

## ISOLATED OPTIC NERVE SARCOIDOSIS

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**ABSTRACT.** *Objective:* To report three cases of sarcoidosis confined to the optic nerve. *Methods:* Chart review of clinical, laboratory, imaging, and optic nerve biopsy findings and a review of the literature. *Results:* All three cases presented with progressive visual loss and showed enhancement of the intraorbital optic nerve on magnetic resonance imaging. There was no evidence for systemic disease, including a negative workup for sarcoidosis or other infiltrative pathologies. Optic nerve biopsy in each case showed non-caseating granulomas consistent with sarcoidosis. *Conclusions:* Sarcoidosis confined to the optic nerve is a rare phenomenon but should still be considered in the differential diagnosis of progressive optic neuropathy, even in the absence of systemic disease. (*Sarcoidosis Vasc Diffuse Lung Dis* 2017; 34: 179-183)

**KEY WORDS:** sarcoidosis, optic nerve, optic neuritis, optic neuropathy

### INTRODUCTION

Sarcoidosis is an idiopathic, systemic inflammatory disease histologically characterized by non-caseating epithelioid-cell granulomas (1). The lungs and mediastinal lymph nodes are the most frequently affected organs, with thoracic findings seen in greater than 90% of cases (2). Eye complications are also a common comorbidity in sarcoidosis, occurring in 30 to 60% of patients with approximately 1.5-12.4% of patients presenting initially with ocular symptoms. (3) Though uveitis is the most common ocular in-

flammatory response in sarcoidosis (2, 4, 5) involvement of the optic nerve occurs in about 1-5% of sarcoid patients (6). Isolated involvement of the optic nerve without any other signs of central nervous system involvement or systemic disease is an atypical phenomenon (6-8). Here we present a series of patients with sarcoidosis confirmed by optic nerve biopsy with no evidence for systemic disease.

### CASE 1

A 37-year-old African American woman presented with a three-week history of vision loss and soreness in the right eye (OD). Five months prior she had experienced an episode of self-resolving painless vision loss OD, which was attributed to optic neuritis. On exam, her visual acuity was now counting fingers OD with a sluggish pupillary response and a 3+ afferent pupillary defect. Visual acuity and pupillary response were normal in the left eye (OS). Examination

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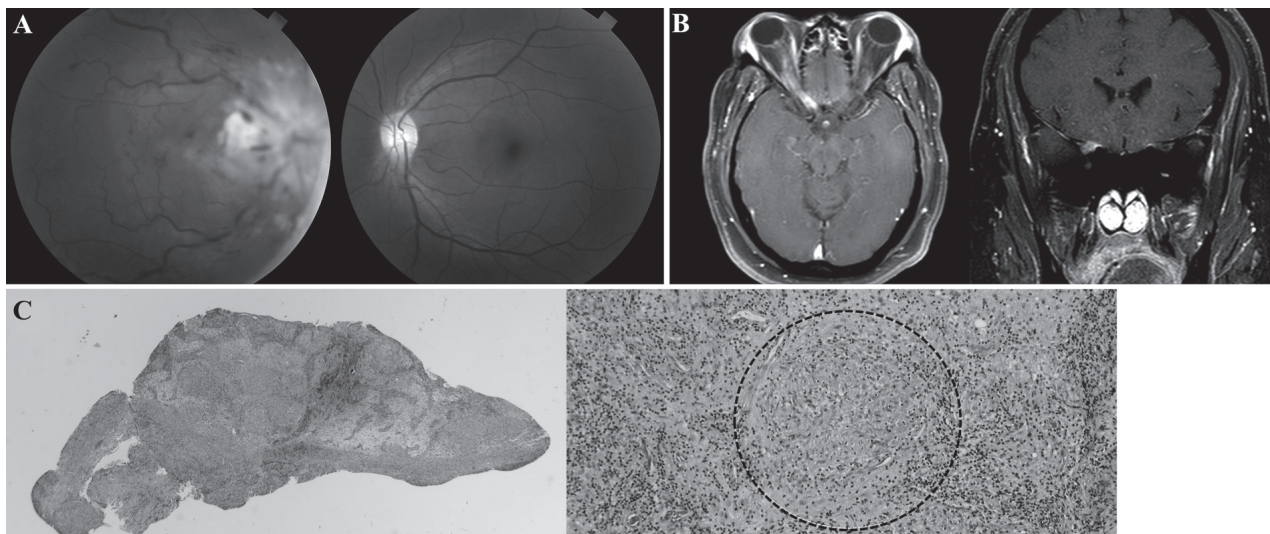
revealed severe disc edema in the right eye extending into the macula and accompanied by hemorrhages around the disc and within the macula (Figure 1). Examination of the left eye was unremarkable. Serum angiotensin converting enzyme (ACE), antinuclear antibody (ANA), lyme and bartonella titers, IgG4 antibodies, anti-neutrophil cytoplasmic antibody (ANCA), Quantiferon gold, anti-Ro/anti-La antibodies, and aquaporin-4 antibody were all negative and chest x-ray showed no hilar lymphadenopathy. An MRI of the brain and orbits showed enhancement of the right optic nerve with edema extending to the optic chiasm but did not involve it (Figure 1). Lumbar puncture showed slightly elevated opening pressure at 27 cmHg, but no oligoclonal bands, and negative gram stain and cytology.

Repeat examination a few weeks later revealed deterioration of vision to no light perception (NLP) and new 3+ inflammatory cells in the vitreous. She was given 1000 mg IV methylprednisolone for 3 days with resolution of vitreous cells but no recovery of vision one month later. Follow up MRI showed improvement but incomplete resolution of the right optic nerve enhancement. She was continued on a slow taper of prednisone but experienced worsening pain and recurrent vitreous cell upon discontinuation of steroids.

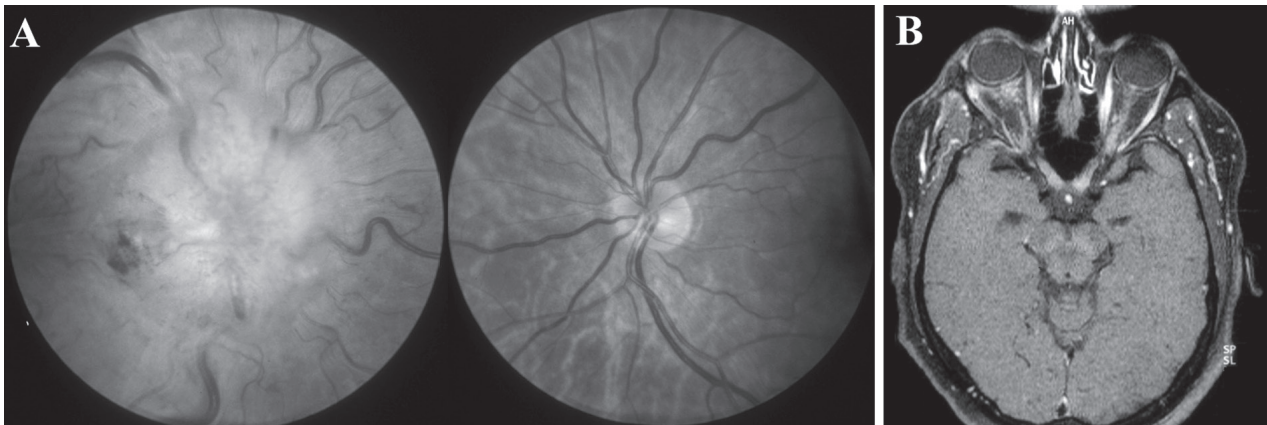
Given the poor visual recovery and ongoing discomfort, biopsy of the optic nerve was undertaken. Histology revealed multiple well-formed non-caseating granulomas (Figure 1) and stains for acid fast bacilli and fungus were negative. No neoplastic features or malignant cells were noted. She was diagnosed with sarcoid optic neuritis and started on azathioprine and prednisone. The prednisone was tapered over several months and she has remained relapse free for 2.5 years. However, she developed uncontrolled neovascular glaucoma eventually necessitating evisceration of the eye.

## CASE 2

A 38-year-old Caucasian man presented with several months of painless vision loss OD. Exam revealed best corrected visual acuity of 20/60 OD and a 2+ relative afferent pupillary defect. Visual fields showed enlargement of the blindspot OS. The right optic nerve was swollen and hemorrhages were seen around the optic disc and macula (Figure 2). There was no uveitis. Ultrasound showed thickening of the optic nerve. Brain and orbit MRI demonstrated enhancement of the right optic nerve extending up to but not including the chiasm (Figure 2). Systemic



**Fig. 1.** [Case 1]: A) Fundus photographs show severe disc edema extending into the macula in the right eye. Hemorrhages around the disc and within the macula are also visible. The left eye is normal. B) Contrast enhanced T1-weighted brain and orbit MRI. Axial section shows enhancement of the intraorbital right optic nerve with edema extending to the optic chiasm. Coronal view shows involvement of the right optic nerve without lesions in the brain parenchyma or meninges. C) Haematoxylin and eosin stain of optic nerve biopsy specimen. Low power view shows numerous well-formed non-caseating granulomas consistent with sarcoidosis. High power view of non-caseating granulomas



**Fig. 2.** [Case 2]: A) Fundus photographs show severe swelling of the disc with surrounding hemorrhage. The left eye is normal. B) Contrast enhanced axial T1-weighted brain and orbit MRI. Intense enhancement of the right intraorbital right optic nerve can be seen in conjunction with partial enhancement of the left intraorbital optic nerve

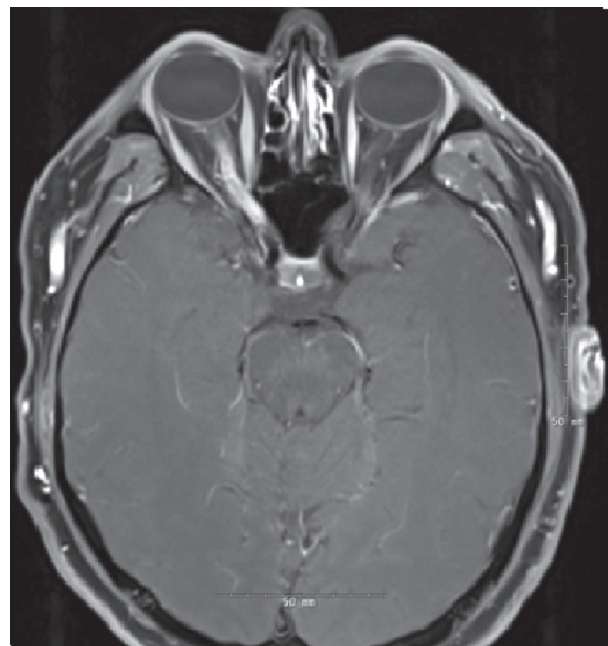
workup including ACE, lysozyme, energy response, lyme titers, rapid plasma reagin, ANA, ANCA and chest x-ray were normal. He was initially treated with prednisone 60 mg/day and increased to IV methylprednisolone 500 mg QID for three days, but continued to lose vision to NLP. Repeat MRI showed intense enhancement of the right optic nerve extending up to the chiasm. Extirpation of the intraorbital right optic nerve from a medial approach showed non-caseating epithelioid-cell granulomas with perivascular infiltrates. He was started on dexamethasone 1 mg QID post-operatively which led to normalization of his visual field OS, return to 20/15 acuity OS, and resolution of his disc edema. The patient was lost to follow up after several months.

### Case 3

A 34-year-old man presented with one year of progressive painless vision loss OD. He had been previously diagnosed with optic atrophy based on MRI findings and intermittently placed on prednisone 80-100 mg and methotrexate. His vision initially improved but then proceeded to decline over the course of the year. Neurological and pulmonary evaluations were not indicative of multiple sclerosis or sarcoidosis.

Visual acuity was now NLP OD and 20/20 -1 OS with an afferent pupillary defect present OD. No retinal abnormalities were seen but 3+ optic atrophy and a cup to disc ratio of 0.3 were noted. There was

no uveitis. MRI of the brain and orbits showed enhancement of the right optic nerve from the orbit up to the chiasm (Figure 3). Biopsy of the optic nerve showed chronic inflammation with benign appearing lymphocytes and non-necrotizing granulomas. No evidence of neoplasm or microorganisms was seen. The patient was lost to follow up.



**Fig. 3.** [Case 3]: Contrast enhanced axial T1-weighted MRI of head and orbit. Isolated enhancement of the right optic nerve is visible beginning in the posterior orbit and extending to the intracranial portion

## DISCUSSION

In this series we present three cases of biopsy-proven sarcoidosis exclusively confined to the optic nerve. Vision loss due to sarcoid involvement of the anterior visual pathway can be explained by intrinsic granulomatous infiltration, extrinsic compression, or intracranial hypertension involving the optic nerve, optic tracts, or the chiasm (9, 10). As seen in our cases, inflammation of the intraorbital optic nerve is significantly less common than intraocular or chiasmal involvement (6, 7, 10, 11). Typically, intraorbital involvement occurs in more widespread neurosarcoidosis affecting the hypothalamus or central nervous system (6).

The most common MRI findings in neurosarcoidosis are leptomeningeal involvement, occurring in about 40% of neurosarcoid patients, and intraparenchymal mass lesions seen in about 35% of cases (12). Of the cranial nerves, the optic nerve is most likely to show MRI abnormalities in neurosarcoidosis, though facial nerve involvement is more clinically prevalent (13). Carmody et al. described MRI findings in a series of 15 patients with orbital and optic pathway sarcoidosis. Of these, only three had intraorbital nerve involvement whereas nine had chiasmal enlargement or enhancement, and all displayed imaging findings of sarcoid involvement outside the visual pathway (14). Unique to our cases is the demonstration of intraorbital nerve infiltration without any MRI findings of neurosarcoid involvement elsewhere in the CNS.

Isolated involvement of the optic nerve without systemic signs often makes it exceedingly difficult to establish a diagnosis, as sarcoidosis can mimic the clinical and radiological findings of other entities, particularly optic nerve meningiomas or gliomas (7, 11, 14-16). In a literature review of biopsy-proven optic nerve sarcoidosis, Ing et al. found that 14 out of 18 published cases were presumed to be either gliomas or meningiomas pre-operatively (11). However, the differential for a progressive optic neuropathy is broad, including tumors (metastasis, glioma, lymphoma, meningioma, schwannoma, hemangioma, multiple myeloma), infections (tuberculosis, Lyme disease, syphilis, HIV, cat-scratch disease, *Aspergillus*), demyelinating disorders (multiple sclerosis, neuromyelitis optica), inflammatory disorders (sarcoidosis, arteritic ischemic optic neuropathy, system-

ic lupus erythematosus, Behcet's disease, Sjogren's syndrome, Wegner's, inflammatory bowel disease, and orbital pseudotumor) (17,18). Other etiologies of optic neuropathy to consider include compressive, traumatic, ischemic, toxic-nutritional (ethambutol, amiodarone, methanol, ethanol, and tobacco) and hereditary (Leber's hereditary optic neuropathy, autosomal dominant optic atrophy) (18). The presence of non-caseating with negative stains for fungus and mycobacteria on biopsy is most consistent with sarcoidosis.

Due to the absence of involvement in other tissues, biopsy of the optic nerve was necessary to characterize the progressive optic neuropathy in each case. Although the cases herein all experienced total vision loss prior to surgery, partial thickness optic nerve biopsy deserves consideration in eyes with residual vision. Roberti et al. described a case of isolated optic nerve sarcoidosis with negative systemic workup confirmed using a "shave" biopsy of the intracranial optic nerve that preserved the patient's central vision (19). Khong et al. also presented a case of sarcoidosis affecting the intraorbital nerve that was biopsied using a medial transconjunctival approach which preserved post-operative vision (20). Such vision sparing approaches to optic nerve biopsy should be duly considered in order to preserve the opportunity for recovery.

In addition to the lack of laboratory or clinical features typical of sarcoidosis, the preoperative diagnosis was further obfuscated by the nonresponsiveness to empiric corticosteroid therapy. In cases where clinical suspicion for sarcoidosis is sufficiently high without overt signs of organ involvement elsewhere, chest CT scans or PET scan can be helpful in identifying thoracic findings not visible on chest X-ray and could provide an alternative biopsy site if lymphadenopathy is identified (21).

## CONCLUSION

Sarcoidosis can initially present as isolated involvement of the intraorbital optic nerve and should remain on the differential for a progressive optic neuropathy, even in cases not responsive to steroids. In such instances, optic nerve biopsy may be the only modality able to establish a diagnosis of sarcoidosis.

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