

# A CASE OF PROBABLE NEUROSARCOIDOSIS PRESENTING AS UNILATERAL OPHTHALMOPLEGIA

Mirjana Jovičević<sup>1</sup>, Marija Žarkov<sup>1</sup>, Tamara Rabi Žikić<sup>1</sup>, Duško Kozić<sup>2</sup>, Sonja Rajić<sup>3</sup>  
and Dušica Simić Panić<sup>4</sup>

<sup>1</sup>Clinical Department of Neurology; <sup>2</sup>Diagnostic Imaging Center, Oncology Institute of Vojvodina; <sup>3</sup>Clinical Department of Neurology, Emergency Center, <sup>4</sup>Department for Medical Rehabilitation, Clinical Center of Vojvodina, Medical Faculty, University of Novi Sad, Novi Sad, Serbia

**SUMMARY** – Sarcoidosis is a multisystem disease of unknown etiology, characterized by the presence of noncaseating epithelioid granulomas and accumulation of T lymphocytes and mononuclear phagocytes, which damages the normal structure of tissues. Isolated form of neurosarcoidosis is very rare and difficult to diagnose and requires histologic confirmation of noncaseating granulomas in the nervous tissue. We report a case of a 55-year-old female who had probable isolated neurosarcoidosis based on magnetic resonance imaging findings of relapsing pachymeningitis with an inflammatory process in the apex of the right orbit and pseudotumor inflammation of the superior and lateral recti of the right eye. Diagnosis was further verified by positive response to dual corticosteroid and immunosuppressive therapy. Our case demonstrates the importance of considering isolated neurosarcoidosis as a potential underlying etiology of painful ophthalmoplegia, even without systemic manifestation of the disease.

**Key words:** *Neurosarcoidosis – diagnosis; Ophthalmoplegia; Magnetic resonance imaging; Central nervous system diseases; Case reports*

## Introduction

Sarcoidosis is a multisystem disease of unknown etiology, characterized by the presence of noncaseating epithelioid granulomas and accumulation of T lymphocytes and mononuclear phagocytes, which damage the normal structure of tissues. It may involve any tissue, and it most commonly affects the lungs, skin, lymph nodes, eyes, liver, nervous system, and parotid gland<sup>1</sup>. Sarcoidosis of the nervous system occurs in 5%-15% of all sarcoidosis cases<sup>2</sup>, and its isolated form is very rare and difficult to diagnose<sup>3,4</sup>. Neurosarcoidosis most frequently clinically manifests with cranial neuropathies<sup>2</sup>. Painful ophthalmoplegia

refers to periorbital or hemicranial pain accompanied by ipsilateral ocular motor palsies; it involves diverse etiologies and requires comprehensive evaluation<sup>5</sup>.

The diagnosis of neurosarcoidosis is established on the basis of the clinical and radiological picture, as well as histologic confirmation of noncaseating granulomas<sup>2-4</sup>. The diagnosis may be relatively evident if neurologic symptoms appear in a patient with definitive systemic sarcoidosis. However, patients with isolated neurosarcoidosis present a greater diagnostic challenge<sup>6</sup>. Depending on the presence of systemic sarcoidosis, neurologic manifestations and response to treatment, patients may be classified into those with possible, probable and definitive neurosarcoidosis<sup>7</sup>. A definitive diagnosis requires histologic confirmation of noncaseating granulomas in the nervous tissue. Magnetic resonance imaging (MRI) is a highly sensitive method in the diagnosis of neurosarcoidosis; however, it lacks specificity. It is useful in following

Correspondence to: *Prof. Mirjana Jovičević, MD, PhD*, Clinical Department of Neurology, Clinical Center of Vojvodina, Hajduk Veljka 1, 21000 Novi Sad, Serbia  
E-mail: [jovpedja@eunet.rs](mailto:jovpedja@eunet.rs)

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the patient's response to treatment, as well as in the differential diagnosis. Abnormal findings of the cerebrospinal fluid (CSF) are present in 80% of patients with neurosarcoidosis, including mild pleocytosis and proteinorrachia and, occasionally, decreased glucose levels. Increased CSF levels of angiotensin-converting enzyme (ACE) are seen in 55% of patients with neurosarcoidosis, whereas increased serum levels of ACE are present in 70%-80% of these patients. Also significant is the evidence of hypercalcemia and hypercalciuria, which indicates that the disease is active<sup>8</sup>.

There are no clear guidelines and indications for the treatment of neurosarcoidosis. Empirically, the treatment of choice is corticosteroid therapy. Initial recommended dosage is oral prednisolone 1 mg/kg/day for 6-8 weeks. For more severe cases, intravenous methylprednisolone 1000 mg/day for three days is recommended<sup>8</sup>. In patients with contraindications for corticosteroid treatment, cytotoxic medication is used, such as methotrexate, azathioprine, cyclosporine, and cyclophosphamide<sup>3,8,9</sup>.

## Case Report

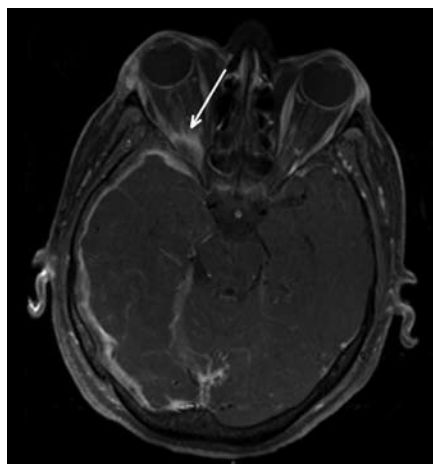
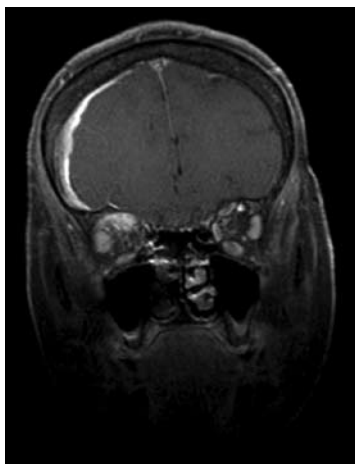
We report a case of probable neurosarcoidosis in the absence of pulmonary features. A 55-year-old female was admitted to our neurology department for severe headaches, double vision and ptosis on the right eye, which had lasted for one month. Neurological findings showed external ophthalmoplegia on the right side

with chemosis and exophthalmos of the right eye. The patient had previously been examined by a neurosurgeon because of the same complaints, and brain computed tomography (CT) finding obtained at that time was interpreted as subdural hematoma on the right.

One year before current admission, the patient had been hospitalized for depression, and at the same time she had been diagnosed with pneumonia. In addition, the patient had Hashimoto's thyroiditis and suffered from recurrent bilateral otitis media. Brain MRI showed thickening of the leptomeninges on the right side (previously interpreted as subdural hematoma), obliteration of the venous sinuses without thrombosis on the right side, inflammation of the superior and lateral recti of the right eye, and granulomatous tissue in the apex of the right orbit, a finding suggestive of neurosarcoidosis (Figs. 1, 2 and 3).

Lumbar puncture was performed, but cytochemical findings of the CSF were normal. There was elevated calciuria, whereas serum levels of ACE and ionized calcium were within the normal ranges. Thoracic and abdominal CT findings were normal, which excluded the presence of pulmonary sarcoidosis.

Treatment was initiated with prednisolone 60 mg *per* day and thereupon the clinical picture improved and CT findings showed regression of the changes. Repeated brain MRI performed after one month showed significant regression of the inflammatory process in the leptomeninges, so tapering off the corticosteroid therapy was started.



*Fig. 1. Coronal MRI sequence showing inflammation of the superior and lateral recti of the right eye.*

*Fig. 2. Axial MRI sequence showing granulomatous tissue in the apex of the right orbit.*

*Fig. 3. Brain MRV shows obliteration of the venous sinuses (sigmoid and transverse) without thrombosis on the right side.*

However, one month later the patient had a relapse of disease with severe retro-orbital headache, more pronounced exophthalmos and ptosis of the right eye. Brain MRI showed relapsing pachymeningitis with an inflammatory process in the apex of the right orbit and pseudotumor inflammation of the superior and lateral recti. CSF findings showed mild pleocytosis, with no signs of proteinorrhachia. All immunologic analyses were normal, and testing for *Mycobacterium tuberculosis* in the CSF was negative.

Pulmonologist was consulted, and dual therapy was introduced with prednisone 20 mg 2+1+0 and methotrexate 7.5 mg 1x1 two times *per week*, upon which the patient's condition improved.

## Discussion

The differential diagnosis of painful ophthalmoplegia is extensive and includes various different etiologies<sup>5-7</sup>. Most sinister of those are neoplasms (primary intracranial tumors, metastasis) and vascular etiologies (aneurysms, carotid dissection, carotid-cavernous fistula and cavernous sinus thrombosis)<sup>6,7</sup>. In addition, there are clinical entities such as ophthalmoplegic migraine, paranasal sinus mucocele, trauma and iatrogenic injuries to be considered<sup>5</sup>. In our patient, these etiologies were ruled out by neuroimaging findings. Painful ophthalmoplegia may also be observed in pathologic conditions such as diabetes, meningitis and infectious diseases (fungal, bacterial and viral infections). Further differential diagnosis of painful ophthalmoplegia consists of inflammatory masses such as sarcoidosis, Tolosa-Hunt syndrome, systemic lupus erythematosus, Wegener's granulomatosis, orbital pseudotumor, Churg Strauss syndrome, giant cell arteritis, and thyroid orbitopathy<sup>7</sup>. Considering the clinical presentation and laboratory findings, we considered sarcoidosis and Tolosa-Hunt syndrome as likely diagnoses. In this case, characteristic granulomatous changes were typical of sarcoidosis. In addition, Tolosa-Hunt syndrome is characterized by abnormal blood cell counts, positive antinuclear antibodies and increased serum globulins, which was not the case in our patient<sup>8,9</sup>.

Since neuroimaging findings were consistent with neurosarcoidosis and other diagnostic methods ruled out the presence of a systemic form of the disease, followed by the good treatment response, we may con-

clude that our case was probable neurosarcoidosis. In our patient, neurosarcoidosis presented itself with painful ophthalmoplegia as the first symptom, which is extremely rare and we believe that there is only one such case previously described in the literature<sup>7</sup>. Our case demonstrates that in patients with painful ophthalmoplegia, neurosarcoidosis should be considered as a differential diagnosis, even if there is no systemic manifestation of the disease.

However, despite the diagnostic procedures applied and the patient's favorable response to corticosteroid and immunosuppressive drugs, in order to establish a definitive diagnosis of isolated neurosarcoidosis, biopsy confirmation would be required<sup>10</sup>.

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## Sažetak

## SLUČAJ VJEROJATNE NEUROSARKOIDOZE KOJI SE MANIFESTIRA KAO JEDNOSTRANA OFTALMOPLEGIJA

*M. Jovičević, M. Žarkov, T. Rabi Žikić, D. Kozić, S. Rajić i D. Simić Panić*

Sarkoidoza je multisistemska bolest nepoznate etiologije koju karakterizira prisutnost nekazeoznih epitelioidnih granuloma s nakupljanjem T limfocita i mononuklearnih fagocita te narušavanjem normalne tkivne arhitektonike. Izolirani oblik neurosarkoidoze je vrlo rijedak i teško ga je dijagnosticirati te zahtijeva histološku potvrdu nekazeoznih granuloma u živčanom tkivu. Prikazujemo slučaj 55-godišnje žene koja je vjerojatno imala izoliranu neurosarkoidozu, što je zaključeno na temelju nalaza magnetske rezonancije koji je pokazao recidivirajući pahimeningitis s upalnim procesom u vrhu desne orbite i pseudotumorskom upalom gornjeg i vanjskog ravnog mišića desnog oka. Dijagnoza je dodatno potvrđena pozitivnim odgovorom na dvojni kortikosteroidnu i imunosupresivnu terapiju. Slučaj naše bolesnice pokazuje važnost razmatranja izolirane neurosarkoidoze kao potencijalnog etiološkog uzroka bolne oftalmoplegije, čak i bez sistemske manifestacije bolesti.

*Ključne riječi: Neurosarkoidoza – dijagnostika; Oftalmoplegija; Magnetska rezonancija, snimanje; Živčani sustav, bolest; Prikazi slučaja*