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Case Report

Uveitis and internuclear ophthalmoplegia as ocular manifestations of sarcoidosis

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Abstract

Sarcoidosis is a multisystemic granulomatous chronic disease of unknown etiology with a wide range of clinical presentations. Diagnosis of sarcoidosis in patients with ocular manifestations can be challenging.
We first describe a case of sarcoidosis presented with pulmonary involvement and both uveitis and internuclear ophthalmoplegia as ocular manifestations.
A 55-year-old caucasian woman with non-productive cough and weakness presented with bilateral granulomatous anterior uveitis. Few days later, the patient presented again complaining of horizontal diplopia due to internuclear ophthalmoplegia. The diagnosis of sarcoidosis was made as a result of clinical examination and systemic investigations. Particularly, high-resolution computed tomography scanning of the chest was able to identify bilateral hilar lymphadenopathy not previously detected by chest X-ray. Biopsy confirmed diagnosis showing classic non-caseating granulomas.

Keywords: Biopsy, Diplopia, Internuclear ophthalmoplegia, Sarcoidosis, Uveitis

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Introduction

Sarcoidosis is a multi-systemic granulomatous chronic disease with a wide range of clinical presentations due to the host immune cellular response to a persistent unknown antigen. Etiology is unknown but Mycobacterium tuberculosis seems to be the major disease driver in many patients. Genetic predisposition has been demonstrated and HLA-B8 is the most common allele associated with sarcoidosis.[1]

Sarcoidosis is more frequent in females. The incidence rate varies strongly with age for both sexes, with a first peak between the 2nd and 3rd decade and a second peak between the 5th and 6th decade of life.[2] The incidence varies with race: African-Americans are more commonly affected than Caucasians.[3]

Sarcoidosis is characterized by non-caseating granulomas in involved organs: lungs, lymph nodes, skin, and eyes are more commonly involved, but any organ or system can be affected. The nervous system is affected in 5% of cases.[4]

The most frequent symptoms of sarcoidosis are fever, arthralgia, parotid enlargement, cough, dyspnea, chest pain, weakness, malaise, fatigue and weight loss. However, approximately one-half of patients are asymptomatic.

Ocular involvement occurs in 20–80% of patients at any time during the course of the disease.[5] Sarcoidosis can involve any ocular structure; anterior uveitis is the most common ocular manifestation of sarcoidosis.[6]

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Diagnosis of sarcoidosis in patients with ocular manifestations can be challenging due to the variability in presentation: it is based on laboratory and imaging findings and confirmatory biopsy, showing classic non-caseating granulomas.

In sarcoidosis neuro-ophthalmologic manifestations are also reported. Several authors described cranial neuropathies, meningitis, neuroendocrinological dysfunction, hydrocephalus, seizures, neuropsychiatric symptoms, myelopathy and neuropathies.[7,8] Recently Jovićević et al. described a case of probable neurosarcoidosis presenting as unilateral ophthalmoplegia.[9]

The diagnosis of neurosarcoidosis is often problematic, especially when occurring as an isolated form without other organ involvement.

We describe a case of sarcoidosis presented with pulmonary involvement and both uveitis and internuclear ophthalmoplegia as ocular manifestations.

Internuclear ophthalmoplegia (INO) is a disorder of eye movements caused by a lesion in an area of the brain called the medial longitudinal fasciculus (MLF). The most common causes of INO are multiple sclerosis and brainstem infarction. Other causes include head trauma, brainstem and fourth ventricular tumors, Arnold-Chiari malformation, infection, hydrocephalus, and lupus erythematosus. Internuclear ophthalmoplegia is clinically characterized by total or partial failure to adduct one eye in lateral gaze and a monocular nystagmus of the abducting eye. It may be unilateral or bilateral. The method of choice for diagnostic imaging of MLF lesion in patients with INO is magnetic resonance.[10]

Case report

A 55-year-old caucasian woman presented to our Clinic complaining of redness, blurred vision and pain in both eyes (OU). Few weeks before, she had a flu-like episode. She also had non-productive cough and weakness. Her history was positive for recurrent respiratory problems during the last months, leading her physicians to make a diagnosis of ''non-specific recurrent bronchitides''. She had a ten-year history of systemic hypertension.

Her visual acuity (VA) was 20/40 in right eye (OD) and 20/25 in left eye (OS). Biomicroscopy revealed granulomatous anterior uveitis in OU (Fig. 1a and b). Gonioscopic examination showed small nodules at trabecular meshwork in OD. Intraocular pressure (IOP) was 26 mmHg in OD and 14 in OS. Vitreous was silent and fundoscopic examination was normal in OU. Topical corticosteroid and mydriatic/cycloplegic agents were prescribed for OU and topical beta-blockers for OD. After three days of treatment, VA was 20/20 in OU, uveitis dramatically improved in OU and IOP in OD was 16 mmHg. Serum investigations for granulomatous uveitis, including ACE, lysozyme, Quantiferon TB Gold, Tuberculin test (Mantoux) and chest X-ray were negative. Few days later, the patient complained of horizontal diplopia. Ophthalmological examination revealed decreased adduction of OD and a left-beating jerk nystagmus on attempted abduction of OS (Fig. 2a and b). Thus, diagnosis of right internuclear ophthalmoplegia (INO) was made and the patient was referred for a complete neurological work-up. Blood pressure was normal and neurologic examination was unremarkable. Magnetic resonance imaging (MRI) of the brain revealed a focal lesion with contrast enhancement in the midbrain (Fig. 2c), then lumbar puncture was planned. Cerebrospinal fluid pressure was normal; an elevated number of leukocytes and inflammatory cells with increased protein content and oligoclonal bands were present. Microbiologic and cytologic analysis rule out infections and tumors.

Diplopia spontaneously disappeared but the patient was consulted again for anterior uveitis recurrence in OD. We prescribed topical corticosteroid and mydriatic/cycloplegic medicaments for OD and required high-resolution CT (HRCT) scanning of the chest.

HRCT scans identified a bilateral hilar lymphadenopathy (BHL) not previously detected by chest X-ray (Fig. 3a). Hilar lymph node biopsy showed typical non-caseating granulomas and diagnosis of sarcoidosis was confirmed (Fig. 3b). Oral corticosteroid 1 mg/kg daily was given, followed by a slower taper to lower doses and the disease was well controlled. No recurrence of uveitis occurred in the follow-up period (8 months). Systemic symptoms gradually reduced.

Discussion

Sarcoidosis is a multisystemic granulomatous chronic disease with a wide range of clinical manifestations.

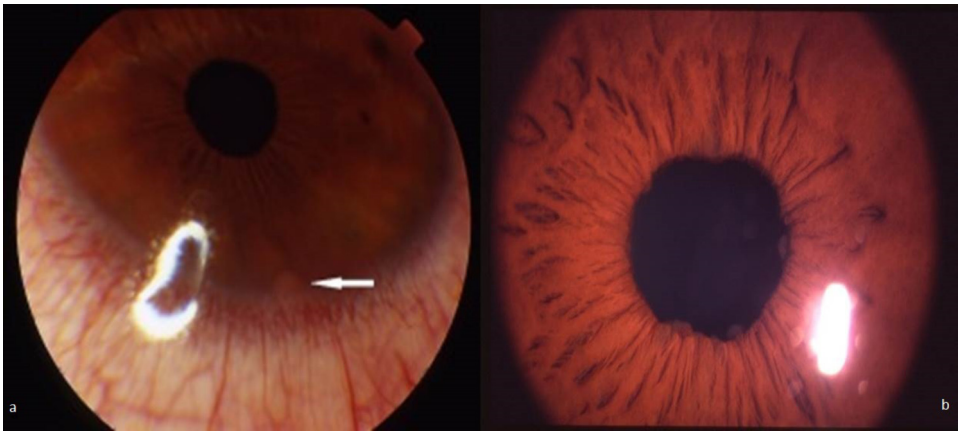

Fig. 1. Slit-lamp biomicroscopy shows granulomatous anterior uveitis. a: In the right eye, a large peripheral granuloma is present inferiorly in the anterior chamber (arrow). In this eye small nodules at trabecular meshwork were found, causing high intraocular pressure. b: Koeppe nodules located on iris pupillary margin (high magnification).

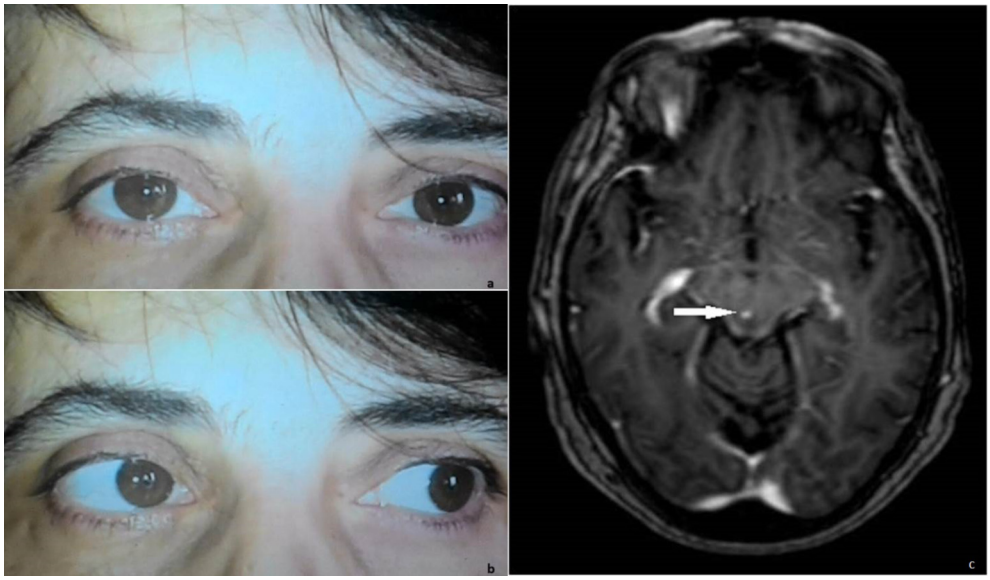

Fig. 2. a & b: Right internuclear ophthalmoplegia with decreased adduction of the right eye on attempted left gaze and left-beating jerk nystagmus of the left eye in abduction. c: Magnetic resonance imaging of the brain. T1-weighted sequence after gadolinium-based contrast administration shows a millimetric hyperintense lesion can be visible in the midbrain. These findings are suggestive for sarcoidosis diagnosis with involvement of the central nervous system.

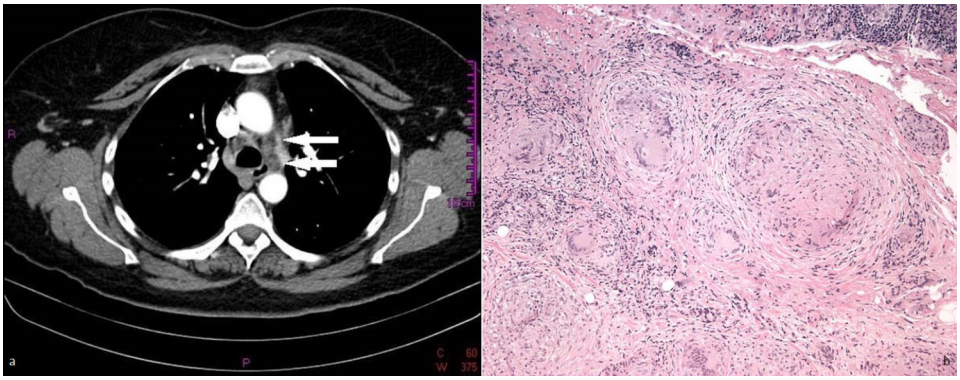

Fig. 3. a: Bilateral hilar lymphadenopathy detected by high-resolution computerized tomography (HRCT) scanning of chest. Arterial phase acquisition of HRCT (mediastinal window) after contrast enhancement shows left hilar lymphadenopathy (pathological lymph nodes, arrows) with associated minimum parenchymal collapse of the ipsilateral lung. b: Hilar limph node biopsy shows typical non-caseating granuloma. Multinucleated giant cells are located at the center of the inflammatory lesion and epithelioid cells, derived from monocytes, lymphocytes and plasma cells are visible around (hematoxylin-eosin stain, $\times 25$).

An early and accurate diagnosis remains challenging, because initial presentation may vary and many patients are asymptomatic; moreover there is no single reliable diagnostic test.

Ocular disease occurs in approximately 30% of sarcoidosis patients; if untreated, ocular disease can lead to permanent visual impairment, including blindness.[11]

Central nervous system may be also involved and neuro-ophthalmologic manifestations are possible.

To the best of our knowledge, it has not been previously reported a case of sarcoidosis presented with pulmonary involvement and both uveitis and internuclear ophthalmoplegia, as ocular manifestations.

Our patient had a typical bilateral granulomatous anterior uveitis and a less frequent manifestation, such as INO. The INO occurs when the medial longitudinal fasciculus on one side in the brainstem (midbrain or pons) is damaged by stroke, tumor, infection, multiple sclerosis, vitamin deficiency or inflammation.[12] In our case brain MRI revealed an inflammatory lesion in the midbrain. Sarcoidosis affects mostly the leptomeninges and is rarely intraparenchymatous. Moreover a solitary cerebral sarcoid mass lesions in the brainstem is very rare. Radiological features of sarcoid mass lesions usually include slightly hyperdense areas on MRI; these lesions enhance diffusely following contrast injection. Perilesional edema may be present. These radiological findings are, however, not specific and the differential diagnosis must include other granulomatous diseases (tuberculosis, leprosy), chronic inflammatory disease like SLE, parasitosis or tumoural lesions.[13]

Atabay et al. described a case of a patient with Eales disease who had internuclear ophthalmoplegia as a neurologic manifestation of the disease.[14]

Usually, the diagnosis of sarcoidosis is based on laboratory and imaging findings and confirmatory biopsy. ACE is elevated in a great percentage of patients with active sarcoidosis, but normal serum level do not exclude the diagnosis. Our patient had a compatible uveitis and an isolated

inflammatory lesion in the brainstem. So, although ACE and lysozyme were normal and chest X-ray not suggestive, we prescribed HRCT scanning of the chest in order to confirm sarcoidosis and rule out other entities, such as tuberculosis, leprosy and chronic pulmonary disease. In fact, HRCT scanning of the chest may detect BHL and be helpful when X-ray chest is negative and it should be prescribed in any case in which sarcoidosis is strongly suspected. In our case, HRCT showed BHL, then biopsy confirm the diagnosis of sarcoidosis demonstrating typical non-caseating granulomas composed of epithelioid cells, lymphocytes, fibroblasts and multinucleated giant cells.

In conclusion, diagnosis of sarcoidosis is challenging and normal serum level of ACE and chest X-ray negative do not rule out the disease. So, we recommend HRCT in all cases of suspected sarcoidosis. Furthermore, biopsy is mandatory to confirm diagnosis.

Conflict of interest

The authors declared that there is no conflict of interest.

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