JAMA Ophthalmology Clinical Challenge

Older Woman With Proptosis, Ptosis, and Blurred Vision

Alison B. Gibbons, BS; Charles Eberhart, MD, PhD; Emily Li, MD

Figure 1. Axial (A) and coronal (B) T1 fat-suppressed postcontrast magnetic resonance imaging (MRI) demonstrating abnormal enhancing soft tissue with right greater than left involvement of intraconal (yellow-outlined asterisks) and extraconal (white-outlined asterisks) orbital fat and posterior extraocular muscles. The enhancement encases the optic nerves and extends to the cavernous sinus. There is abnormal dural enhancement in the right middle cranial fossa and the right sphenoid wing (arrowhead).

A Black woman in her early 70s with a history of coronary artery disease after coronary artery bypass operations, hypertension, and colon polyps presented to oculoplastic surgery with 1 week of progressive right-sided proptosis and headache, described as severe pain radiating to the back of her head. This was associated with right eyelid ptosis and blurry vision. Prior to presentation, an outside ophthalmologist treated her with 1 week of oral prednisone, 20 mg/d, for presumed orbital inflammation with no improvement. She denied additional symptoms. Notably, she described headache and sudden vision loss in the right eye after coronary artery bypass grafting 1 year ago for several days before spontaneous improvement with incomplete resolution. Personal and family histories were negative for malignant neoplasm and autoimmune disease.

Examination revealed right-sided uncorrected Snellen visual acuity of 20/60 associated with restricted supraduction, abduction, and infraduction. Pupils were equal in size without a relative afferent pupillary defect, and intraocular pressures were 10 mm Hg OD and 11 mm Hg OS. Visual fields had temporal restriction to confrontation of the right eye. Vision, motility, and visual fields were normal on the left. Pertinent findings included right-sided proptosis of 2 mm, cranial nerve V1 and V2 hypoesthesia, eyelid ptosis with a margin to reflex distance 1 of 0 mm, optic disc pallor, and vessel attenuation. Outside magnetic resonance imaging (MRI) demonstrated an infiltrative mass involving right greater than left orbital apices, the right optic nerve, and right extraocular muscles. There was enhancement of the cavernous sinuses, right pterygopalatine fossa, right sphenoid wing, and right middle cranial fossa dura (**Figure 1**).

WHAT WOULD YOU DO NEXT?

A. Restart corticosteroids at a higher dose

B. Refer to the neurosurgery department for cranio-orbito-zygomatic craniotomy

C. Perform urgent orbital exploration and biopsy

D. Order urgent radiotherapy

CME Quiz at jamacmelookup.com

Diagnosis

Neurosarcoidosis

What to Do Next

C. Perform urgent orbital exploration and biopsy

Discussion

The differential diagnosis for proptosis with motility restriction in adults includes neoplasms, infectious and noninfectious orbital inflammation, trauma, and vascular abnormalities. The most common cause is thyroid eye disease, associated with eyelid retraction (90% of cases), exophthalmos (60%), and motility restrictions (40%).[1] Orbital inflammatory conditions typically present with pain, soft tissue edema, and steroid response.[2] The patient had no history of orbital inflammatory disease to warrant restarting corticosteroids (choice A) without workup, especially in the setting of an infiltrative orbital mass with intracranial involvement.

A new orbital mass in an older adult warrants investigation to rule out a malignant neoplasm, including lymphoproliferative disease, melanoma, and metastases.[2] MRI demonstrated an enhanc-

ing infiltrative lesion predominantly involving the right orbit, cavernous sinuses, right sphenoid wing, and right middle cranial fossa dura. Common spheno-orbital lesions include meningiomas and metastases; an enhancing dural tail on MRI is a classic feature of meningioma.[3] Meningioma management consists of microsurgery, radiosurgery, and radiotherapy (choice D) after tissue diagnosis.[4] In this case, orbital exploration and biopsy (choice C) would obtain tissue with less morbidity and surgical risk than craniotomy. Neurosurgery (choice B) would be indicated for management of a biopsy-proven tumor.

Biopsy revealed noncaseating granulomas, chronic inflammation with no fungi or acid-fast organisms, and rare immunoglobulin G4–positive cells (**Figure 2**). Serology was negative for granulomatous disease; radiography was negative for hilar lymphadenopathy. Neurosarcoidosis was diagnosed based on the presence of noncaseating granulomas on tissue biopsy and negative workup for other granulomatous disease. The patient began oral prednisone, 40 mg/d, which alleviated her symptoms, and she established care with the sarcoidosis clinic for evaluation and surveillance.

Sarcoidosis, an immune-mediated condition characterized by noncaseating granulomas in various organs, presents at a mean age of 48 years and incidence of 35.5 cases per 100 000 Black individuals and 10.9 cases per 100 000 White individuals in the US.[5] Diagnosis is made through (1) demonstration of noncaseating granulomas on tissue and exclusion of other disease or (2) presentation as a pathognomonic syndrome, such as Lofgren syndrome, lupus pernio, or Heerfordt syndrome.[6]

Ophthalmic involvement, the first clinical sign in 20% to 30% of cases, usually presents with anterior uveitis, keratoconjunctivitis, or sicca syndrome.[7] Uveoparotid fever, or Heerfordt syndrome, manifests with facial palsy, parotid gland enlargement, uveitis, and fever.[6,7] Neurosarcoidosis affects 3% to 10% of cases, of which 84% to 94% have additional systemic involvement.[6] Isolated neurosarcoidosis and simultaneous orbital and intracranial involvement are rare features of this case. Of 11 cases of cavernous sinus involvement reported, only 2 had concurrent orbital inflammation.[8,9]

Initial treatment typically consists of oral prednisone, 0.25 to 1 mg/kg/d. This patient's initial dose of 20 mg/d was subtherapeutic given her weight (97.5 kg). Many cases require additional agents, and severe cases may require prolonged immunosuppression.[10] Visual prognosis is favorable with treatment.[7]

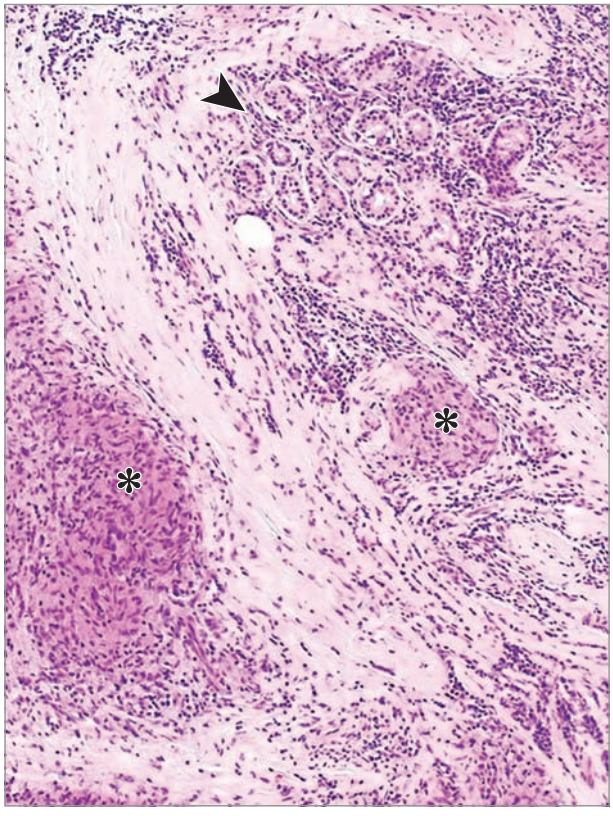

Figure 2. Lymphoplasmacytic inflammation involving lacrimal gland (arrowhead) and stroma, along with scattered noncaseating granulomas (asterisks) (hematoxylin-eosin, original magnification ×100).

Patient Outcome

At 4-month follow-up after completing a prednisone taper, the patient's headaches had resolved. Examination revealed visual acuity of 20/60 OD, improved motility deficits, full visual field, and resolution of proptosis with symmetric ophthalmometric measurements. She remained stable without corticosteroids at 6-month follow-up.

ARTICLE INFORMATION

Author Affiliations: Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, Maryland (Gibbons, Eberhart, Li); Department of Pathology, Johns Hopkins Hospital, Baltimore, Maryland (Eberhart).

Corresponding Author: Emily Li, MD, Wilmer Eye Institute, Johns Hopkins School of Medicine, 600 N Wolfe St, Maumenee 5, Baltimore, MD 21287 (eli20@jhmi.edu).

Published Online: January 25, 2024. doi:10.1001/jamaophthalmol.2023.6035

Conflict of Interest Disclosures: None reported.

Additional Contributions: We thank the patient for granting permission to publish this information.

REFERENCES

1. McAlinden C. An overview of thyroid eye disease. *Eye Vis (Lond)*. 2014;1:9. doi:10.1186/s40662-014-0009-8

2. Topilow NJ, Tran AQ, Koo EB, Alabiad CR. Etiologies of proptosis. *Intern Med Rev (Wash D C)*. 2020;6(3). doi:10.18103/imr.v6i3.852

3. McNab AA, Jones RS, Hardy TG. Spheno-orbital lesions. *Ophthalmic Plast Reconstr Surg*. 2021;37(6):522-533. doi:10.1097/IOP.0000000000001924

4. Magill ST, Vagefi MR, Ehsan MU, McDermott MW. Sphenoid wing meningiomas. In: McDermott MW, ed. *Handbook of Clinical Neurology*. Vol 170. Elsevier; 2020:37-43. doi:10.1016/B978-0-12-822198-3.00026-4

5. Llanos O, Hamzeh N. Sarcoidosis. *Med Clin North Am*. 2019;103(3):527-534. doi:10.1016/j.mcna.2018.12.011

6. Sève P, Pacheco Y, Durupt F, et al. Sarcoidosis. *Cells*. 2021;10(4):766. doi:10.3390/cells10040766

7. Pasadhika S, Rosenbaum JT. Ocular sarcoidosis. *Clin Chest Med*. 2015;36(4):669-683. doi:10.1016/j.ccm.2015.08.009

8. Barbosa NT, Gomes BCR, Cagy M, Spitz M, Ferreira ACAF. Orbital apex syndrome associated with diffuse hypertrophic pachymeningitis in isolated neurosarcoidosis. *Arq Neuropsiquiatr*. 2021;79(8):754-755. doi:10.1590/0004-282x-anp-2020-0395

9. Rajasingham J, Souayah N. Neurosarcoidosis revealed by isolated abducens nerve palsy. *Neurology*. 2012;78(suppl 1):P07.154.

10. Bradshaw MJ, Pawate S, Koth LL, Cho TA, Gelfand JM. Neurosarcoidosis. *Neurol Neuroimmunol Neuroinflamm*. 2021;8(6):e1084. doi:10.1212/NXI.0000000000001084