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LETTER TO THE EDITOR

Cavernous sinus syndrome due to neurosarcoidosis in adolescence: a diagnosis not to be missed

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Dear Sir,

Cavernous sinus syndrome (CSS) is a pathological condition characterized by usually unilateral painful ophthalmoplegia associated with headache, diplopia, ptosis, pupillary changes, trigeminal nerve dysfunction and retro-orbital pain. Primitive or metastatic malignancies, vascular abnormalities and inflammatory processes are the most common causes of CSS [1]. Differential diagnosis between the various conditions may be tangled; in this respect, laboratory and brain MRI findings are discriminatory [2]. We describe here a rare case of unilateral CSS as the presenting sign of neurosarcoidosis in adolescence.

A 16-year-old female referred to our neuro-ophthalmological outpatient service for right ptosis, non-reacting midriasis, pain during eye movements, cephalalgia, and diplopia. She also referred mild exertional dyspnea and fatigue in the last months. Neurological and neuro-ophthalmological examinations showed complete right III cranial nerve palsy with non-reacting midriasis, congested right optic disc with a normal neurorim, in absence of other neurological defects. Visual field was normal, while visual evoked potential showed delayed latency of P100 in the right eye. Head MRI (Fig. 1) showed a pachymeningeal thickening of the right cavernous sinus region, extending toward ipsilateral orbital fissures and oval foramen, and an analogous focal pachymeningeal thickening in both the temporal regions. All these lesions showed gadolinium enhancement. Autoimmune screening, thyroid function, hematological testing and Mantoux reaction were normal. While serum ACE and lysozyme dosage were in the normal range, serum chitotriosidase was increased (64 nmol/h/ml, cut-off limit 48.8 nmol/h/ml) [3]. Cerebrospinal fluid (CSF) analysis and investigation for *Mycobacterium tuberculosis*, neurotropic viruses and culture for bacteria were negative. Pulmonary function tests (PFTs) were normal, but diffusing capacity of lung for carbon monoxide (DLCO) was reduced (57% of predicted). Chest high-resolution CT scan (HRCT) showed a mild parenchymal involvement with peripheral and perifissural micronodules suggestive of sarcoidosis. Bronchoalveolar lavage (BAL) revealed an increased percentage of lymphocytes with high CD4/CD8 ratio (macrophages 46.5%, lymphocytes 46.5%, neutrophils 3.5%, eosinophils 3%, basophils 0.5%; CD4/CD8 lymphocytes ratio 3.98). Therefore, diagnosis of pachymeningeal and lung sarcoidosis was considered consistent and pulsed intravenous corticosteroid therapy (1 g/day) for 5 days, followed by oral therapy, was introduced. The therapy achieved a rapid, marked and durable improvement of symptoms. Six-month follow-up showed resolution of all clinical aspects, with only remaining reacting-midriasis, complete disappearance of meningeal thickening at MRI and DLCO improvement (70% pred.). Steroid therapy was tapered till complete suspension 24 months

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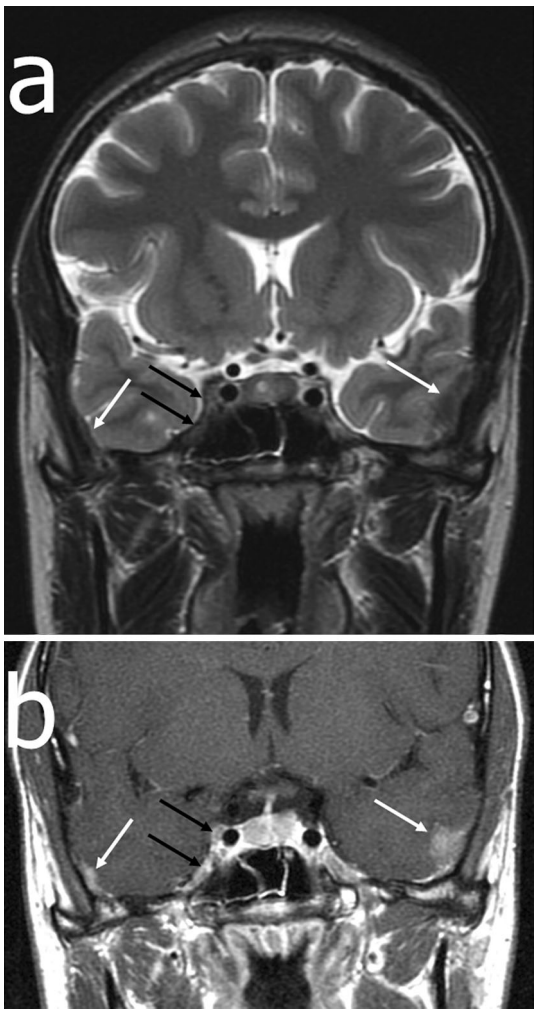

Fig. 1 T2-weighted (**a**), and gadolinium-enhanced (**b**) coronal magnetic resonance images of the cavernous regions. *Black arrows* indicate the thickened dura mater of the right cavernous sinus, showing low signal intensity on T2-weighted images and gadolinium enhancement. *White arrows* indicate dural focal thickenings of low signal intensity on T2-weighted images and gadolinium enhancement in both the anterior temporal regions, more pronounced in the *left side*. Note also a median-right paramedian adenoma of the anterior pituitary gland, as an incidental finding

after acute onset with neither clinical nor radiological relapse during the following 36 months of observation.

CSS is often the presentation sign of numerous severe diseases including malignancies, acute carotid problems, thrombosis, inflammatory or infectious diseases. Therefore, it could represent a clinical emergency in which the diagnosis must be addressed as soon as possible [2].

Sarcoidosis is a chronic idiopathic systemic granulomatous inflammatory disease, rarely causing CSS [4]. Although it may affect every organ and system, neurological localization is rare and appears symptomatic in about 5% of cases. Neurosarcoidosis is more common in females in their fourth decade and can coexist with pulmonary, ocular or other organ involvements, or, very rarely, it can be limited only to the central and/or peripheral nervous system (1% of cases). Clinical onset is most frequently acute or subacute and in about 30% of cases leads to the chronic phase [4].

The cranial base represents the most common site of sarcoidosis involvement, resulting in cranial neuropathy (23–73%); however, any brain area may be affected, with heterogeneous clinical manifestations [4], rarely including CSS. MRI is the neuroradiological technique of choice in sarcoidosis, but differential diagnosis is wide.

The occurrence of CSS, especially as presenting symptom of neurosarcoidosis, is uncommon and has been reported only in few adulthood cases [2, 5]. As far as we know, this is the first report in an adolescent patient; the very young age, together with the dramatic neuro-ophthalmological clinical onset and the presence of only very mild constitutional symptoms, made the diagnostic process challenging. Brain MRI revealed a pachymeningeal inflammatory disease, and the increase of serum chitotriosidase levels, a novel biomarker of sarcoidosis [3], drove the diagnostic work-up in that direction. The demonstration of the pulmonary involvement, by the abnormality of DLCO, the HRCT showing a mild but typical sarcoidosis picture, and the BAL findings, allowed us to confirm the diagnosis, avoiding the execution of a cerebral biopsy. Fortunately, prompt introduction of i.v. steroids, which are the mainstay of sarcoidosis treatment, followed by a slow oral tapering, led our patient to a marked and stable improvement of symptoms with no relapse during the following 5 years of observation.

In conclusion, CSS from neurosarcoidosis, with or without systemic involvement, is a critical condition that should be early recognized and aggressively treated in order to avoid neurological sequelae. Although the occurrence is more frequent in adulthood, younger patients can be affected as well. Neurosarcoidosis should be always investigated in CSS differential diagnosis.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest. Anonymity of patient was protected in this case report.

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