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CASE REPORT **OLGU SUNUMU**

NEUROSARCOIDOSIS PRESENTING WITH SEIZURE: CASE REPORT

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ABSTRACT

Sarcoidosis is a granulomatous disease primarily affecting the lungs and lymph nodes as well as several other systems. By affecting both the central and the peripheral nervous system, it may present with various different neurological features. We report a case with neurosarcoidosis presenting with seizures.
Keywords: Sarcoidosis, neurosarcoidosis, epilepsy, encefalopathy, neurorheumatology, lymphadenopathy.

NÖBET İLE PREZENTE OLAN NÖROSARKOİDOZ OLGUSU

ÖZ

Sarkoidoz öncelikli olarak akciğer ve lenf nodlarının tutulumu ile giden ve pek çok sistemi etkileyebilen bir granülamatoz hastalıktır. Nörolojik olarak, santral sinir sistemi ve periferik sinir sistemini tutarak farklı tablolarla prezente olabilir. Bu çalışmada epileptik nöbetlerle başvuran ve ileri tetkikler sonucunda nörosarkoidoz tanısı alan bir olgu sunulmuştur.
Anahtar Sözcükler: Sarkoidoz, nörosarkoidoz, epilepsi, ensefalopati, nöroromatoloji, lenfadenopati.

INTRODUCTION

Sarcoidosis is a granulomatous disease of unknown etiology, which often affects many systems and organs as well as lung, skin, and eye involvement. The incidence of sarcoidosis is estimated to be 4/100,000 in Turkey. It is usually seen in young adults under 50 years of age and is quite common between 20 and 40 years of age. It is slightly more common in women compared to men (1).

Central and/or peripheral nervous system involvement has been reported in 5-20% of patients with systemic sarcoidosis. Neurosarcoidosis may be clinically presented with a cranial neuropathy, aseptic meningitis, hydrocephalus, headache, seizure, neuropsychiatric symptoms, neuroendocrine dysfunctions, myelopathy, and peripheral neuropathy. Peripheral neuropathy is detected in approximately 20% of patients even though cranial neuropathy (usually peripheral facial paralysis) is seen in 50-75% of patients diagnosed with neurosarcoidosis. Approximately 20% of patients experience focal or generalized seizures. Neurosarcoidosis, which starts with epileptic seizures, is rare (2,4-7).

CASE REPORT

A 54-year-old female patient was admitted to our clinic with the complaint of looking at a fixed point 2 months ago, seizures in the form of contractions, and unconsciousness and gait abnormality added for 20 days. It was reported that the patient received Brucella treatment at one center for fever, weakness, sleepiness, joint ache, and headache 12 years ago but did not benefit from it, and then recovered when the patient was treated at another center with the diagnosis of

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brain edema and encephalitis. After that, it was learned that the patient, who had no complaints for years, had a seizure lasting 1-2 minutes with a loss of consciousness 1 year ago, accompanied by postictal confusion lasting approximately 10 minutes after locking of the jaw and contraction of the hands. Various examinations at that time were reported to be normal.

It was learned that the patient, whose absence seizure started two months ago, had a seizure accompanied by a short period of unconsciousness with a burning sensation on the back, an increase in absence seizures and contraction for the last 20 days, and then a fluctuating state of consciousness emerged with gait abnormality. The patient was admitted to an infection ward at an external center with brain magnetic resonance (MR) results and pre-diagnosis of encephalitis. Lumbar puncture revealed high protein levels and low glucose levels (simultaneous fingertip glucose level was 118 mg/dL), ceftriaxone, acyclovir, and levetiracetam treatment was started. The case with increased consciousness and neurological results was referred to our clinic for further examination and treatment. Consciousness was slightly apathetic and reaction time prolonged but the patient was cooperative-oriented in their neurological examination. Bilateral symmetrical paraparesis at the level of 3/5 in proximal muscles and 4/5 in distal muscles, bilateral DTR hyperactivity, bilateral Trömner signs, bilateral moderate kinetic tremor were detected. The sense of vibration was reduced in the distal parts of the bilateral lower extremity and the patient could walk a short distance with support.

Brain contrast MRI showed results of nodular and leptomeningeal involvement around the brain stem, prominently in the parasellar region and central sulcus in bilateral cerebral hemispheres (Figure 1,2). In addition, leptomeningeal contrast involvement was observed in cervical and thoracic spinal localization (Figure 3).

Laboratory examination revealed pancytopenia (Hb:10.9 g/dl [N:11.67-15.47], WBC:3.81 103/mcL [N:4.07-11.23], PLT: 151 103/mcL [N:158.7-387.7]), low vitamin D (3.5 ng/ml [N:10-60]), and hyperlipidemia (Total Cholesterol:247 mg/dL [150-240], LDL:150 mg/dl, Triglyceride:316 mg/dl). Infectious (Salmonella, Brucella, Lyme, VDRL, herpes, Toxo, HIV, TB) and collagen tissue tests (ANA, Anti-ds DNA, ANCA, anti-RNP, Anti-SSA, Anti-SSB, Anti-SM) were negative. ARB and PPD were negative in sputum. Protein electrophoresis was normal, no paraproteinemia was detected in the

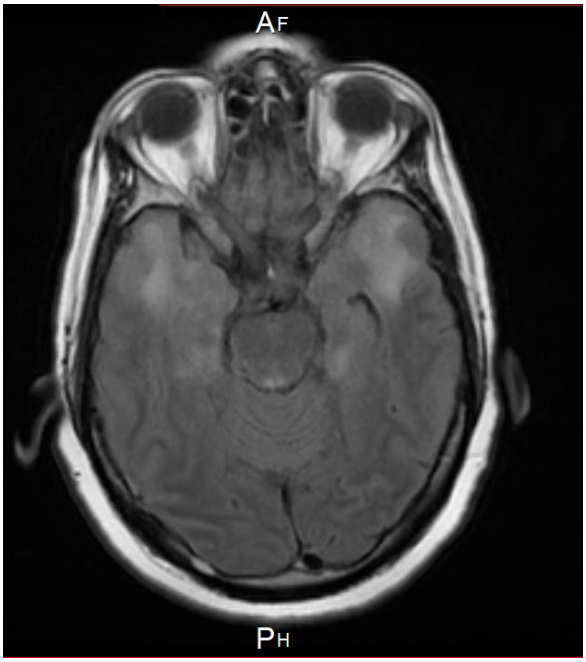

Figure 1. Signs of involvement in T2 FLAIR sequences in brain parenchyma in bilateral temporal, hippocampal, and paracellular regions.

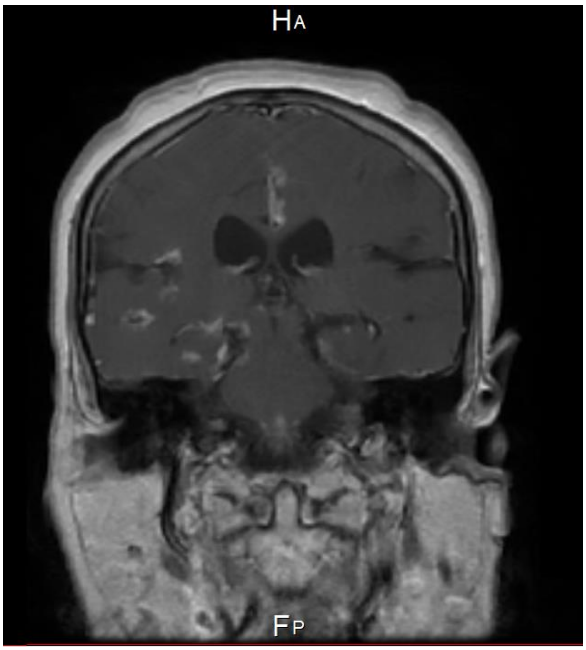

Figure 2. Signs of nodular leptomeningeal contrast involvement around basal cisterns and central sulcus in T1-weighted coronal sections.

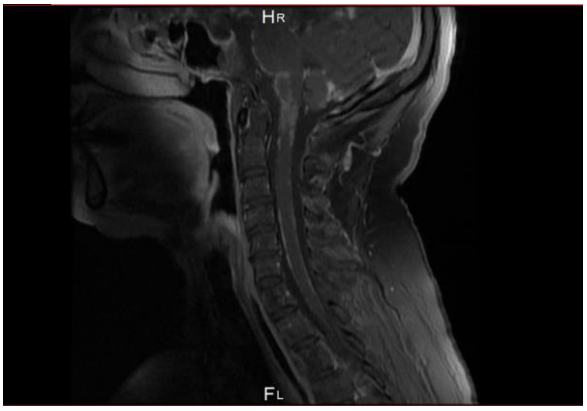

Figure 3. Signs of contrast involvement in the short segment of the cervical spinal cord and brain stem in T1-weighted imaging.

immunofixation test. Urine Bence Jones was negative. Angiotensin-converting enzyme (ACE) level was 100 U/L (N:9-67). Lumbar puncture revealed high protein levels (247 mg/dL) and low glucose levels (25 mg/dL) (simultaneous fingertip glucose level was 124 mg/dL). No cells were observed in CSF direct microscopy. Rare blood cells were detected in the CSF cell cytology.

EEG was reported as EEG examination in which slow activity with subcortical feature (diffuse bilateral synchronous discharges of sharp theta activities of 1-1.5 sec were observed at rest and HPV) paroxysms were observed.

Thoracic computed tomography (CT) revealed paratracheal lymphadenomegalies (Figure 4). Abdominal CT revealed splenomegaly and peripancreatic, periceliac, paraaortic, bilateral iliac, and inguinal multiple lymph nodes. Noncalcified granulomas were detected in the biopsy of the inguinal lymph node (Figure 5).

In addition, chronic uveitis results were detected by eye consultation. Neurosarcoidosis was diagnosed with clinical, radiological, and histopathological results and the patient was given intravenous methylprednisolone 20 mg/kg/day for 3 days. Afterward, 80 mg prednisolone from 1 mg/kg/day was given for 4 weeks. Post-treatment control brain MRI was performed and significant improvement was observed in the lesions. Levetiracetam 2000 mg/day was continued. The patient whose seizure was not observed was discharged to continue with the outpatient clinic follow-ups. In addition, no immunosuppressive agent was used in the maintenance treatment of the patient. An informed consent form was signed by the patient for this case report.

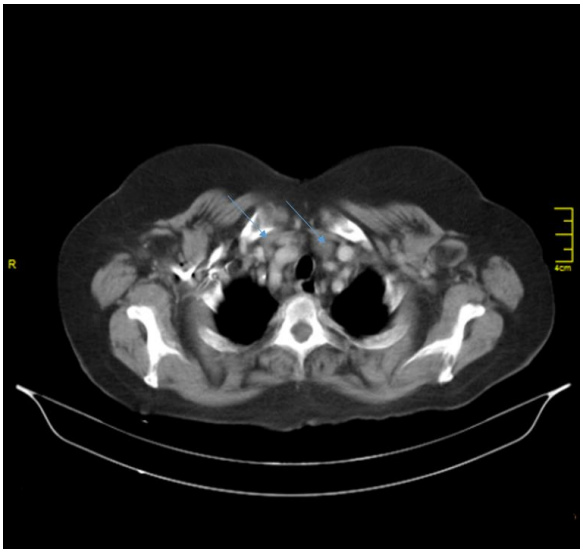

Figure 4. Paratracheal lymphadenomegalies in thoracic CT.

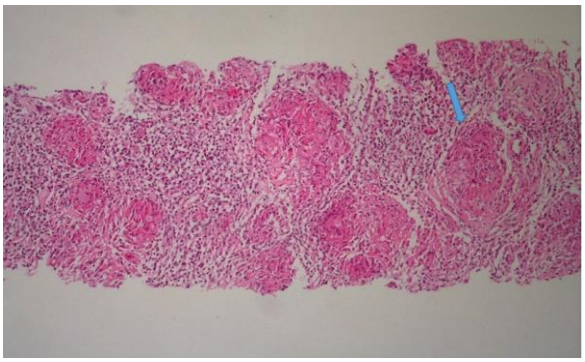

Figure 5. Noncalcified granulomas seen in the inguinal lymph node biopsy.

DISCUSSION AND CONCLUSION

It was planned to investigate acute disseminated encephalomyelitis, neurobrucellosis, tuberculous meningitis, viral encephalitis, vasculitis, neurosarcoidosis, central nervous system (CNS) vasculitis, CNS lymphomas, and paraneoplastic processes in the differential diagnosis in our case with recurrent seizures, fluctuations in consciousness and gait disorders, clinically encephalomyelopathy, radiologically diffuse white matter involvement, and significant nodular contrast enhancement along with leptomeningeal involvement. Pancytopenia, CSF results, widespread lymphadenopathy in the thorax and abdomen, and elevated ACE detected in the examinations suggested neurosarcoidosis. The diagnosis of sarcoidosis was confirmed with noncalcified granulomas detected in the inguinal

LAP biopsy. The clinic diagnosed the patient with neurosarcoidosis in light of CSF and MRI results.

Sarcoidosis is a non-infectious inflammatory disease characterized by noncalcified granulomas. It affects 87% intrathoracic (hilar node 72%, lung parenchyma 46%), 18% skin, and 28% peripheral lymph nodes even though it can involve many systems (2).

It often clinically presents as a slowly progressive picture within months. However, asymptomatic patients have also been reported as well as acute or subacute forms. It usually occurs with symptoms such as fever, weakness, loss of appetite, weight loss. It then gives results according to the involved organ. Lung involvement occurs at some stage of the disease in 90% of cases. It manifests itself with dyspnea and dry cough in this case. Hemoptysis and sputum are rare. Pleural involvement is rare, but lymphadenomegaly is common in both the thorax and abdomen. Erythema nodosum, maculopapular rash, and subcutaneous nodules may develop as skin involvement. Uveitis may occur in 25% of cases. Bone cysts, joint involvement, and asymptomatic myositis may also be seen. It rarely leads to clinical results even though liver involvement is frequent. Renal, gastrointestinal, and cardiac involvement are also rare (3).

CSF abnormalities exist in more than 50% of patients with neurosarcoidosis. These abnormalities are pleocytosis, increased protein, and decreased glucose levels. In addition, some patients with neurosarcoidosis may have an increase in oligoclonal band or IgG index in CSF. ACE levels, lactic acid, and interleukin 2 receptor levels may also increase. However, none of these abnormalities are specific to neurosarcoidosis (2,5).

Sarcoidosis is confirmed by histopathological diagnosis. Therefore, biopsy material may be taken from here if the patient has organ involvement other than CNS. Chest radiography or thoracic CT should be performed for systemic sarcoidosis. ACE levels in the blood increase in approximately two-thirds of patients but may also be positive in other granulomatous diseases (3). The ACE level was also observed to be high in our case.

Neurosarcoidosis occurs in approximately 10% of patients with systemic sarcoidosis. They are often presented with cranial nerve involvement, especially peripheral facial paralysis and aseptic meningitis even though various neurological involvements are seen. Leptomeningeal involvement is 40% and is frequently seen in the basal. Hypopituitarism or diencephalic syndromes, seizures, cognitive destruction, myelopathy symptoms are seen. Intramedullary involvement is observed in the cervical and upper thoracic in 25% of patients with neurosarcoidosis. Hydrocephalus has been reported in 5-12% of cases (4).

Cases of neurosarcoidosis presenting with epilepsy are rare in the literature (7,8). Epileptic seizures are estimated to occur in 5-20% of neurosarcoidosis cases (9).

Epileptic seizures were observed in 13 (15%) of 79 cases diagnosed with neurosarcoidosis and the disease was presented with epileptic seizures in 8 (10%) of these cases in the most comprehensive study on this subject. Generalized tonic-clonic (92%) was the most common and partial seizure (31%) was the second most common. Seizures of 85% of patients were controlled with steroid therapy and anti-epileptic therapy (10).

The usually selected treatment for neurosarcoidosis is high-dose intravenous or oral methylprednisolone therapy. Immunosuppressant agents such as methotrexate, cyclophosphamide, azathioprine, leflunomide, infliximab, hydroxychloroquine, adalimumab, mycophenolate mofetil can be added to the treatment (11-12). The efficacy of methotrexate in neurosarcoidosis is approximately 60%, similar to pulmonary sarcoidosis (13). Positive responses were observed in several cases with infliximab in cases of corticosteroid-resistant neurosarcoidosis (13). It has been reported that positive results have been obtained with TNF alpha-blockers in patients with cognitive impairment (13). 20-25 Gy radiotherapy is among the treatments that can be considered in patients who do not respond to drug therapy (13). It has been observed due to this case that the possibility of neurosarcoidosis should be considered in cases presenting with a partial seizure at an advanced age and where CNS is affected radiologically and clinically in a diffuse and diffuse manner. Immunosuppressive agents are the primary options even though there is no standardized treatment protocol for its treatment (11). The seizure type and other systemic involvements of the patient should also be taken into consideration when planning anti-epileptic treatment.

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Ethics

Informed Consent: The authors declared that informed consent form was signed by the patient.

Copyright Transfer Form: Copyright Transfer Form was signed by the authors.

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