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An unusual presentation of neurosarcoidosis: Concurrent optic perineuritis and optic neuritis

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Abstract:

Neurosarcoidosis is a rare complication of sarcoidosis and typically presents as acute cranial neuropathies. Neurosarcoidosis can rarely cause an inflammatory optic neuropathy, resembles an optic neuritis and even more rarely can cause an optic perineuritis. Although concomitant optic neuritis and optic perineuritis have been reported in other inflammatory conditions, such as myelin oligodendrocyte antibody-associated disease, spatially-distinct optic neuritis, and optic perineuritis has not been previously described in neurosarcoidosis. Here, we present a case of spatially-distinct concomitant optic neuritis and optic perineuritis from neurosarcoidosis in a 51-year-old man initially suspected to harbor metastatic disease based on imaging findings.

Keywords:

Neurosarcoidosis, optic perineuritis, optic neuritis, sarcoid

Introduction

Sarcoidosis is a systemic granulomatous disease with a reported overall incidence of approximately 11 per 100,000 people;^[1] the incidence of sarcoidosis in Asians and Taiwanese is less than the overall incidence, with a reported incidence of 3.2 per 100,000 in Asians and 2.17 per 100,000 in Taiwanese.^[2,3] Neurosarcoidosis, a rare complication of sarcoidosis, occurs in approximately 5% of patients with sarcoidosis and can affect the central or peripheral nervous systems. Although acute cranial neuropathies^[4-6] are the most common presentation of neurosarcoidosis, occurring in up to 74% of confirmed cases,^[7] involvement of the optic nerve is rare. Indeed, a subacute inflammatory optic neuropathy, the presentation of which resembles other causes of optic neuritis, has been reported in only 1%–5% of patients with neurosarcoidosis and is seldom the

initial clinical manifestation.^[8,9] Optic perineuritis is an even rarer manifestation of neurosarcoidosis, with few cases reported in the literature.^[10-12] We report a unique case of neurosarcoidosis presenting as unilateral optic neuritis and optic perineuritis, combined with bilateral lower extremity weakness, initially suspected to harbor metastatic disease based on neuro-imaging findings.

Case Report

A 51-year-old man with a past medical history of fibromyalgia and chronic low back pain was transferred from an outside hospital to our institution for evaluation of 6 months of painless blurred vision in the right eye and bilateral lower extremity weakness which progressed from decreased sensation and pain at onset to weakness and gait instability. He denied progressive worsening of the vision in his right eye over the prior 6 months, however he reported that his bilateral lower extremity weakness

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acutely worsened over the 3 days before admission. He denied skin rashes, facial swelling, fever, or a chronic cough. He denied a personal or family history of sarcoidosis, multiple sclerosis, or other neurological diseases.

Neuro-ophthalmologic examination showed decreased visual acuity (20/160) in his right eye, a right relative afferent pupillary defect and significant disc edema with vessel obscuration and disc hemorrhages in his right eye [Figure 1]; the visual function and examination of his left eye were unremarkable. There were no ocular examination findings to specifically suggest sarcoidosis, such as conjunctivitis, keratoprecipitates, uveitis, or vascular sheathing in either eye. Humphrey visual field testing showed complete visual field suppression in his right eye. Spectral-domain optical coherence tomography showed significant disc edema and diffuse ganglion cell complex thinning of his right eye.

Serologic testing demonstrated an elevated C-reactive protein. Serum calcium, erythrocyte sedimentation rate, angiotensin-converting enzyme, HIV testing, QuantiFERON gold, rheumatoid factor, antinuclear antibody, anti-neutrophil cytoplasmic antibody, centromere antibody, anti-Smith antibody, Scl70 antibody, anti-Ro antibody, anti-La antibody, cyclic citrullinated peptide antibody, and NMO/AQP4 antibody titers were all normal or negative. Sputum cultures were negative for acid-fast bacilli (AFB).

Spine magnetic resonance imaging (MRI) showed multiple enhancing intramedullary and spinal cord surface lesions with extensive involvement of the cauda equina. Brain and orbital MRI showed eight small dural and cortical-based supra- and infratentorial enhancing nodular lesions [Figure 2]; enhancement of the optic nerve sheath surrounding the orbital segment of the right optic nerve, suggestive of optic perineuritis; and mild abnormal intrinsic enhancement within the right optic nerve [Figure 3]. The largest intracranial lesion measured 10 mm × 6 mm and was located along the superior left tentorial leaflet. The dural- and cortical-based enhancing nodular lesions on his brain MRI, as well as the multiple enhancing spinal cord lesions on the spine MRI, were concerning for metastatic disease.

Because of concern for a metastatic process, a thorough workup to identify a primary malignancy was performed. Lumbar puncture showed a slightly elevated opening pressure (27 cm H₂O). Cerebrospinal fluid (CSF) studies showed an elevated protein (200 mg/dL) and a lymphocytic pleocytosis (58 cells/μl; 90% lymphocytes, 6% neutrophils, and 4% macrophages), with numerous small lymphocytes on cytology. CSF glucose was normal (58 mg/dL). CSF bacterial, viral, and fungal

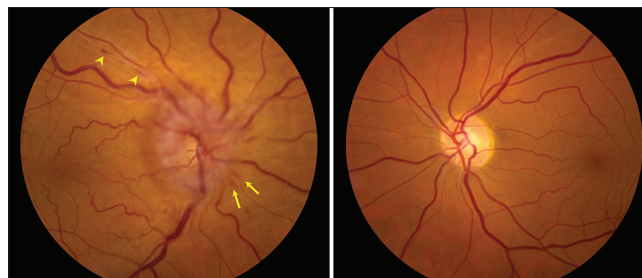


Figure 1: Left: Color fundus photograph of the right eye showing diffuse optic disc edema, vessel obscuration, disc hemorrhages (arrows), and small flame-shaped retinal hemorrhages (arrowheads). Right: Color fundus photograph of the left eye showing a normal-appearing optic nerve and posterior pole

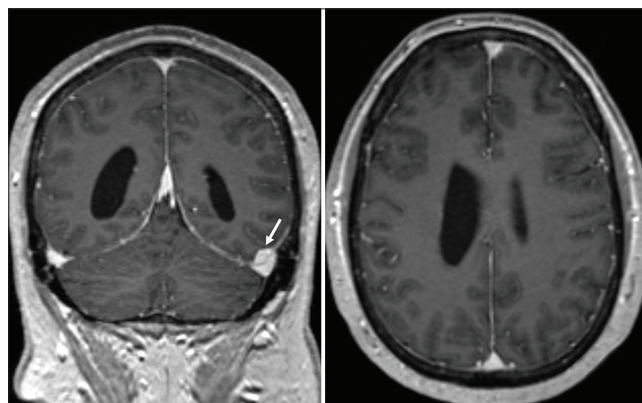


Figure 2: Left, Coronal MPRAGE T1 image of the dural-based mass (arrow) along the superior left tentorial leaflet, measuring 10 x 6 mm. Right, transverse MPRAGE T1 image of the dural-based enhancing lesion (arrow) along the left paramedian falx, measuring 6 mm x 5 mm

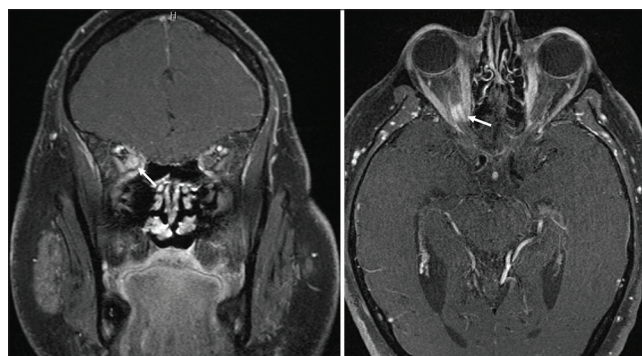


Figure 3: Left, coronal T1 postcontrast imaging showing right optic nerve sheath enhancement surrounding the orbital segment of the optic nerve, with mild optic nerve enhancement (arrow). Right, axial T1 postcontrast imaging demonstrating right optic nerve sheath enhancement and the "tram-track" sign (arrow)

cultures were negative. Computerized tomography of the chest, abdomen, and pelvis demonstrated a 2 mm subpleural pulmonary nodule; prominent indeterminate mediastinal and hilar lymph nodes felt to be reactive inflammatory lymph nodes; and mild acute diverticulitis; however, an underlying mass could not be ruled out. Esophagogastroduodenoscopy and colonoscopy showed duodenitis and colon polyps; there was no evidence of an occult gastrointestinal malignancy. Subcarinal lymph

node fine needle aspiration obtained by bronchoscopy showed nonnecrotizing granulomatous inflammation with negative AFB and Grocott's Methenamine Silver stains for mycobacteria and fungal organisms, respectively, most compatible with sarcoidosis [Figure 4]; there were no abnormal B- or T-cell populations suggestive of lymphoma by flow cytometry analysis.

He was treated with a course of high dose intravenous solumedrol (250 mg every 6 h) for 5 days with marked improvement of the vision in his right eye. At his follow-up appointment, approximately 4 months after being discharged from the hospital, the visual acuity and visual field in his right eye had improved; the visual acuity in his right eye was 20/40, and he had a superior visual field defect [Figure 5]. The edema of his right optic nerve resolved, with subsequent development of optic atrophy [Figure 5].

Discussion

Optic perineuritis is an extremely rare manifestation of sarcoidosis. While the definition of optic perineuritis has changed over time, it is now commonly described as an orbital inflammatory disease that targets the optic nerve sheath, occurring idiopathically in the majority of cases or secondary to a systemic disorder.^[13] Optic perineuritis is most often associated with giant cell arteritis, Crohn's disease, granulomatosis with polyangiitis, myelin oligodendrocyte glycoprotein (MOG) antibody-associated disease, and Behçet's disease.^[13-15] Prompt corticosteroid treatment usually leads to a dramatic improvement in vision, but there have been cases of spontaneous recovery.^[13,16]

Our case is unusual as our patient exhibited concurrent optic perineuritis and intrinsic optic neuritis found in spatially-distinct regions of the same optic nerve. Although this has been reported in other forms of inflammatory optic neuropathies, such as MOG antibody-associated disease, spatially-distinct concurrent

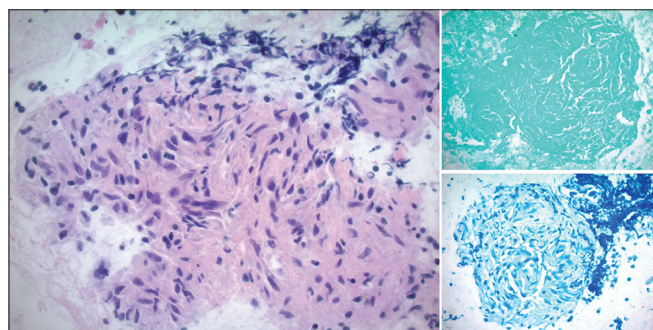


Figure 4: Photomicrographs from the subcarinal lymph node fine-needle aspiration. Left, nonnecrotizing granuloma composed of clusters of epithelioid histiocytes with admixed lymphocytes (hematoxylin-eosin, ×400 magnification). Top right, acid-fast bacilli stain is negative for mycobacteria (×200 magnification). Bottom right, Grocott's Methenamine silver stain is negative for fungal organisms (×200 magnification)

optic neuritis and optic perineuritis to our knowledge has not been previously described in neurosarcoidosis.^[15]

Optic perineuritis and optic neuritis are often clinically indistinguishable at presentation since both can cause optic nerve dysfunction and can present with a swollen optic disc.^[17] Radiographic findings are pivotal to differentiating between the two disease entities; while optic neuritis manifests as contrast enhancement of the nerve itself, optic perineuritis manifests a distinctive pattern of peri-optic nerve enhancement, seen as the tram-track sign on axial slices and doughnut sign on coronal slices. However, these findings are not pathognomonic and can be seen in other ocular pathologies, such as optic nerve sheath meningioma and metastatic carcinoma to the optic nerve sheath.^[14,18]

Visual field testing can also be a valuable diagnostic tool to help differentiate optic neuritis from optic perineuritis; optic neuritis typically affects central vision, while optic perineuritis often spares central vision and manifests as enlargement of the physiologic blind spot, or paracentral or arcuate scotomas.^[13] In our case, Humphrey visual field testing revealed global suppression in the right eye, which correlated best with the radiographic finding of optic neuritis.

Literature on pathologies that concurrently affect the optic nerve and optic sheath is limited but includes case

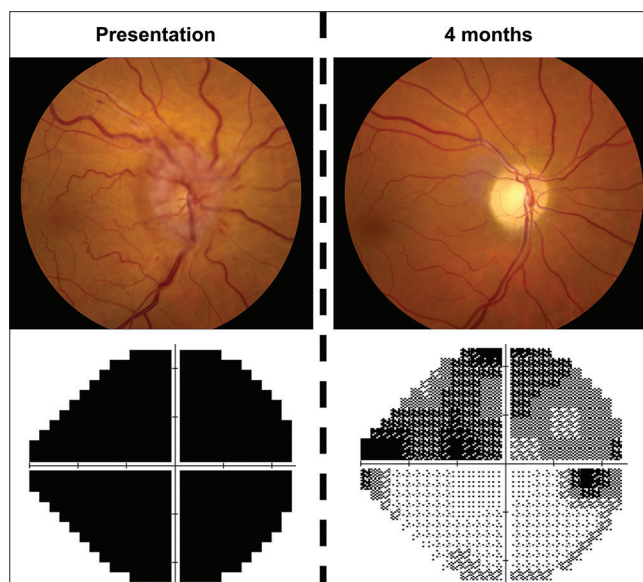


Figure 5: Upper left: Color fundus photograph of the right eye (same photograph as in Figure 1, left) showing diffuse optic disc edema, vessel obscuration, disc hemorrhages, and small flame-shaped retinal hemorrhages. Upper right: Color fundus photograph of the right eye 4 months after discharge from the hospital showing interval resolution of the optic disc edema and the subsequent development of optic atrophy. Lower left: Humphrey visual field from the right eye obtained at the initial evaluation showing complete suppression of the visual field. Lower right: Humphrey visual field obtained at his follow-up evaluation, approximately 4 months after his initial evaluation, showing improvement in his visual field defect

reports on malignant optic nerve glioma; leukemia; lymphoma; metastatic tumors; as well as inflammatory diseases, such as MOG antibody-associated disease; and granulomatous diseases, including sarcoidosis and granulomatosis with polyangiitis.^[13,19] When the optic nerve and sheath enhancement appear contiguous on MRI imaging, it has been suggested that this occurs secondary to inflammation of the intraneural pial septa adjacent to the inflamed nerve sheath.^[19] However, our case demonstrated spatially-distinct optic nerve and optic nerve sheath enhancement, suggesting that other mechanisms, in addition to or in conjunction with intraneural pial septa inflammation may be responsible for the radiographic findings in our patient.

In summary, our case of spatially-distinct optic perineuritis and optic neuritis represents a novel clinical presentation of neurosarcoidosis. MRI imaging of the brain and orbits is crucial in identifying simultaneous optic nerve and peri-optic enhancement. Since optic perineuritis is frequently associated with systemic diseases, it is important to perform a tailored systemic workup focused on the most likely etiologies of optic perineuritis. It was only after computed tomography imaging and biopsy of a subcarinal lymph node that our diagnosis was confirmed.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient has given his consent for his images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

The authors declare that there are no conflicts of interest related to this paper.

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