CASE REPORT

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Isolated neurosarcoidosis

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Abstract

Sarcoidosis is an inflammatory granulomatous disease affecting multiple organ systems. Neurosarcoidosis (central nervous system involvement) is seen in approximately 25% of patients with systemic sarcoidosis, although it is subclinical in most of these cases. Clinical presentations and imaging findings in nervous system were varied. Cranial nerve abnormalities were the most common clinical presentation and involvement of the optic nerve in particular was associated with a poor prognosis for visual recovery. A patient is described who presented with decreased visual acuity, hypoesthesia of the face and multiple tumors of the eyelids on both eyes. Initial biopsy of one of the tumor of the eyelids revealed a non-caseating granulomatous inflammatory process with nodular infiltrates made up of epithelioid cells, Langhans-type giant multinucleated cells and mononuclear cells; the diagnosis of sarcoidosis was suspected. After two years of clinical and MRI (Magnetic Resonance Imaging) follow up, the diagnosis of isolated neurosarcoidosis was confirmed by histology. In this study, we analyzed clinical and radiologic records of this patient with biopsy proven and clinically diagnosed neurosarcoidosis for the following reasons: (1) to assess the concordance between abnormalities noted on MRI with neurologic symptoms at presentation; (2) to correlate changes in imaging findings during follow-up with clinical worsening; and (3) to show up the characteristic feature of this case with no general sign/symptoms of sarcoidosis.

Keywords: neurosarcoidosis, tumors of the eyelids, disorders of the cranial nerves.

Introduction

Sarcoidosis is a multisystemic disease of unknown etiology characterized by the formation of immune granulomas in involved organs [1]. The clinical impact of the disease is dependent on the site of granulomatous inflammation and its severity throughout the body [4–6]. Although neurosarcoidosis is a less common manifestation of sarcoidosis [7–9], its symptoms can be devastating and occasionally life-threatening. The diagnosis of neurosarcoidosis can be challenging because the disease can present with a myriad of symptoms and diverse imaging findings [10]. The prevalence of clinical involvement of the nervous system in sarcoidosis is estimated to 5–15%, and very rarely it may selectively involve the nervous system [11].

We describe a patient who presented multiple tumors of the eyelids and posterior optic neuropathy on both eyes. After two years of clinical and cerebral MRI follow up, the diagnosis of isolated neurosarcoidosis was verified by histology.

Patient, Methods and Results

A 65-year-old female patient presented with decreased visual acuity and multiple small tumors of the tarsus of the upper and lower eyelids, on both eyes. Neuro-ophthalmologic examination revealed decreased visual acuity on both eyes (visual acuity both eyes = 2/20), alteration of the visual field as an altitudinal visual field and hypoesthesia of the face.

General exams and laboratory examination were normal, except for a mildly elevated erythrocyte sedimentation rate (ESR). Chest X-ray was normal. Cerebrospinal fluid cultures for *Mycobacterium tuberculosis* and cerebrospinal fluid (CSF) serology for fungi, parasites, herpes simplex virus (HSV) and toxoplasmosis were negative. The patient was scheduled for biopsy of one of the tumors of the eyelids. Biopsy specimen revealed a non-caseating granulomatous inflammation with epithelioid cells surrounded by Langhans-type giant multinucleated cells, lymphocytes and plasma cells (Figure 1), so the diagnosis of sarcoidosis was suspected and corticosteroid treatment was started for the next year. Ophthalmological exam (Figure 2), and brain MRI were normal. She had no new symptoms in the following year; then she developed palsy of the oculomotor nerves (convergent strabismus and diplopia), severe decrease of the visual acuity and anesthesia of the face, intense headaches, seizures and vertigo. In this period (second follow-up year), she did not receive corticosteroid therapy.

Brain MRI revealed enhancement of the intraorbital, intracanalicular and intracranial segments of the optic nerve sheath, on both sides (Figures 3–5), enhancement of the subarachnoid course of oculomotor nerves at the level of interpeduncular fossa (Figure 6), enlargement of

the surface origin of the trigeminal nerve (Figure 7) and dural and leptomeningeal enhancement (Figure 8). Repeat laboratory examination revealed elevated ESR of 34 mm/hr. and serum calcium, diagnostic tests for immune disorders, anticardiolipin antibodies. Abdominal ultrasound and chest and abdominal CT-scan (Computer Tomography) were normal. Repeat cultures for *Mycobacterium* and CSF serology for *Borrelia* and HSV were negative. Corticosteroid therapy was initiated (methylprednisolone 500 mg for five days, gradually tapered to 15 mg every other day).

Throughout the period of illness, there were no signs of involvement of any organs other than the brain. Treatment with azathioprine 50 mg was tried, but the patient developed liver enzyme elevation and this therapy was discontinued. Cyclosporine therapy was suggested, but the patient refused it due to potential side effects. At the last control visit, the patient had severe cognitive impairment and paraplegia. She died of heart failure. The histological examination of the brain, meninges, optic nerves revealed characteristic lesions of sarcoidosis (Figures 9–12).

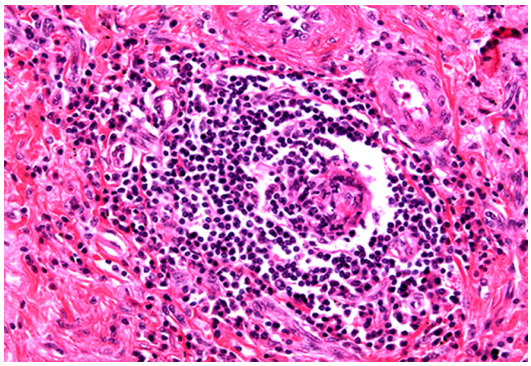

Figure 1 – ***Histopathological findings of the tumor on the eyelid, which reveal a non-caseating granuloma, consisting of epithelioid cells, Langhans-type giant multinucleated cells, and lymphocytes (HE stain, original magnification ×100).***

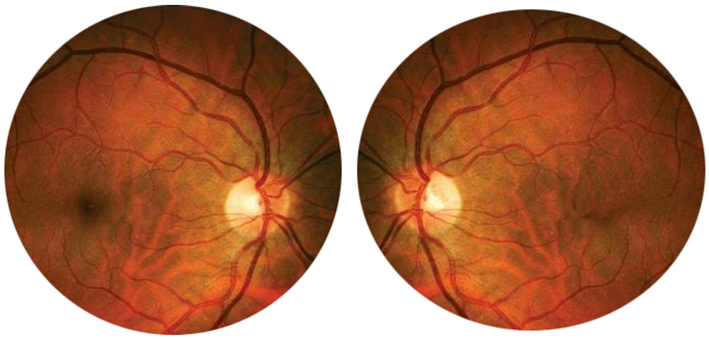

Figure 2 – ***Ophthalmoscopic aspect of the posterior optic neuropathy, on both eyes.***

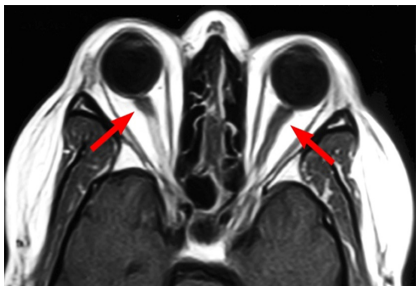

Figure 3 – ***Cerebral MRI, T1 post-contrast image in axial view shows enhancement of the intra-orbital segment of the optic nerves, bilaterally (arrows).***

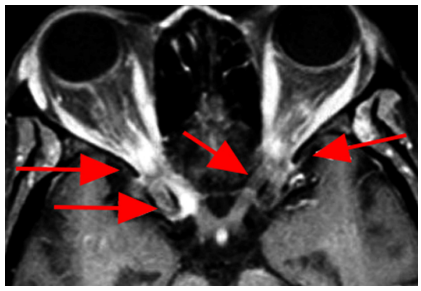

Figure 4 – ***Cerebral MRI, T1 post-contrast image in axial view shows enhancement of the intracanalicular segment of the optic nerves, bilaterally (arrows).***

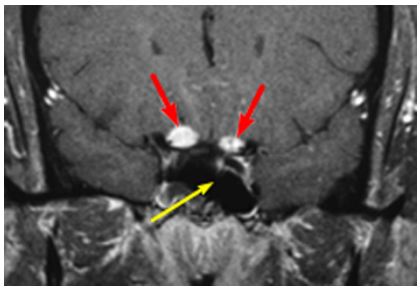

Figure 5 – ***Contrast-enhanced fat-saturated T1-weighted coronal image with enhancement and thickening of both optic nerves in prechiasmatic segment (upper arrows). Lower arrow points the sphenoid sinus.***

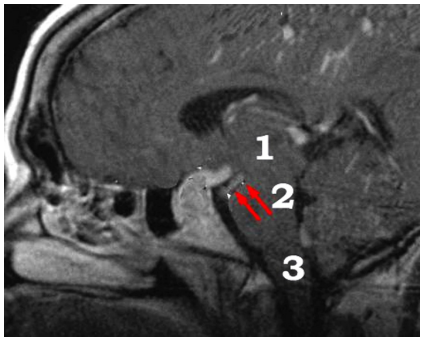

Figure 6 – ***Contrast-enhanced T1-weighted parasagittal image shows enhancing lesion causing thickening and enhancement of cisternal segment of third cranial nerve (arrows); 1 – The midbrain; 2 – The pons; 3 – The bulbus.***

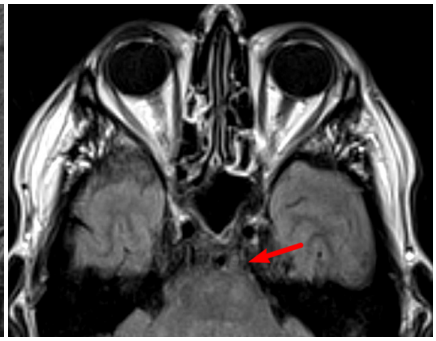

Figure 7 – ***Contrast-enhanced T1-weighted axial image shows enhancing lesion causing thickening of the trigeminal nerve (arrow) at the level of the anterior surface of the pons.***

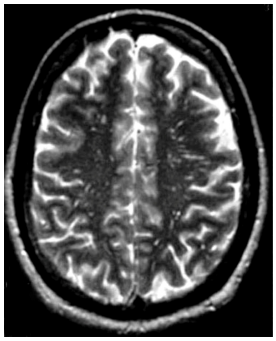

Figure 8 – ***Contrast-enhanced T2-weighted axial image shows diffuse thickening and enhancement of dura mater.***

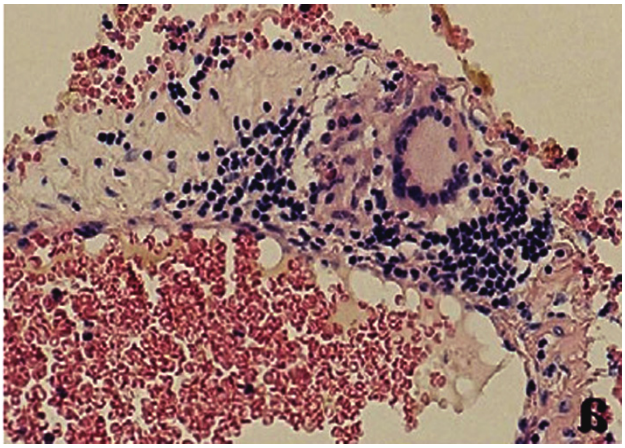

Figure 9 – ***Small meningeal granuloma with a Langhans-type giant multinucleated cell (HE stain, original magnification ×100).***

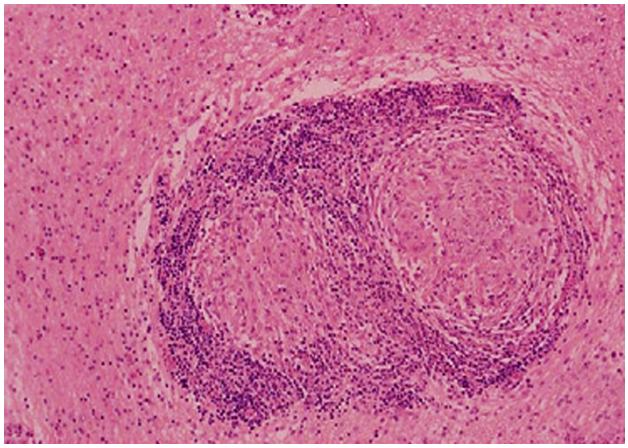

Figure 10 – ***Granulomatous lesion without necrosis located within the cerebral white matter (HE stain, original magnification ×40).***

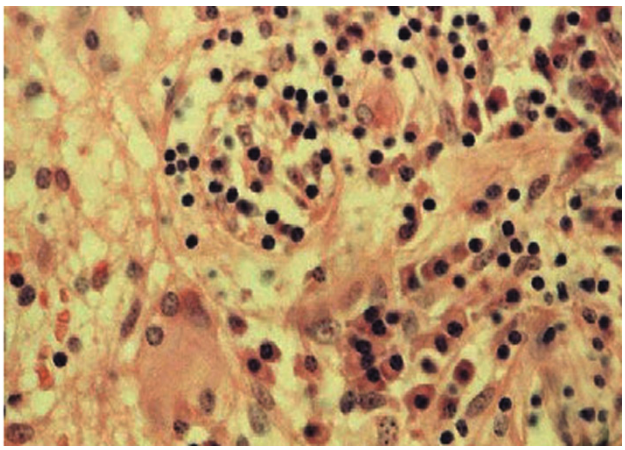

Figure 11 – ***Higher magnification of a granuloma showing lymphocytes, plasma cells and a giant multinucleated cell (HE stain, original magnification ×200).***

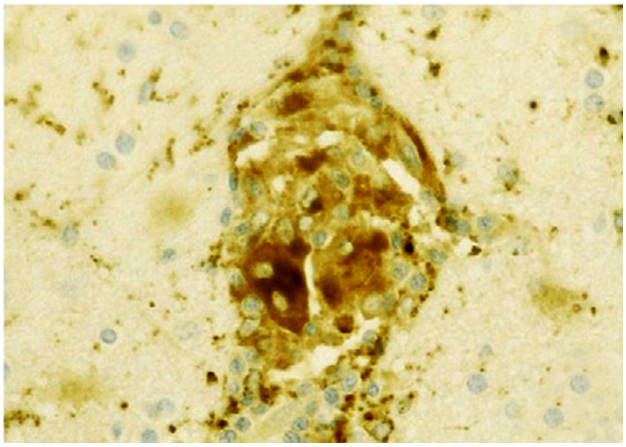

Figure 12 – ***Small perivascular granuloma with epithelioid and giant multinucleated cells positive for CD68 (immunohistochemical stain, original magnification ×200).***

Discussion

Our patient met the criteria for definitive diagnosis of neurosarcoidosis: clinical presentation compatible with neurosarcoidosis, exclusion of other possible causes and positive nervous system histology [12]. However, the diagnosis of isolated neurosarcoidosis remains very difficult despite the established criteria [13]. As it can affect any part of the nervous system, clinical presentation may range from decrease of the visual acuity and headaches to altered consciousness and severe motor deficits. Some clinical presentations are often associated with a higher rate of morbidity and death. In contrast to an isolated mass lesion, which has a favorable outcome, poor outcome is associated with seizures, hydrocephalus, chronic meningitis and multi-focal parenchymal disease [14]. In our patient, the initial manifestation were the decrease of the vision on both eyes and tumors of the eyelids, in order to develop palsy of the oculomotor nerves and seizures This finding, along with later development of disseminated white matter disease, put this patient at a high risk of poor outcome [15].

Mass lesions are frequently reported in patients with neurosarcoidosis and they may mimic primary or metastatic tumors [16]. However, adjacent leptomeningeal involvement is frequently seen, a finding that may help reach an accurate diagnosis [17, 18]. These individuals often present with seizures, which were a clinical feature in our patient, who also had leptomeningeal involvement.

The typical and most common imaging features in neurosarcoidosis are thickening and enhancement of basilar leptomeninges, followed by enhancing or non-enhancing parenchymal lesions and hydrocephalus [19]. Imaging findings in neurosarcoidosis can mimic astrocytoma, meningioma, intracranial metastatic disease, CNS (Central Nervous System) vasculitis, other granulomatous diseases such as tuberculosis, parasitic and fungal infections, and Wegener's or lymphomatous granulomatosis, and multiple sclerosis [20]. If there is a known history of pulmonary sarcoidosis, the diagnosis of neurosarcoidosis is straight forward. Nevertheless, when CNS involvement is a first manifestation, all the diseases mentioned above should be excluded. This makes neurosarcoidosis one of the great mimickers in neurology.

Conclusions

Although sarcoidosis is rarely confined to the nervous system, its neurological features frequently occur early

in the course of the disease leading to diagnostic confusion. Presentation with cranial neuropathies (particularly nerves II, VII) is the most common, although other cranial nerves (III, V) can be affect. In our case the diagnoses of definite neurosarcoidosis was supported by the clinical facts (posterior optic neuropathy on both eyes), brain MRI and biopsy findings. Patients who presented bilateral decreased vision, due to optic neuropathy, generally had a poor prognosis. Neurosarcoidosis is a diagnosis by exclusion: when CNS involvement is a first manifestation, all the diseases mentioned above should be excluded.

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