Isolated Neurosarcoidosis: Case Report and Literature Review

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Abstract

Sarcoidosis is a multisystemic granulomatous disease of unknown etiology with a rare tendency to the nervous system. Isolated neurosarcoidosis is rare and difficult to be diagnosed clinically. A 53-year-old Jordanian male admitted to Jordan University Hospital with a history of urine retention, low back pain and feet parasthesia. Brain magnetic resonance imaging showed bilateral enlargement of certain cranial nerves and meningeal masses. Magnetic resonance imaging of the whole spine revealed meningeal and lumbar nerves thickening.

Keywords: Neurosarcoidosis, central nervous system, magnetic resonance imaging.

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Introduction

Sarcoidosis is a multisystemic granulomatous disease of unknown etiology, has tendency to lungs but relatively rare to the nervous system particularly in Asians.[1]

Involvement of the Central Nervous System (CNS) consequential to complicating thoracic or systemic sarcoidosis occurs typically within two years of onset of the disease.[1] It was estimated that 5% of sarcoidosis patients demonstrated clinical involvement of the nervous system as Neurosarcoidosis (NS).[2, 3]

Whereas post mortem studies suggested that only 50% of patients with nervous system involvement were diagnosed clinically. [4] Only few cases of isolated neurosarcoidosis were reported in the literature. [3, 5]

The demographic distribution; age and sex of NS are similar to thoracic sarcoidosis.[2, 3] It was concluded that 88% of NS patients would have systemic sarcoidosis at the onset of neurologic disease. [6] NS rarely relapses and when it happens, it typically involves the cranial nerves. [7]

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Case Report

A 53-year-old male patient, presented with symptoms of acute urinary retention, low back pain radiating to gluteal regions and feet parasthesia. On clinical examination, the patient was slow, apathetic and lethargic. Mini Mental Status Examination score was abnormal (27/30). Cranial nerves examination showed bilateral facial weakness, worse on the right side. Rest of cranial nerves were normal in particular the optic nerve. The patient manifested mild to moderate asymmetric weakness of both legs with hyporeflexia and flexor plantar responses. He demonstrated saddle anesthesia, preserved bulbo-cavernous reflex and atonic anal sphincter. The rest of medical examination was normal.

Laboratory results including neuroendocrine tests, serum calcium and immunoglobulins were normal except for CSF, which showed 230 WBC per cubic millimeter, lymphocytes 98%, protein 1280 mg/dl, sugar 10 mg/dl (blood sugar 122 mg/dl). CSF pressure was normal (170 mm H2O), ACE plasma was normal while in CSF was not done. Zeihl-Neelsen stain and culture for AFB as well as PPD were negative. Transbronchial biopsy and bronchoalveolar lavage for granulomas or malignant cells were negative. Chest x-ray, high-resolution chest CT scan and pulmonary function test including diffusion capacity were normal.

Brain Magnetic Resonance Imaging (MRI) without and with intravenous contrast showed loss of bright spot of neurohypophysis and a mass in the floor of the third ventricle involving the infundibulum, hypothalamus and optic chiasm (Figure 1). In addition, bilateral enlargement of the intracranial portion of the optic, oculomotor, trigeminal (Figure 2), facial and vetstibulo-cochlear nerves more prominent at the right cerebello-pontine angle (Figure 3).

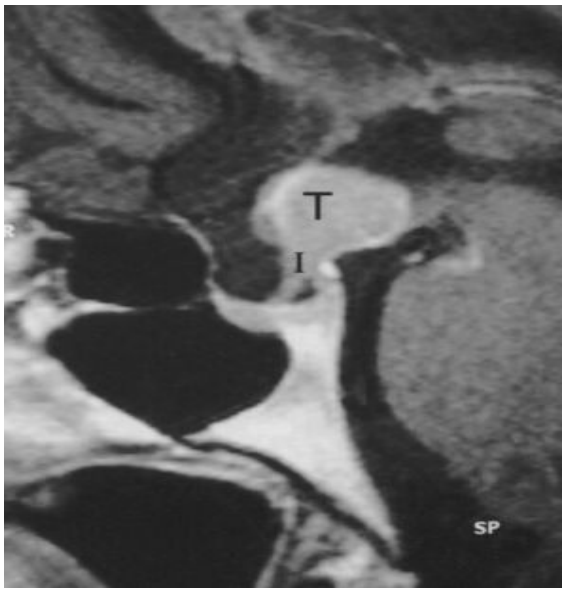

Figure 1: Sagittal MRI, T1 sequence with intravenous contrasted agent showing enhancing mass (T) in the floor of third ventricle extending to pituitary infundibulum (I) and optic chiasm.

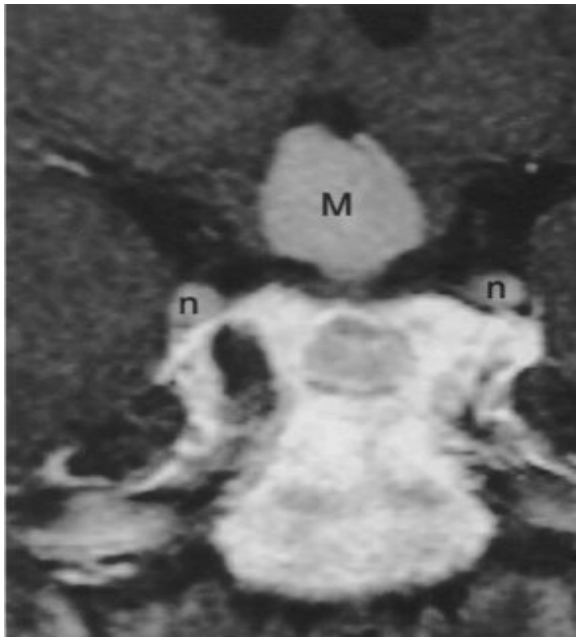

Figure 2: Coronal MRI, T1 sequence with intravenous contrasted agent showing an enhancing mass (M) in the floor of third ventricle and enlargement of both trigeminal nerves (n) which also show post contrast enhancement.

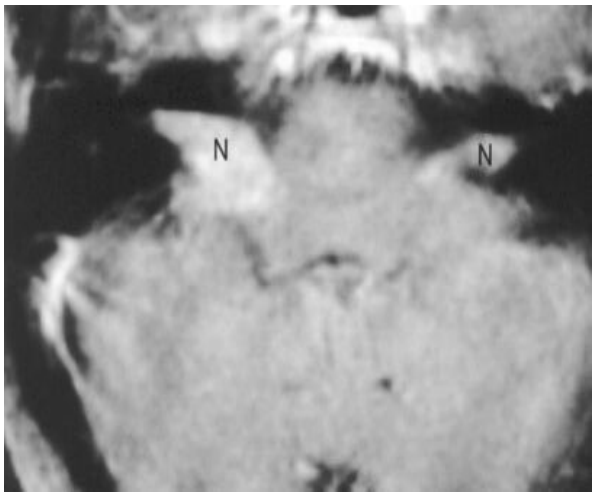

Figure 3: Axial MRI, T1 sequence with intravenous contrasted agent showing bilateral enlargement and enhancement of both facial and vestibulo-cochlear nerves (N) more prominent on the right side.

Multiple meningeal masses were also distinguished in the interpeduncular and ambient cisterns as well as in the left Sylvian fissure. All these meningeal and cranial nerves lesions were hypointense on T1 and isointense on T2, and showed strong post contrast enhancement except the optic nerves and no brain lesion could be seen even in FLAIR images. MRI of the whole spine revealed meningeal and lumbar spinal nerves thickening with vivid enhancement. By meningeal biopsy, the diagnosis of NS was confirmed. The patient was treated with high dose steroids and immunosuppressive agents but without improvement in his condition. He was discharged home and advised to be followed up in his district hospital.

Discussion

Neurosarcoidosis was first reported in 1909 by Heerfordt who described three cases of "subchronic uveo-parotid fever complicated by paresis of cerebrospinal nerves"; demonstrating a form of NS characterized by optic neuritis, facial palsy, and dysphagia. [1, 8] Histopathological studies showed NS developing primarily in the leptomeninges and along the perivascular spaces of Virchow- Robin with subsequent disruption of the blood brain barrier and its extension into the brain parenchyma. The disease progression has a predilection to the basal and midline structures as well as of facial and optic nerves involvement. [9, 10] Central nervous system involvement may affect the cerebral cortex, cerebellum and rarely the spinal cord.[1] Positive nervous system histology is considered a gold standard for the diagnosis. [4]

Sixty three percent of patients with NS show neurologic symptoms as their first manifestation. These patients may present with seizures, cranial nerves involvement, motor signs, papilledema, [11] diabetes insipidus, encephalopathy, hydrocephalus, aseptic meningitis, peripheral neuropathy and myopathy. [2] Brain stem and /or cerebellar presentations found in 21% of cases. [4] The most common cranial nerve deficit noted in the facial nerve, either unilaterally or bilaterally, due to direct nerve compression by parotid gland swelling , by a lesion within facial canal or intracranially. [1] In the presented case facial nerves were bilaterally involved and more prominent at the right side, most likely correlated to the mass in the right cerebellopontine angle. Bilateral facial palsy in young adults is likely most to be caused by sarcoidosis, [10] and its isolated involvement carried a more favorable prognosis than the others. [4]

The optic nerve is the next most common cranial nerve to be involved which was also involved in the reported case. [5, 10] In an early stage and rapid onset of NS, the optic nerve and its chiasm either respond to treatment or resolve spontaneously.[10] But another study reported that optic nerve involvement often had residual symptoms or did not respond to treatment which may be due to the fact that other cranial nerves are surrounded by schwann cells. [5] Other cranial nerves involvement was seen in one third of patients and had good prognosis. [4, 5] In the present case, occulomotor, trigeminal and vestibule-cochlear nerves were bilaterally involved.

The behavioral involvement of NS in the spinal tissues is similar to that of intracranial tissues but with less common mass lesions.[12] Clinically, evident peripheral neuropathy occurs in 6-18% which was noticed as; 56% in cervical, 37% in thoracic and 7% in lumbosacral segments.[2, 4, 10, 12] A recent report concluded that, the initial clinical manifestation of NS occurs in the spinal cord [2] similar to the present case due to lumbar nerve involvement, however, others reported it as unusual manifestation. [5]

Positive CNS MRI results found in 65% of patients, the most common abnormality was multiple white-matter lesions in 43% (periventricular and periaqueductal), meningeal enhancement in 38% and brain parenchyma enhancing mass in 25%.[4, 7] Nonenhancing brain parenchymal lesions occur in the periventricular white matter but may be seen also in the brain stem and basal ganglia. In addition, these differ from the enhancing parenchymal lesions for which symptoms often correlate with the imaging findings and symptomatic improvement correlated with the regression on MR images.[5] None of these findings were noticed in the present case.

Anterior pituitary gland is rarely involved, but loss of bright spot of the posterior pituitary lobe on noncontrasted T1 weighted images is also a recognized feature.[10] Pituitary stalk and hypothalamic involvement as seen on MRI is more suggestive of NS than other disease.[7] Occasionally, granulomas coalesce to form mass like lesions particularly in the chiasm region, floor of third ventricle and pituitary stalk. [5, 9] All of the aforementioned findings were found in our patient.

On MR images, the most common abnormality evolved is the involvement of the optic nerve including chiasm.[5] On the other hand, enhancement of cranial nerves rarely seen on MRI [9] which was not the case as we report enhancement of all the affected cranial nerves except optic nerves. Dural masses appear isointense to gray matter on T1, hypointense on T2 weighted MR images and they enhance uniformly.[5] Spinal neurosarcoid granulomatous lesion located in the leptomeninges and within the parenchyma of the spinal cord is a rare finding [2, 12] but carries inferior prognosis.[4]

An optimistic report on NS prognosis stated that, about two third of patients with NS have a self-limited monophasic illness, the rest have a chronic remitting relapsing course. With treatment, death from neurologic disease is unusual. [1] On the contrary, our patient didn't show any clinical improvement over a period of 6 months due to the aggressive nature of his disease and unfortunately died at his district hospital from neurological disorders and infection.

The differential diagnosis of NS includes multiple sclerosis, Lyme disease, Wegener granulomatosis, Behcet disease, meningeal carcinomatosis, tuberculosis and lymphomatosis. [4, 7, 9, 12] The radiologic presence of NS is not always evident clinically. [5]

MRI is the modality of choice and the use of contrast agent and FLAIR sequence has increased its sensitivity. [13] Leptomeningeal involvement could be missed if contrast agent is not used. A FLAIR sequence is valuable in detecting low contrast lesions, improves its accuracy, [1] and guides us towards diagnosis. [14] Diagnosis of NS can reasonably be supported in many patients by MRI findings and exclude other disorders.[15]

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