Cranial Nerve-VI Palsy as the Main Clinical Manifestation of Neurosarcoidosis.

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Cranial Nerve-VI Palsy as the Main Clinical Manifestation of Neurosarcoidosis

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Introduction: Sarcoidosis is a chronic, systemic, inflammatory disorder that is characterized by the formation of noncaseating granulomas. Patients may present with cranial nerve palsy, paresthesia, paresis, pyramidal signs, progressive cognitive decline, urinary retention, seizures, or hypothalamic-pituitary syndrome. Although the diagnosis of neurosarcoidosis can be challenging, neurological manifestations of sarcoidosis occur more frequently than previously described.

Case Report: A 23-year-old African American man presented to our emergency department with diplopia, which was worsened on left horizontal gaze. On the day of admission, he had a witnessed seizure. Laboratory studies were significant only for mild leukopenia and erythrocyte sedimentation rate of 17 mm/h. Brain magnetic resonance imaging revealed diffuse thickening and enhancement of the dura, mild mass effect, and soft tissue enhancement through the foramen rotundum and left orbital apex. The patient was treated with intravenous methylprednisolone and discharged on 60 mg oral prednisone daily followed by a taper over a 2-month period.

Conclusions: Our case demonstrates that mild neurological deficits can be the initial presentation of neurosarcoidosis in patients with undiagnosed or proven sarcoidosis.

Key Words: neurosarcoidosis, cranial nerve-VI palsy, sarcoidosis, cranial neuropathy, diplopia

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Sarcoidosis is a chronic, systemic, inflammatory disorder that is characterized by the formation of noncaseating granulomas. Neurological manifestations occur in approximately 5% of sarcoidosis patients.[1] About half of patients with neurosarcoidosis present with neurological signs and symptoms when a new diagnosis of sarcoidosis is made. Although the diagnosis of neurosarcoidosis can be challenging, particularly in patients presenting with mild neurological deficits such as isolated cranial nerve (CN) palsy, neurological manifestations of sarcoidosis occur more frequently than previously described.[2] Neurosarcoidosis should be considered in patients with a known diagnosis of sarcoidosis who develop neurological signs and symptoms of an unclear etiology.

Signs and symptoms of neurosarcoidosis are variable and depend on the location and size of the granulomas. Patients may present with CN palsy, paresthesia, paresis, pyramidal signs, progressive cognitive decline, urinary retention, seizures, or hypothalamic-pituitary syndrome.

CASE REPORT

A 23-year-old African American man presented to our emergency department with painless bulging of the left eye of 3 months duration but no feeling of pulsation. Symptoms were associated with diplopia, which was worsened on left horizontal gaze. He denied any facial droop, weakness, paresthesia, or unsteady gait.

On the day of admission, the patient had a witnessed generalized tonic-clonic seizure preceded by a feeling of lightheadedness but no nausea, sweating, or palpitations. He had no history of seizures or head trauma. He denied concomitant fever, weight loss, joint pain, diarrhea, illicit drug use, or alcohol use. On examination, he was found to have left CN-VI palsy (Fig. 1). Diplopia resolved when the right eye was covered. Pupils were round and reactive to light and accommodation. No facial weakness was appreciated and facial sensation was intact. Motor, sensory, coordination, and gait examination was unremarkable.

Laboratory studies were significant only for mild leukopenia and erythrocyte sedimentation rate of 17 mm/h. Concentration of angiotensin-converting enzyme was 49 U/L (normal, 12 to 68 U/L). Renal, liver, and thyroid functions were within normal limits. Antibodies for human immunodeficiency virus and Lyme disease were negative. Reactive reagent protein was negative. Cerebrospinal fluid (CSF) analysis revealed clear fluid appearance with protein of 40 mg/dL, glucose of 64 mg/dL, and white blood cell count of 9 cells/μL (92% were lymphocytes and 8% monocytes). CSF analysis revealed no malignant cells or oligoclonal bands with normal IgG index and was negative for cryptoccocus neoformans antigens.

An electroencephalogram was normal. Brain magnetic resonance imaging (MRI) with and without gadolinium revealed diffuse thickening and enhancement of the dura involving the left cavernous sinus, mild mass effect on the left temporal lobe, and soft tissue enhancement extending anteriorly through the foramen rotundum and left orbital apex (Fig. 2). A computed tomography of the chest, abdomen, and pelvis with and without contrast was unremarkable for any granulomatous disease, lymphadenopathy, or malignancy. A left cavernous sinus dural biopsy revealed extensive chronic inflammation containing non-necrotizing granulomas (Fig. 3), consistent with neurosarcoidosis. There were no *Toxoplasma gondii*, histoplasmosis, or cryptococcus organisms identified on giemsa or hematoxylin and eosin stains. There was no sequestration of lymphocytes in and near blood vessels to suggest vasculitis.

The patient was treated with intravenous methylprednisolone, 1000 mg daily, for 5 days. Diplopia and CN-VI palsy improved with

FIGURE 1. Photograph showing left cranial nerve-VI palsy on initial presentation.

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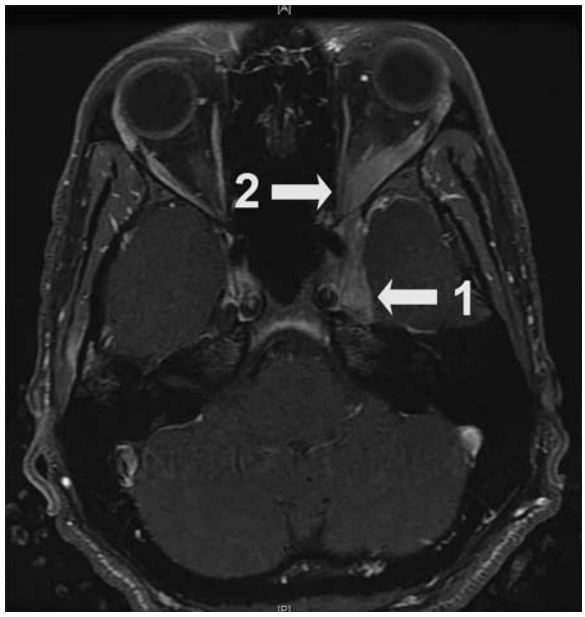

FIGURE 2. Magnetic resonance imaging of the brain, T1 with contrast, showing diffuse enhancement of the lateral wall of the left cavernous sinus (1) and orbital apex (2) with mass effect on the left temporal lobe.

residual subtle difficulty in left eye abduction. No recurrent seizures were reported in the hospital. He was discharged on oral prednisone, 60 mg daily, followed by a taper over a 2-month period. Neurological evaluation 18 months after discharge revealed resolution of the CN-VI palsy (Fig. 4). No recurrent seizures were reported.

DISCUSSION

Neurological manifestations of sarcoidosis include cranial neuropathies. Because the basilar meninges are prone to be involved in neurosarcoidosis, cranial neuropathy is the most common neurological manifestation, with an overall frequency of 50% to 75%.[3] Infiltration of CNs in the subarachnoid space is another common site for granulomatous infiltration.[2] Facial nerve palsy, often bilateral, is the most frequent cranial neuropathy in patients with neurosarcoidosis,[4,5] followed by optic neuropathy.[3] Other CNs including olfactory or auditory can also be involved. Involvement of CNs III, IV, or VI is rare.[6] Ocular motility involvement is most commonly due to involvement of the abducens nerve, which is more common than third and fourth CN palsies.[3] The incidence of eye involvement in patients with neurosarcoidosis seems to be higher in women than in men.[6]

FIGURE 4. Photograph showing total resolution of cranial nerve-VI palsy after treatment, at 18-month follow-up.

Our case demonstrates that CN palsy, although rare, may be a prominent neurological complication of neurosarcoidosis at initial presentation. It also further reveals the importance of tissue biopsy in establishing the diagnosis, as neurosarcoidosis can mimic other central nervous system inflammatory diseases such as multiple sclerosis or Tolosa-Hunt syndrome.[7] Neuro-ophthalmologic manifestations of neurosarcoidosis essentially indicate involvement of the central nervous system,[8] but other systems can be involved and thus further workup is warranted. Isolated central nervous system involvement of sarcoidosis has been reported, as was the case in our patient.

Diplopia, seen in our patient, may be a presenting feature of neurosarcoidosis when ≥ 1 ocular motor CNs are affected, or if the intracranial pressure is increased. This raises the possibility of the cavernous sinus or subarachnoid space being

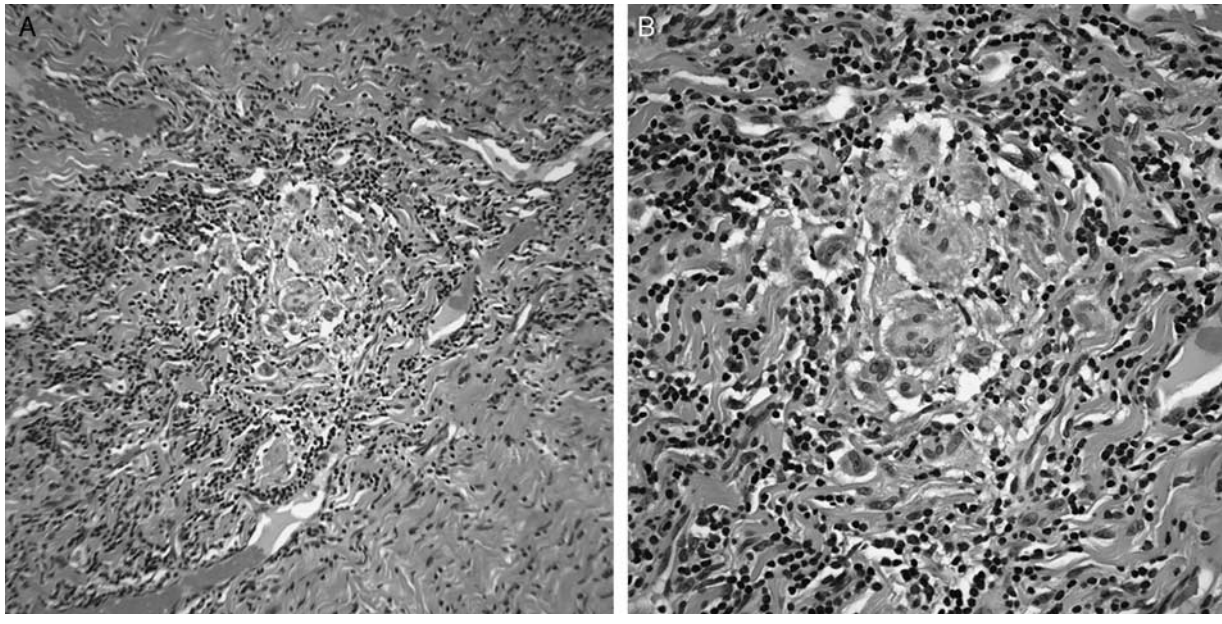

FIGURE 3. Dural biopsy showing mononuclear inflammatory cells and noncaseating granulomas (A); higher resolution (B).

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involved.[7] In this case, our patient had cavernous sinus involvement. Naqasawa et al[9] have previously reported abducens nerve palsy as the first manifestation of neurosarcoidosis affecting the cavernous sinus. What distinguishes our case from theirs is that, except for seizures, other potential systemic manifestations of sarcoidosis were absent. Although our patient's history, MRI, and CSF findings were suggestive of neurosarcoidosis, tissue biopsy remains the gold standard diagnostic procedure for establishing the diagnosis.[2,5,7] Granulomatous lesion of unknown significance remains a possibility; however, the patient's race, response to steroids, and location of the granuloma in the central nervous system all support the diagnosis of neurosarcoidosis.

We recommend the use of brain MRI with contrast over computed tomography when clinical suspicion for neurosarcoidosis is high for better visualization of the cavernous sinus and brain stem, which are common sites for sarcoidosis involvement.[2,4] We advise clinicians to exercise caution when performing a lumbar puncture in a patient with suspected neurosarcoidosis and any clinical or radiographic evidence of increased intracranial pressure, such as papilledema, mass effect, or enlarged ventricles. Practicing neurologists should consider this diagnosis in patients with a constellation of clinical and radiographic findings consistent with neurosarcoidosis, even in the absence of a known history of diagnosed sarcoidosis, particularly in the African American and Northern European populations. Clinical follow-up is warranted, and the use of steroid-sparing agents in patients experiencing adverse reactions should be considered.

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