Journal of Neurological Sciences [Turkish] **31:(3)**# 41; 604-608, 2014
http://www.jns.dergisi.org/text.php3?id=806

Case Report

Recurrent Neurosarcoidosis: Two Cases with Different Patterns of Clinical and Imaging Presentation

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Summary

Neuroarcoidosis can affect any part of the central and/or peripheral nervous system and in cases with neurological symptoms as their first manifestations, it is very challenging for the clinicians to make a differential diagnosis. Herein we report two different clinical presentations of neurosarcoidosis without an evidence of active systemic sarcoidosis. With our report, we would like to emphasize, particularly high rates of progression or recurrence of neurosarcoidosis with or without systemic involvement and requirements of early treatment and imaging follow-up.

Key words: Neurosarcoidosis, magnetic resonance imaging, angiotensin converting enzyme, diagnosis

Rekürren Nörosarkoidoz: Farklı Klinik ve Radyolojik Prezentasyonlar ile İki Olgu Sunumu

Özet

Nörosarkoidoz, santral ve/veya periferik sinir sisteminin herhangi bir bölümünü etkileyebilmektedir ve hastaların başlangıç semptomlarının, nörolojik semptomlar olması durumunda, olası ayırıcı tanıları dışlama ve tanı koyma süreci, klinisyenler için zorlu bir süreç olabilir. Bu makalede, aktif sistemik sarkoidoz bulguları olmaksızın, farklı klinik prezentasyonlar ile kliniğimize başvuran iki nörosarkoidoz olgusu sunulmaktadır. Bu olgu sunumlarıyla, sistemik sarkoidoz tutulumu olsun ya da olmasın; nörosarkoidoz vakalarında görülen oldukça yüksek progresyon ve rekürrens oranlarına, erken tedavi ve görüntüleme takiplerinin gerekliliğine dikkat çekilmek istenmiştir.

Anahtar Kelimeler: Nörosarkoidoz, manyetik rezonans görüntüleme, anjiyotensin dönüştürücü enzim, tanı

INTRODUCTION

Sarcoidosis is a chronic, inflammatory systemic disease, characterized histologically by non-caseating granulomas. There may be involvement of multiple organ systems but the disease most commonly affects respiratory tract and lymphatic system. Women are more frequently affected than men[5,6]. Neurosarcoidosis occurs in less than 5% of patients with systemic sarcoidosis[2]. Isolated neurosarcoidosis only occurs approximately in 1% of cases[5]. Herein, we report two different clinical presentations of neurosarcoidosis without

an evidence of active systemic sarcoidosis. Both of which had recurrent attacks during dose reduction of oral steroid therapy. With early treatment, mortality of neurosarcoidosis is unusual[2]. Therefore when clinically suspected, early diagnosis and multidisciplinary approach to the management of disease is essential.

CASE PRESENTATION

Case 1

A 38-year-old male patient was admitted to our clinic with complaints of ongoing weakness in the right arm and leg for two months. The right upper and lower extremity muscle strengths were 4/5 on his neurological examination. The patient had similar complaints about six years ago. He reported no clinical findings of optic neuritis. Cranial and cervical spine magnetic resonance imaging (MRI) exhibited multiple contrast enhancing lesions and there was no pathological finding in computed tomography (CT) imaging of the thoracic spine. His lumbar puncture was performed in that period, and cerebrospinal fluid (CSF) glucose was found to be 50 mg/dl, CSF protein was 59.6 mg/dl and oligoclonal band was negative. CSF angiotensin converting enzyme (ACE) level was high (7 U/L) but serum ACE level was within normal limits and vasculitis markers were negative. He was treated with intravenous methylprednisolone therapy and recovered fully. At that time, neuromyelitis optica antibody test which was sent for differential diagnosis and resulted as negative. The patient was diagnosed as ‘possible' neurosarcoidosis with supportive findings in laboratory and imaging studies and exclusion of other possibilities with similar clinical settings. He was followed with oral steroid therapy with a gradual tapering. He was clinically stable until his last admission to our clinic. On the second admission of our patient, bronchoalveolar lavage and transbronchial biopsy were performed which were non-diagnostic with nonspecific results. However serum ACE level was as high as 124.9 U/L. Hyperintense, contrast enhanced lesions were observed in mesencephalon, right occipital lobe and subcortical white matter adjacent to the right lateral ventricle on T2 and FLAIR sequences of cranial MRI. MRI of the cervical spine revealed a diffuse longitudinal nonenhancing lesion between C2-C5 cervical segments. The patient was treated with intravenous methylprednisolone for three days. Significant improvement in the patient's complaints was observed and he was discharged with oral steroid therapy.

Case2

A 36-year-old female patient presented with symptoms of severe headache, visual obscurations and agitation. She had a history of similar presentation two years ago and she had been evaluated as ‘possible' neurosarcoidosis with cranial neuroimaging findings. Later on, the diagnosis of ‘definite' sarcoidosis had been confirmed with thoracic lymph node biopsy. Oral steroid therapy had been started at that time and gradually tapered. On her last admission, neurological examination was normal except for papilledema. Lumbar puncture was performed and its results were as follows: CSF opening pressure was 185 mmH_2O, CSF glucose was 32 mg/dl, CSFprotein was 200 mg/dl. Significant optic chiasm and optic nerve contrast enhancement and widespread leptomeningeal enhancement was detected on cranial MRI. MR venography was normal. Thorax CT imaging of patient revealed that there was no evidence of active pulmonary sarcoidosis. She was treated with intravenous methylprednisolone therapy for five days. At the end of this treatment, cranial MRI revealed significant decrease in leptomeningeal enhancement. On the tenth day, patient was discharged with oral steroid and azathioprine therapy.

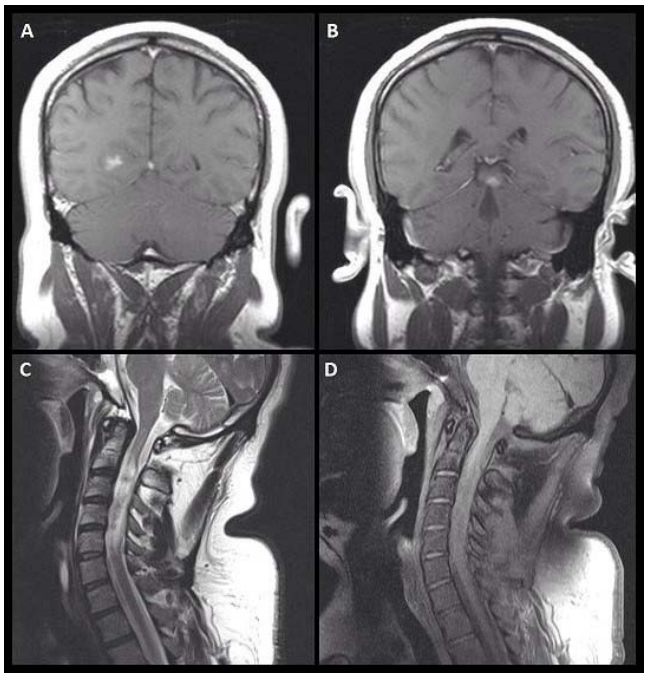

Figure 1: *Contrast-enhanced T1-weighted MRI of patient 1 revealed hyperintense contrast enhanced lesions in right occipital lobe and mesencephalon (A-B). Cervical MRI of the same patient revealed a diffuse longitudinal nonenhancing lesion between C2-C5 cervical segments (C-D)*

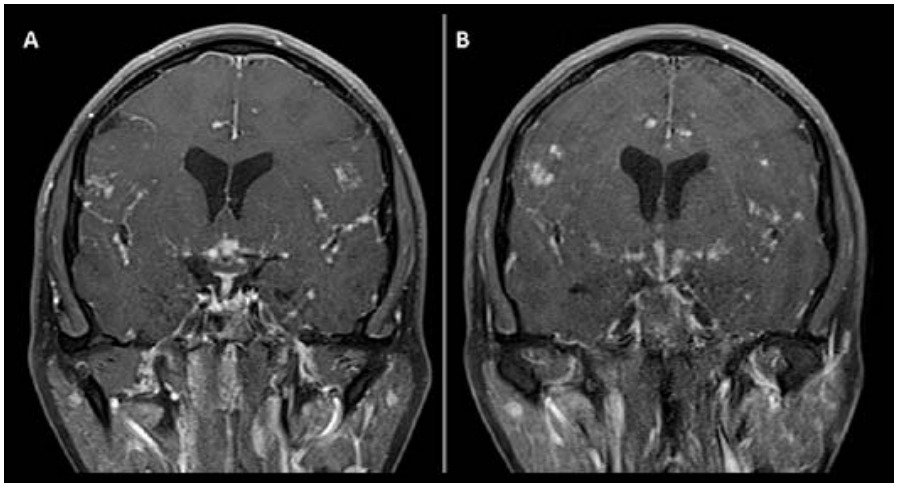

Figure 2: *Contrast-enhanced T1-weighted MRI of patient 2 revealed contrast enhancement in pituitary infundibulum and optic chiasm (A) widespread leptomeningeal enhancement can also be seen (A-B)*

DISCUSSION

Sarcoidosis is a chronic inflammatory disease of unknown etiology with typical non-caseating granulomatous lesions[2]. The disease typically affects individuals between the ages of 20 and 40[1,5].The prevalence of involvement of the nervous system emerges in approximately5% of affected individuals[2]. Zajicek et al identified classification criteria for the diagnosis of neurosarcoidosis that distinguished ‘definite', ‘probable' and ‘possible'[7].

Neurosarcoidosis often affects the leptomeninges with infiltrative lesions, but the disease typically involves the cranial nerves[1,2,5]. Facial nerve is the most commonly affected nerve, however optic neuropathy was more prominent than facial nerve palsy in several recent studies[5,6]. Pawate el al suggested that optic neuritis may be the most common presentation. It was seen in 35% of patients in their case series[3]. The optic nerve involvement may occur at the chiasm similar to our second case or any intra orbital portions of the optic nerves[5,6]. The dural sheath of the optic nerve can also be involved, therefore papilledema can be visible as was observed in our second case[6]. Additionally, myelopathy from intramedullary lesions is an important clinical manifestation of neurosarcoidosis. Sakushima et al suggested that patients with spinal cord sarcoidosis tend to have a longer disease duration since diagnosis than patients with other forms of neurosarcoidosis[4]. Initial symptoms of our first patient started six years ago, which was a relatively long duration, in conformity with this report.

Serum ACE elevates in 30-40% and CSF ACE elevates in 55–75% of neurosarcoidosis cases[2,5,6].However, value of either serum or CSF ACE as a biomarker of disease activity is controversial[5]. CSF findings in neurosarcoidosis are usually nonspecific, and may demonstrate high protein content andnormal or low glucose values[1,5]. Oligoclonal bands in CSF and/or high CSF to serum IgG index have been found in 25–50% of cases[5]. Cranial MRI has a great importance for diagnosis of neurosarcoidosis[5]. Additionally new diagnostic approaches have been described recently, about the use of [18F]-fluorodeoxyglucose PET to detect potential biopsy sites[5]. The typical MRI feature is thickening and enhancement of the leptomeninges, particularly around the base of the brain on contrast-enhanced T1-weighted MRI and dural enhancement has been described in approximately one-third of patients[5,6]. Contrast enhancement of whole visible portions of optic nerves in optic canal, and also thickening of optic nerves can also be seen[6].

Therapeutic drug choice for neurosarcoidosis are similar to sarcoidosis at other locations[1,5]. Corticosteroids are the basis of early treatment for acute inflammation suppression with a gradual tapering[5]. In aggressive cases, a 3 to 5 day course of pulse intravenous methylprednisolone therapy may be needed[5]. Immunosuppressant agents such as methotrexate, azathioprine, cyclosporin and cyclophosphamide can be added as an adjunctive therapy or can be used during steroid tapering or when steroids are contraindicated[1,5]. Recently several case reports have been published about the successful treatment of neurosarcoidosis with rituximab, monoclonal anti-CD20 antibody[5]. Also, immunomodulatory monoclonal antibody infliximab has recently been used to treat the disease, however, the effect of long-term treatment with infliximab is still unknown[1].

CONCLUSION

Neurosarcoidosis with or without systemic involvement is extremely rare but there is a high rate of progression and recurrence after treatment. There fore multidisciplinary approach to the management of disease, long term treatment and imaging follow-up is essential. Both of our patients were referred to our clinic with recurrence of neurological findings during steroid therapy dose reduction. Based on the high rates of recurrences or for the prevention of side effects of steroids, immunosuppressant agents may be used at early stages of the neurosarcoidosis. But there is a need for global prospective studies about therapeutic standards to keep this severe disease under control. Also, it should be noted that CSF ACE evaluation cannot replace tissue biopsy for diagnosis of CNS neurosarcoidosis, the clinicians

must be careful and aware of differential diagnosis.

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Received by: 11 March 2014
Revised by: 19 June 2014
Accepted: 15 July 2014

The Online Journal of Neurological Sciences (Turkish) 1984-2014
This e-journal is run by Ege University Faculty of Medicine,
Dept. of Neurological Surgery, Bornova, Izmir-35100TR
as part of the Ege Neurological Surgery World Wide Web service.
Comments and feedback:
E-mail: editor@jns.dergisi.org
URL: http://www.jns.dergisi.org
Journal of Neurological Sciences (Turkish)
Abbr: J. Neurol. Sci.[Turk]
ISSNe 1302-1664

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