurgery* 18:798–801, 1986.
20. Richards AB, Skalka HW, Roberts FJ, and Flint A. Pseudotumor of the orbit and retroperitoneal fibrosis: A form of multifocal fibrosclerosis. *Arch Ophthalmol* 98:1617–1620, 1980. □