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CASE REPORT

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Neurosarcoidosis in an adult man with a family history of MS: A case report

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Key clinical message

According to this report, a biopsy revealed a diagnosis of neurosarcoidosis in a patient with a history of MS. The development of the disease can be slowed down by early diagnosis and appropriate treatment.

Abstract

Neurosarcoidosis is a rare type of sarcoidosis that affects the central nervous system (CNS). Herein, we present a case of neurosarcoidosis with a history of multiple sclerosis (MS). Based on the pathological findings of the biopsy, a diagnosis of neurosarcoidosis was established. The administration of appropriate treatment at an early stage can assist in decelerating its progression.

KEYWORDS

neuro, sarcoidosis, Sarcoidosis multiple sclerosis

1 | INTRODUCTION

In 1905, Winkler described the first reported case of central nervous system (CNS) sarcoidosis. This is a multi-organ disease with chronic systemic granulomatous features. Sarcoidosis affects not only the lungs but also the skin, lymph nodes, eyes, and liver. In older studies, up to half of the patients could have the asymptomatic disease, identified on chest X-ray (CXR) performed for other reasons. Approximately 5%–15% of cases are associated with CNS involvement (neurosarcoidosis).[1] Lesions in the CNS may be subdural or extradural, leptomeningeal, or parenchymal in this disorders.[1] In the case of spinal cord involvement, the disease is typically intradural and can be treated with corticosteroids or surgical decompression.[2] According to the studies, one of the critical complications of neurosarcoidosis is cranial neuropathy in 50% to 75% of patients.[1]

Here, we present a case of an adult man. This particular case is unique because he was initially diagnosed with toxoplasmosis. Nevertheless, a brain and cervical magnetic resonance imaging (MRI) performed 5 years later diagnosed him with MS, contrary to a lung biopsy that showed neurosarcoidosis 6 years later.

2 | CASE PRESENTATION

A 42-year-old right-handed man with a family history of multiple sclerosis (MS) in his sister was admitted due to swelling of the right wrist joint. An MRI of the right wrist revealed that the radiocarpal joint had signs of inflammatory changes, with erosive changes on the distal end of the radius, scaphoid, and lunate. Additionally, the patient's tissue sample revealed focal fibrin deposition and

lymphocyte infiltration. In this regard, he was recently treated by surgery on his right wrist.

Later, he suffered from a decrease in visual acuity in his right eye, which was 4/10 and 7/10 in his right and left eyes, respectively. After being examined for the diagnosis of toxoplasmosis, he was treated with corticosteroids, and the patient partially recovered. One year later, the patient developed hemiparesis and paresthesia on the right side of the face and right limbs, which was treated with a course of corticosteroids, and after 2–3 months, the patient had a relative recovery. The treatment with psychiatric drugs (50 mg Asentra and 5 mg Chlordiazepoxide) seems to be unrelated to the patient's MS symptoms.

After 5 years, the patient developed paraparesis and was referred to a neurologist. An MRI of the brain and cervical vertebrae was performed, including sagittal T1 and T2- weighted sequences and axial T2 sequence (Figures 1 and 2). The findings showed abnormally high signal intensity at C2-C3 and C3-C4 levels of the posterior spinal cord. Degenerative disco-vertebral changes were evident in the C5-C6 level, but no disk herniation was observed. No intra- or extradural mass lesion was detected. The diagnosis was MS, which was treated with interferon β1.

Four years later, a repeated spinal MRI showed dehydration changes in disk spaces at follow-up. A bulging of the C4-C5, C5-C6, and C6-C7 intervertebral disks was also observed. There were oval lesions within the cervical cord at the level of C4-C5 and C5-C6, which were indicated by a high signal intensity in T2W images without enhancement after contrast injection. Brain MRI demonstrated that both internal auditory canals and the 7th and 8th cranial nerve complexes were normal; however, there were few rounds, and small lesions in the cerebellum, corpus callosum, and paraventricular regions.

The patient's symptoms were completely under control using interferon β, until he suffered from severe fever and chills, cough, and body aches for a month, which were exacerbated by interferon β. A blood test was taken, and the library findings showed normal aspartate transferase (SGOT) (25 unit/L; normal: 0–37). Alanine transferase (SGPT) was (33 U/L; normal: 0–41). The hormone analysis results showed that TSH was also normal (1.80 mLU/L; normal:0.3–4). Though the above testing the possibility of sarcoidosis could not be excluded, the lack of definitive findings brought other possibilities into the differential diagnosis.

The patient was referred to a pulmonologist, and suspicious lung lesions was detected in lung imaging. The specimen from bronchial washing fluid included 5 mL clear and colorless fluid and revealed thin mucinous background containing a few inflammatory cells (less than 5%) admixed with some groups of ciliated epithelial cells (32%) and some dust (60%) and squamous epithelial cells (3%). A chest X-ray revealed bilateral hilar lymphadenopathy, confirmed by thoracic computed tomography (CT) scan (Figure 3). Therefore, the patient underwent a thoracic lymph node biopsy, which revealed noncaseating granulomas consistent with sarcoidosis (Figure 4).

During the follow-up, another brain MRI was repeated in 2019, and a few T2-flair high signal lesions were seen

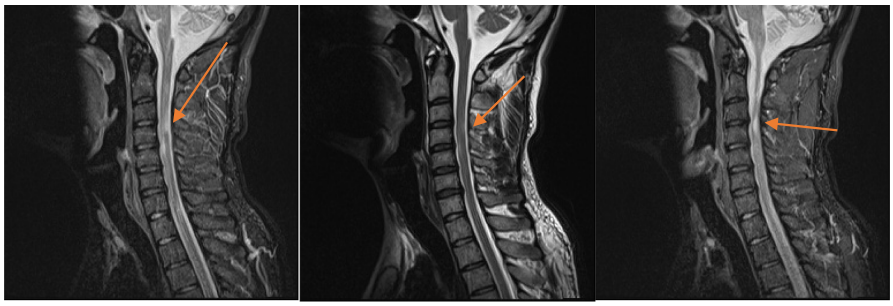

FIGURE 1 In cervical spine MRI with and without contrast injection, multiple sections (axial, coronal, and sagittal) were obtained through multiple (T1 and dual-echo, gradient echo) sequences.

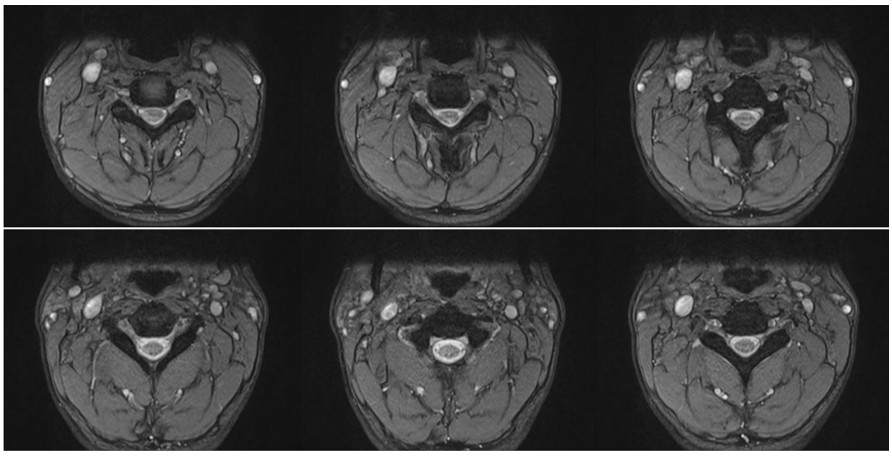

FIGURE 2 Spinal MRI with and without contrast injection. T2 axial, which shows a change in spinal cord signal.

in periventricular regions (Figure 5). The spinal cord MRI also showed high signal lesions (Figure S1).

After the lumbar puncture (LP) and based on cerebrospinal fluid (CSF) studies, the patient's diagnosis of neurosarcoidosis was considered. In the CSF examination, an elevation in the level of serum angiotensin-converting enzyme (ACE) along with radiographic evidence of hilar adenopathy and organ biopsies showing noncaseating epithelial granulomas was also approving of a diagnosis of sarcoidosis.

The patient was diagnosed with probable neurosarcoidosis and started on steroids based on these findings. The patient is currently being treated with Prednisolone 5 mg daily and Famotidine, Cetirizine, and Domperidone, and the patient's symptoms are under control. Through the follow-up, another CSF examination was entirely normal. Repeated MRI was not done after steroid therapy to evaluate improvements in white-matter lesions as the patient returned to his baseline neurological status.

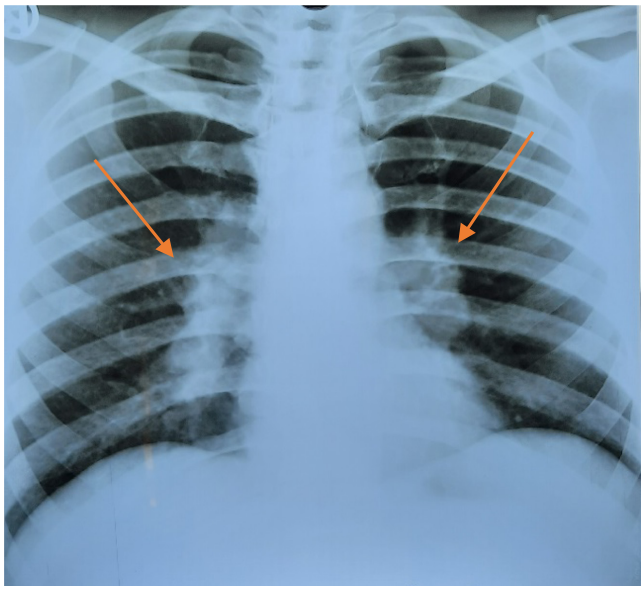

FIGURE 3 CXr of his chest demonstrated bilateral hilar and mediastinal lymphadenopathy concerning lymphoma.

3 | DISCUSSION

Sarcoidosis granuloma is thought to result from an exaggerated immune response to an unknown antigen, leading to an inappropriate T lymphocyte response.[3] In 5%–10% of patients with sarcoidosis, clinical manifestations of neurosarcoidosis have been reported.[1] Approximately 52% of 1088 patients with sarcoidosis, in a meta-analysis, presented with neurological symptoms, while 67% presented with pulmonary involvement.[4] A definitive diagnosis is generally made using a histopathological specimen that typically exhibits non-necrotizing granulomas associated with chronic inflammation.[1]

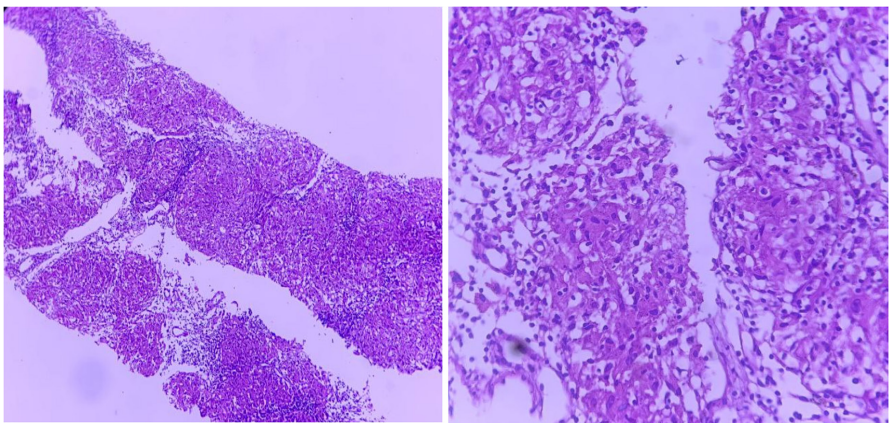

FIGURE 4 Specimen of right lung hilar mass and subcarinal lymph node. In both, non-necrotizing granulomatous inflammations were seen (sarcoidal-like).

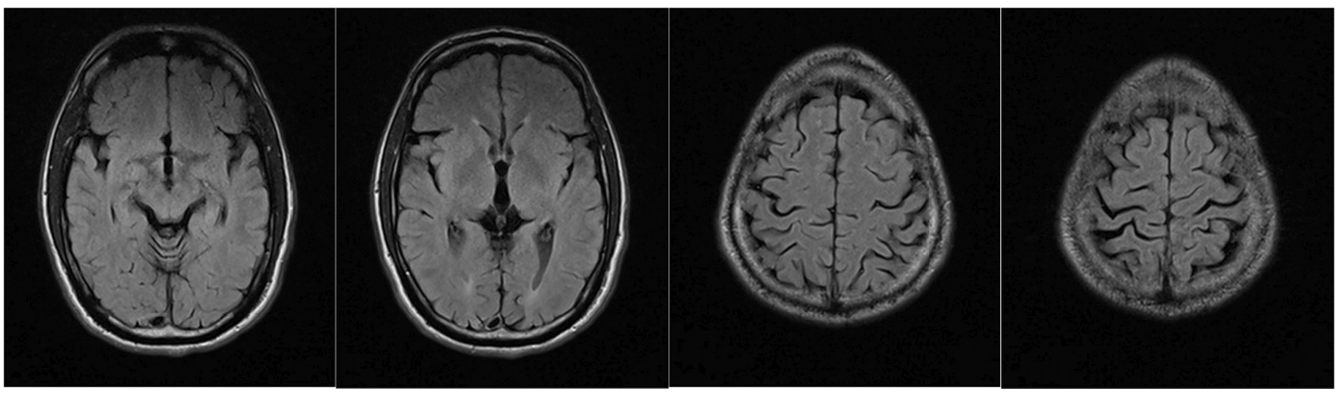

FIGURE 5 Brain MRI, periventricular regions showed a few high signal lesions on the T2-flair scan.

TABLE 1 Demographic and clinical information on cases with a diagnosis of neurosarcoidosis.

No.	Authors	Age	Sex	Symptoms on admission	Paraclinical findings	Treatment	Outcome
1	Ryan Shields et al.[13]	29	F	Numbness Paresthesia Back pain	Brain and Spinal cord MRI: Extradural lesions, with spinal cord compression at T8 Lumbar puncture: increased CSF neutrophils, lymphocytes, mono/macrocytes, and protein	Methotrexate Infliximab Corticosteroids	Improved
2	Ateeq Mubarik et al.[14]	76	M	Confusion	Brain MRI: bilateral periventricular, centrum semiovale Bone and liver Biopsy: Noncaseating granulomas	Corticosteroids	Improved
3	Sarita k. sapkota et al.[15]	49	F	Dizziness Slurred speech Handshaking Seizure	Brain MRI: Smooth dural enhancement EEG: Non-specific slowing without any electrographic seizures or epileptiform discharges Thorax and abdomen CT: bilateral hilar lymphadenopathy	Azathioprine Corticosteroids Phenytoin Lacosamide	Improved
4	J Chald hoyle et al.[16]	40	F	Headache Fatigue Back and neck pain Progressive visual loss	Brain MRI: bilateral optic nerve involvement Chest CT: grade I hilar adenopathy Lung Biopsy: Noncaseating granulomatous	Corticosteroids Thalidomide	Improved
5	A. Lorentzen et al.[17]	40	M	Neck pain Right arm weakness Paresthesia Changing in temperature Sensation in the left arm	Spinal cord MRI: A medullar lesion stretching from the level of C3 to C5 Chest CT: Thickening of the bronchial walls and multiple enlarged glands in the mediastinum Biopsy of the mediastinal glands: Noncaseating epithelioid granulomas	Corticosteroids	Improved
6	Hayam Hamodat et al.[18]	54	M	Right upper quadrant abdominal pain Diffuse lymphadenopathy	Abdomen and pelvis CT: Diffuse lymphadenopathy Chest CT: Bilateral hilar and mediastinal lymphadenopathy concerning lymphoma Biopsy of a lymph node: Noncaseating granulomas Spine MRI: Abnormal thickening and enhancement of paravertebral soft tissues along with the right intercostal spaces that extended from T7 to T12	Corticosteroids, Immunosuppressant	Improved
7	Ernestina Santos et al.[19]	49	M	Cough Numbness Pain at the right knee	Chest CT: Bilateral hilar lymphadenopathy Spine MRI: The increased heterogeneous signal within the S1 nerve root and of the nerve root ganglion on T2 images Skin nodules Biopsy: Erythema nodosum	Methotrexate Cyclophosphamide Infliximab	No significant improvement
8	Melissa Vereecken et al.[20]	71	F	Visual loss in the left eye	Brain MRI: Mass infiltration of the infraorbital and the intracranial optic nerve Chest CT: Hilar lymph nodes Lungs Biopsy: Noncaseating granulomatous lesion	Corticosteroids Azathioprine	Improved

TABLE 1 (Continued)

No.	Authors	Age	Sex	Symptoms on admission	Paraclinical findings	Treatment	Outcome
9	Our case	42	M	Swelling of the right wrist joint Decreased right eye vision Severe fever and chills Cough Body aches	Chest CT: Bilateral hilar lymphadenopathy Brain MRI: Few small round lesions in the cerebellum	Corticosteroids Famotidine Cetirizine Domperidone	Improved

Abbreviations: CT, Computerized tomography; EEG, Electroencephalogram; F, Female; M, Male; MRI, Magnetic resonance imaging.

The most typical complication caused by neurosarcoidosis is cranial neuropathy which is seen in 80% of patients in Joseph's study in 2008.[5] Cervical and thoracic segment involvement is more commonly reported than lumbosacral involvement, similar to our case.[6] Table 1 describes studies on patients with a new diagnosis of neurosarcoidosis.

According to Zajicek et al.[7] study, the most prominent finding was an elevation in protein levels, which is a sign of a dysfunctional blood–brain barrier(BBB). Even if there are no significant number of inflamed cells in the CSF and serum ACE levels are not elevated, the best estimate would be an ACE index equivalent to an IgG index. An evaluation of chest radiographs by Zajicek showed that 30% of patients with neurosarcoidosis had positive results.[7] As demonstrated in the study by Pichler et al.[8] a conjunctival biopsy is of low utility in diagnosing neurosarcoidosis in patients with unknown neuroinflammatory diseases. A recent case series showed that MRI is more sensitive than CT in assessing patients with inflammatory brain diseases.[7]

In a study by Souliere et al.[9] two patients with isolated, sudden-onset sensorineural hearing loss as the clinical manifestation of sarcoidosis were investigated. These abnormalities included white-matter lesions, hydrocephalus, mass lesions in the brain parenchyma, meningeal enhancement of parenchymal lesions, and lesions of the optic nerves. However, based on the brain MRI, our patient did not show any lesions in the vestibulocochlear nerve. Up to 25% of patients with neurosarcoidosis have ocular involvement.[10]

In the case of neurosarcoidosis, treatment is constantly required, and the treatment routine relies upon professional opinion and scientific manifestations.[11] Neurosarcoidosis is typically treated with corticosteroids despite many immunosuppressive agents being used as adjunctive agents.[1] As demonstrated in a meta-analysis, entire improvement in neurosarcoidosis is determined in 27% of patients, complete improvement in 32%, and severe disease in 24%, while deterioration and death happened in 6% and 5% of patients, respectively.[4] Therefore, regardless of the appropriate therapy, some cases do not improve or become worse. In this study, we prescribed Prednisolone for our patient to reduce inflammation. The main focus of this case report was to demonstrate the diagnostic difference between MS and neurosarcoidosis and the clinical manifestation of the disease. Distinguishing between neurosarcoidosis and MS is sometimes complicated. Using CSF analysis may not be very useful since it may reveal similar abnormalities in both disorders.[12] All manifestations are not identical between MS and neurosarcoidosis; nonetheless, persistent meninges enhancements or parenchymal enhancements in tissue are not expected in MS and likely indicate a granulomatous process. In conclusion, early diagnosis assists in decelerating disease progression through the administration of proper treatment.

AUTHOR CONTRIBUTIONS

Omid Mirmosayyeb: Conceptualization; project administration; supervision; validation; writing – review and editing. **Mahtab Mohammadzamani:** Conceptualization; writing – original draft. **Sara Bagherieh:** Conceptualization; methodology; visualization. **Elham Moases Ghaffary:** Methodology; validation; writing – review and editing. **Elham Sadat Azimi:** Investigation; methodology; writing – review and editing. **Aysa Shaygannejad:** Investigation; methodology; writing – review and editing. **Vahid Shaygannejad:** Conceptualization; project administration; supervision; validation.

CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest.

FUNDING INFORMATION

We did not have any financial support for this study.

DATA AVAILABILITY STATEMENT

The authors confirm that the data supporting the findings of this study are available in the article.

CONSENT

Written informed consent was obtained from the patient to publish this report in accordance with the journal's patient consent policy.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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