Cavernous Sinus Syndrome Due to Sarcoidosis: A Case Report

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Abstract- Neurosarcoidosis, rare in patients with sarcoidosis, may present with protean manifestations according to the regions of involvement from peripheral nerves to the central nervous system. Cavernous sinus is rarely involved by sarcoidosis, and it can result in different cavernous sinus syndromes based mainly on the involvement of the trigeminal nerve.

We report a 54-year-old man with pulmonary sarcoidosis and cavernous sinus syndrome and review the clinical course, laboratory findings, and neuroradiologic features of the condition. This patient presented with complete ophthalmoplegia of left eye. Magnetic resonance imaging revealed a lesion with gadolinium-enhancement in the left cavernous sinus. Serial chest examinations showed bilateral hilar enlargement. Pulmonary sarcoidosis was diagnosed according to the findings of lymph nodes biopsies. Elevated erythrocyte sedimentation rate and serum angiotension converting enzyme level were observed. After steroid administration, his ocular palsy ameliorated in a few days and cavernous sinus lesion completely disappeared within 3 months after treatment.

Although rare, neurosarcoidosis should be considered in the differential diagnosis of cavernous sinus syndromes with neuro-ophthalmologic signs. For early diagnosis of neurosarcoidosis, it requires a high index of suspicion for searching sarcoidosis at sites outside the nervous system. Corticosteroid treatment is generally followed by improvement in clinical status, but there is a high rate of progression and recurrence after the treatment.

Key Words: Sarcoidosis, Neurosarcoidosis, Cavernous sinus syndrome, Angiotension-converting enzyme, Granulomatous inflammation

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INTRODUCTION

Sarcoidosis is an idiopathic multisystem granulomatous disease, characterized by many non-specific signs and symptoms, as well as by the presence of epithelioid granulomas without caseation or staining for infectious agents histopathologically[1]. The lungs are affected most frequently, but the disease is relatively rare in the nervous system. Sarcoidosis with involvement of the nervous system occurs in less than 10% of patients. Up to

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50% of patients with neurosarcoidosis manifest with a neurological disease at the time sarcoidosis is diagnosed. Seventh cranial nerve palsy and meningeal infiltration are the most frequent findings[2]. Reports regarding sarcoidosis in the cavernous sinus are rare[3].

CASE REPORT

Two months before admission, this 54-year-old man had blurred vision and dizziness. Visual defects were noticed at that time. He was diagnosed with a pituitary tumor over anterior lobe of the pituitary gland by magnetic resonance imaging (MRI). During this presentation, the patient experienced double vision, headache, and photophobia one month later despite medications at our neurologic outpatient department. On neurologic examination, the patient was found to have impaired vision acuity of the left eye (6/20), chemosis of the left conjunctiva, swelling of the left eyelid, proptosis of the left eye, and complete palsy of the oculomotor, trochlear, and abducens nerves of the left eye. His pupils size was isocoria. The visual fields were full. There was a slight reduction of the sensation in the ophthalmic branch of the left trigeminal nerve. The left corneal response was impaired, consistent with a left trigeminal nerve abnormality. There were no facial palsy, no hearing impairment, no tinnitus, no dysphagia, no uvula deviation, and no tongue deviation.

The follow-up MRI of the brain with gadolinium enhancement revealed a lesion with increased density over the left cavernous sinus region (Fig 1). The chest roentgenogram (CXR) revealed bilateral enlarged hilum. The computed tomogram of the chest and mediastinum with contrast enhancement showed marked homogeneous enlargement of lymph nodes in the mediastinum and bilateral hilar regions (Fig 2). The gallium-67 scan of the chest disclosed markedly increased activity in bilateral hilar regions and the middle mediastinum. Biopsy of the left lower paratracheal and superior posterior mediastinum lymph nodes through mediastinoscope was done and the pathology showed noncaseating granulomatous inflammation with negative periodic acid-Schiff (PAS) and acid-fast stain, compatible with sarcoidosis (Fig 3). Serological studies, including antineutrophil cytoplasmic antibodies, anti-nuclear antibodies, and endocrine survey, were negative. The cerebrospinal fluid (CSF) examination showed protein level of 83.87 mg/dl, white blood cells of 28/mm^3 with lymphocyte predominant (96%), IgG concentration of 14.8 (normal range: 0.63~3.35) and an IgG index of 1.0 (normal range: 0.3~0.7). The serum angiotension-converting enzyme (ACE) level was 37.8 IU/l (normal range: 8.3-

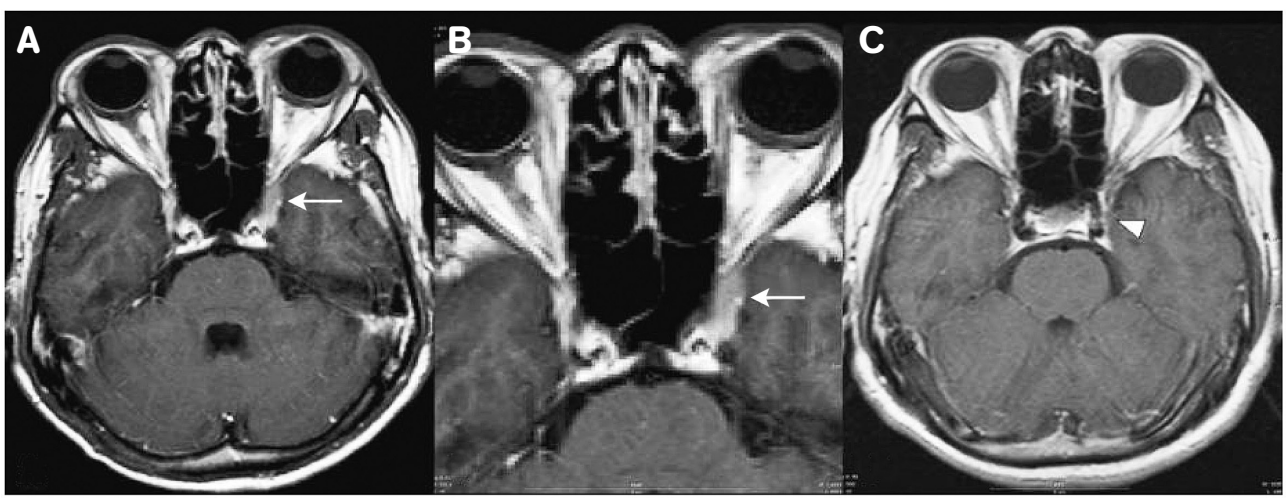

Figure 1. Gadolinium-enhanced T1-weighted axial (A) and coronal (B) images show an enhanced mass involving the left cavernous sinus. Gadolinium-enhanced T1-weighted axial image (C) six months later after steroid therapy shows significant shrinkage of the left cavernous sinus lesion.

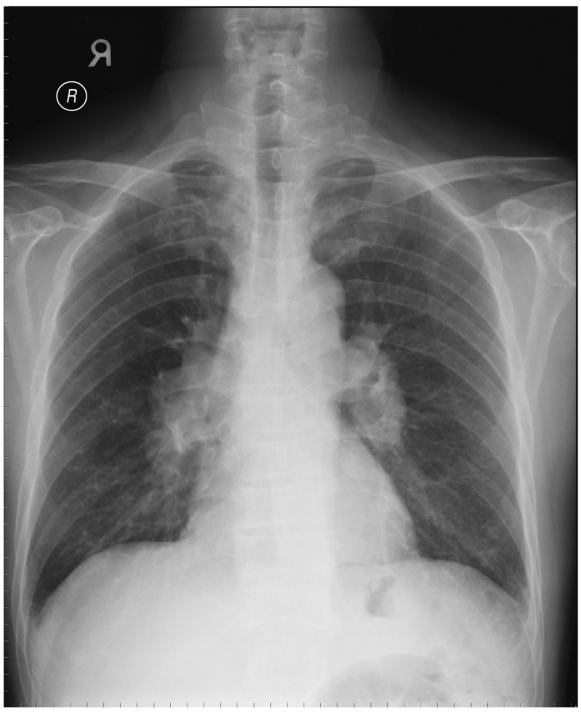

Figure 2. The posteroanterior view of chest X-ray shows typical hilar and paratracheal lymphadenopathy and a pattern of irregular pulmonary parenchymal involvement.

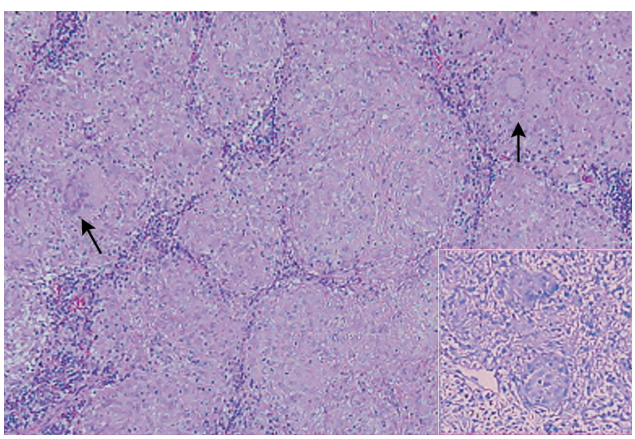

Figure 3. Pathological findings of the biopsied specimen from the lymph nodes of the mediastinum shows noncaseating granulomatous inflammation (↑) with negative periodic acid-Schiff (PAS) and acid-fast stain. (H&E staining).

21.4 IU/l).

Intravenous methylprednisolone, 60 mg daily, was administrated for one week. The patient's diplopia and proptosis were improved 5 days later. The steroid dose was tapered down and shifted to oral prednisolone in the second week. He received prednisolone at the outpatient department as ordered later. The size of bilateral hilar lymph nodes decreased, as revealed by the follow-up CXR two months later. A follow-up MRI of the brain revealed resolution of the mass over cavernous sinus region (Fig. 1). The follow-up serum ACE level had returned to the normal range.

DISCUSSION

In addition to ocular palsy, Jefferson classified three cavernous sinus syndromes based on the divisions of trigeminal nerve involvement. The anterior syndrome comprised deficits of the first division of the trigeminal nerve, and all the nerves supplying mobility of eyeball. The middle syndrome included the first and second divisions of the trigeminal nerve, with denervation of varying ocular muscles. The posterior syndrome involved the oculomotor and abducens nerves and the entire trigeminal nerve, including its motor component[4]. Cavernous sinus syndrome is characterized by ophthalmoplegia, chemosis, proptosis, Horner syndrome, or trigeminal sensory loss. The causes of cavernous sinus syndrome include tumors, infective masses, trauma, thrombosis, carotid aneurysms and fistulas, and inflammatory masses.

The diagnosis of neurosarcoidosis is often difficult, especially in patients without any systemic manifestation. Definite diagnosis of neurosarcoidosis is confirmed by noncaseating granuloma pathology, and the absence of organisms or other causes. The criteria for clinical diagnosis of neurosarcoidosis has not been well established in the absence of positive nervous system histology. Zajicek et al. proposed diagnostic criteria for three categories of neurosarcoidosis: certain neurosarcoidosis; probable neurosarcoidosis; and possible neurosarcoidosis. A diagnosis of probable neurosarcoidosis can be supported by clinical or imaging evidence of lesions, with proof of systemic sarcoidosis obtained from a biopsy of another organ. In the absence of histologic evidence of systemic disease, the diagnosis can be based on two or

more findings, such as typical chest radiograph, gallium scan findings or elevated serum ACE levels[5].

Sarcoidosis is considered rare in Taiwan since there has been no island-wide survey. The true annual incidence of sarcoidosis in Taiwan remains unknown[6], but it has increased in the past 3 decades. Although same specific HLA locus – HLA-CW7 was found in patients with sarcoidosis in Taiwan compared with that in England and Poland, the clinical presentations of patients differed from those reported from the Western countries[7,8].

Neurosarcoidosis affects Africans more commonly but is rare among Chinese. The involvement of the nervous system in sarcoidosis ranges from 1% to 27% of cases. Strictly neurologic forms generally occurs in 5% of cases[9]. The prevalence is underestimated due to the silent manifestation of this disease and unavailability of tissue proof because of the involved location.

Neurosarcoidosis may manifest itself in an acute fashion or as a slow progressive disease, and varies from different location involvement from the peripheral nervous system (PNS) to the central nervous system (CNS). It usually develops within 2 years after the onset of systemic sarcoidosis. In some patients, neurologic symptoms may be the first presenting manifestation. Approximately 80% of neurosarcoidosis patients have presentations outside the nervous system. Most patients presenting with neurologic symptoms and signs also have evidence of pulmonary involvement[10]. Cranial nerve palsies, especially the facial nerve, are the most common presentation of neurosarcoidosis, followed by the optic nerve. Dysphagia and dysphonia could be the sequela as the glossopharyngeal and vagus nerves are involved. Uncommon features, hydrocephalus and aseptic meningitis, are the results of meningeal involvement[2]. Cerebral parenchyma may be infiltrated with a wide range of symptoms, including seizures, cognitive impairment, and personality changes[11]. Abnormalities in the visual pathways are common in patients with systemic sarcoidosis, with perineural or perichiasmal infiltrates. Optic pathway sarcoidosis may present headache and blurred vision[12]. Myelopathy with limbs paresis is the result of spinal cord invasion[13].

It is important to exclude other causes, such as neoplasm or infection, in systemic sarcoidosis patients with clinical signs of neurological involvement. MRI, the most sensitive imaging study for neurosarcoidosis, provides a reasonable level of sensitivity (up to 82%), but relatively poor specificity[14].

Angiotensin-converting enzyme (ACE), produced by the epithelioid cells at the peripheral of granulomatous lesions in response to an ACE-inducing factor released by T-lymphocytes, can be elevated in some disorders, including diabetes, silicosis, and cirrhosis[15]. Serum ACE has been reported as elevated in 5-50% of patients with neurosarcoidosis, and is clinically useful information in investigations. It might be a marker of pulmonary involvement that is also useful in monitoring disease activity[16]. Furthermore, ACE in the CSF may be elevated in 50% of patients with CNS sarcoidosis, although such abnormalities are also found in infection and malignancy status. A normal level of ACE in the CSF results can not exclude the diagnosis of neurosarcoidosis. Owing to a lack of specificity, Dale and O'Brien recommended that it should not be routinely used for investigation[17]. Abnormal CSF examination may be found in up to 80% neurosarcoidosis patients, such as increased total protein, mononuclear pleiocytosis, and elevated IgG index with oligoclonal bands[5].

It is important to diagnose neurosarcoidosis early in the course of the disease process, since early treatment can decrease the damage caused by fibrosis and ischemia of the affected tissues. Most authorities recommend initiating corticosteroid therapy as the first-line therapy to alleviate acute symptoms and avoid irreversible damage to the nervous tissues[18]. Corticosteroid treatment for CNS parenchymal disease and other severe neurologic manifestations of sarcoidosis usually starts with prednisolone 1.0 mg/kg/day. These patients often require prolonged therapy and prednisolone should be tapered very slowly. One third of patients are found to be refractory to corticosteroid therapy and require adjunctive therapy. Potential agents include azathioprine, methotrexate, cyclophosphamide, hydroxychloroquine, pentoxyfillin, thalidomide, and infliximab[19]. Surgery for neurosarcoidosis is indicated for diagnosis and therapy, the latter may ameliorate hydrocephalus or life-threaten-

ing mass lesions causing increased intracranial pressure[20].

Long-term clinical outcome of neurosarcoidosis has rarely been evaluated. According to the report by Ferriby et al. report, CNS involvement at onset is associated with a less favorable disease course with increased morbidity, compared with the involvement of the PNS. The clinical course is more closely related to initial localization than to related to the clinical mode. The systemic involvement is not a predictive factor for the evolution of neurosarcoidosis[21].

There is a high rate of progression and recurrence after treatment, therefore follow-up imaging is necessary. An early diagnosis of neurosarcoidosis requires a high index of suspicion searching for sarcoidosis at sites outside the nervous system.

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