

Coexistence of neurosarcoidosis and multiple sclerosis

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ABSTRACT - Sarcoidosis is a multisystem inflammatory disease of unknown etiology that predominantly affects the lungs and intrathoracic lymph nodes, but in 6% of cases it also occurs in central or peripheral nervous system. Multiple sclerosis (MS) is an immune-mediated inflammatory disease that attacks myelinated axons in the central nervous system. Coexistence of sarcoidosis and other autoimmune diseases like MS is rarely reported in the literature. We present a case report of a patient with coexisting sarcoidosis and MS, with a positive family history of MS. Symptoms of sarcoidosis appeared three years before the onset of symptoms typical for MS. Similarity of demyelinating lesions in the nervous system, increased IgG in cerebrospinal fluid and good response to corticosteroid treatment point to similar etiology. The onset of diseases like sarcoidosis and MS in the same patient over a period of only a few years opens the question whether the two separate entities come in sequence or the onset of sarcoidosis occurs during development of typical clinical presentation of MS.

Key words: sarcoidosis, encephalomyelitis, multiple sclerosis

INTRODUCTION

Sarcoidosis is an inflammatory disorder of unknown origin, characterized by epithelioid cell granulomas in various organs (1). The disease can occur suddenly or gradually, followed by complete or partial remission. Typically, the diagnosis of sarcoidosis is confirmed by a pathologic radiological finding of the lung, hypercalciuria and hyperglobulinemia, anergy to skin tests, higher value of angiotensin-converting enzyme (ACE), epithelial granulomas in histopathologic analysis of mediastinal

lymph nodes (Figs. 1 and 2), or pathologic skin nodes or bone cysts, especially in hands, and positive Kveim test (2). Cerebrospinal fluid (CSF) analysis shows increased IgG, pleocytosis with protein-

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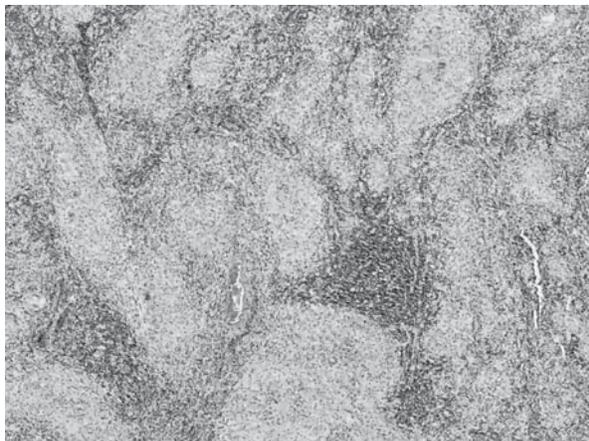


Fig. 1. Sarcoidosis. Microscopic view of granulomatous reaction in the lymph node (HE, X40).

orrhachia, hypoglycorrachia and impaired blood brain barrier (BBB) (3).

Although sarcoidosis primarily affects the lungs, in 6% of cases neurologic symptoms are the first indicators of the disease. Although the symptoms of sarcoidosis are different from those of multiple sclerosis (MS), patients with sarcoidosis and MS are of similar ages and both have damage to cranial nerves, myelopathy, demyelinating lesions of the central nervous system (CNS) and IgG in CSF, which can result in inaccurate diagnosis (4).

Some forms of sarcoidosis are difficult to distinguish from MS, especially if sarcoidosis affects optic nerve and spinal cord. Myelopathy in sarcoidosis usually manifests as chronic progressive paraparesis as a consequence of compression, ischemia and/or parenchymal damage. Along with positive Lhermitte's sign, the only distinction of this myelopathy from the chronic progressive form of MS is clinical presentation. Damage to the optic nerve can be related to optical neuritis in MS (1).

In 50% of cases of neurosarcoidosis, ACE is elevated in CSF, but it is not a specific feature of the disease (5). Intrathecal synthesis of IgG is not common, but the increased permeability of BBB in sarcoidosis can be useful on differential diagnosis against MS. Some researches showed a specific, locally formed IgG in the CSF of patients with sarcoidosis, with positive reaction to Kveim substance (Kveim specific IgG) (6).

The possible relapsing-remitting course of the disease, demyelinating damage detected on magnetic resonance (MR) analysis of CNS and positive IgG in CSF make the differential diagnostic resolution of MS and sarcoidosis. The diagnosis is finally confirmed by laboratory tests that indicate an increase

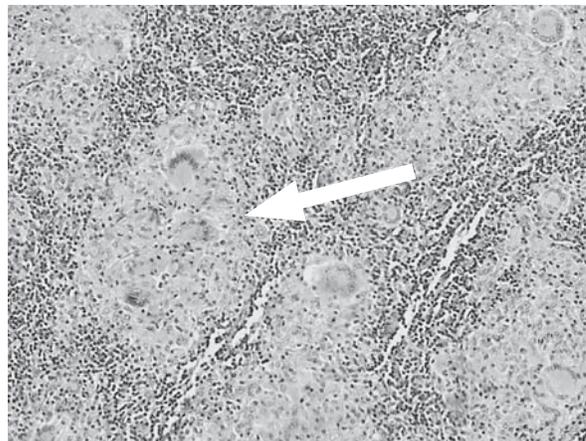


Fig. 2. Sarcoidosis. Microscopic appearance of noncaseous granulomas in the lymph node, arrow (HE, X200).

in the concentration of beta-microglobulin, ACE in serum and CSF, hypercalciuria, positive Kveim test and finding of Kveim specific IgG in CSF (6). Pathognomonic radiological findings of the lung and bone, and histopathologic confirmation of epithelioid granuloma are very important for definitive diagnosis (7).

MR analysis of CNS shows periventricular white matter damages in a quarter of patients with neurosarcoidosis. These changes are difficult to distinguish from damages in MS. Inflammatory leptomeningeal scarring (adhesions), thickening around the chiasm and nerve roots, subependymal granulomas, hydrocephalus and microinfarcts as a result of secondary angiopathy suggest sarcoidosis, but not MS (8). Persistent contrast imbibitions of parenchymal lesions are related to granulomatous damages in sarcoidosis, which is rare in MS (9).

CASE REPORT

A man born in the mountainous area had a positive family history of MS. At the age of 32, mediastinoscopy biopsy was performed due to enlarged mediastinal lymph nodes, with diagnosis of pulmonary sarcoidosis treated with corticosteroids for 18 months. Three years later, at the age of 35, paresthesias of the right lower extremity followed by gradually increasing weakness were observed. These symptoms were transient. At the age of 38, he felt pain in the left eye, with fogging and occasional double vision, and he was admitted to the hospital.

In somatic status, asthenia and less painless subcutaneous nodules in lower legs were found. In neu-

rologic status, a mild right pyramidal deficit, absence of abdominal skin reflexes bilaterally, right sided dysmetria and horizontal nystagmus on the left eye and hemihyesthesia on the right side of the forehead were recorded. Routine examination showed mild lymphocytosis and lower values of serum Ca and Mg, but without hypercalciuria, and slightly elevated levels of serum ACE. Hepatitis markers and serology for toxoplasmosis, syphilis and borreliosis were normal. Cryoglobulins and antinuclear and antimitochondrial antibodies were negative. Values of the complement components were normal. Analysis of HLA typing showed A1, A2, B5, DR 5, DRW6. The papillae of both optic nerves were pale. Radiographic evaluation of the lungs and respiratory functions showed normal findings. In CSF, protein values were normal with 10 sediment cells, lymphocytes, monocytes and plasma cells.

The patient was discharged as a case of neurosarcoidosis. During hospital stay, he received ACTH (Alexander's scheme), followed by improvement.

Five years later, at the age of 43, he was rehospitalized due to walking trouble. Somatic status was normal. Neurologic examination showed paraparesis, more pronounced in the right leg, and ataxia with heeling on the right side and horizontal nystagmus on the left eye. Analysis of visual evoked potentials (VEP) showed dysfunction of both optic tracts and somatosensory evoked potentials (SSEP) dysfunction of afferent pathways bilaterally, more

pronounced on the right side. Laboratory findings showed a slightly elevated component of complement C3. Paraprotein concentrations in serum were normal, as well as the values of ACE and Ca in serum and urine. Brain MRI verified disseminated white matter lesions suggesting MS lesions by their size, shape and arrangement, without spinal cord lesions (Fig. 3). Therapy with oral prednisone resulted in improvement. The patient was discharged as a case of MS.

Six years later, at the age of 49, he was rehospitalized due to numbness of the right leg and ataxia. Somatic status was normal. Walking was atactic and paraparetic, the patient used a crutch, with bilateral horizontal nystagmus, right pyramidal and cerebellar deficit and urinary urgency. He received 500 mg methylprednisolone as pulsed therapy over five days in a total dose of 2.5 g and then tetracosactide hexaacetate depot 1 mg intramuscularly, one vial *per* week for one month. Definitive diagnosis was MS.

CONCLUSION

Today, plenty of additional searching facilitates and simplifies the differential diagnosis of neurosarcoidosis and MS, but coincidence of these two diseases is always possible. However, concurrence of both diseases is rarely reported in the literature (10).

Our patient was diagnosed with clinically definitive MS, with positive family history of MS. Three years before the onset of MS symptoms, he developed symptoms of sarcoidosis. The occurrence of both diseases in the same patient within several years opens a question whether it was a sequence of two independent nosologic entity, or the occurrence of sarcoidosis (initial) during development of the typical clinical features of MS. The influence of T cell groups (myelin reactive T cells) and cytokines could be a unique causal mechanism for the occurrence of immune deficiency in both diseases. The similarity of demyelinating damages in the neural axis, IgG in CSF, and efficient response to corticosteroid therapy in MS and sarcoidosis point to at least a partially common etiopathogenetic circuit. The possibility that a disturbed immune system in the presence of one disease (neurosarcoidosis) led to clinical appearance of the other disease (MS) for which there was a genetic predisposition is also a topic for debate (11,12). According to the current knowledge, the pathologic changes in sarcoidosis are caused by cell-me-

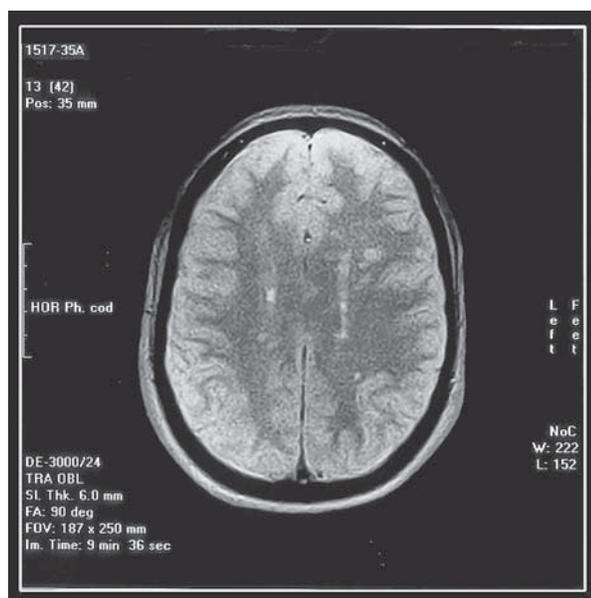


Fig. 3. SE (TR 2500, TE 25/110, SE TR 500, TE 20) Unequal multiple bilateral disseminated lesions in the white substances. The shape, size and arrangement of white matter damages indicate MS.

diated immune response. The pathogenesis of MS has not yet been fully clarified (13). Today, it is interpreted as an autoimmune disease that is at least partly caused by T cell-mediated disorder triggered by environmental factors in genetically prone individuals (14).

In recent years, the influence of T cell group (myelin reactive T cells) and cytokines in the pathogenesis of MS has been intensively studied. There is an assumption that the duration and intensity of the disease are associated with the type and invasiveness of MPB reactive T cells (15). These disturbances of T cell groups could be a unique etiologic immune moment that leads to the occurrence of both diseases.

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