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Isolated Pituitary Neurosarcoidosis: A Case Report and Review of the Literature

İzole Pituiter Nörosarkoidoz: Olgu Sunumu ve Literatürün Gözden Geçirilmesi

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Abstract

Sarcoidosis is a multisystem granulomatous disorder, commonly affecting young adults and usually presenting with bilateral hilar lymphadenopathy and pulmonary infiltration. Central nervous system (CNS) involvement is extremely rare. The cause of sarcoidosis is unknown. The diagnosis of sarcoidosis is firmly established when histopathological evidence of non-caseating granulomas in affected organs supports compatible clinicoradiographic findings. Here, we present a case of a 30-year-old woman referred to our clinic with amenorrhea and polyuria. The radiological appearance of a lesion involving the pituitary stalk was an image of inflammatory infiltration, which is pathognomic for sarcoidosis, syphilis, tuberculosis and foreign body granulomatosis. Laboratory tests were done to rule out syphilis and tuberculosis. A possible diagnosis was sarcoidosis. When we searched other systems for the involvement of sarcoidosis, lungs, lymph nodes, skin and eyes were not involved by the disease. Histopathological examination of a transcranial incisional biopsy revealed a non-caseating granuloma, consisting of macrophages, epithelioid cells, and multinucleated giant cells that secrete cytokines. Around this central core, CD4 and CD8 lymphocytes, B lymphocytes, plasma cells, and fibroblasts were detected. The diagnosis was neurosarcoidosis. We present this case to draw attention to the possibility of isolated neurosarcoidosis as the differential diagnosis of pituitary lesions and review recent advances in the investigation, diagnosis and treatment of this condition.. *(Marmara Medical Journal 2011;24:196-9)*

Key Words: Pituitary lesions, Sarcoidosis, Neurosarcoidosis, Non-caseating granulomas.

Özet

Sarkoidoz genellikle genç erişkinlerde görülen ve sıklıkla bilateral hilar lenfadenopati ve pulmoner infiltrasyonla presente olan, birçok sistemi tutan granülamatoz bir hastalıktır. Santral sinir sistemi (SSS) tutulumu oldukça nadirdir. Sarkoidozun nedeni bilinmemektedir. Sarkoidoz tanısı etkilenen organlarda histopatolojik incelemede gözlenen kazeifiye olmayan granulomların klinik ve radyolojik bulgularla uyumlu olması ile konur. Burada, kliniğimize amenore ve poliüri ile başvuran 30 yaşında bir kadın hastayı sunmaktayız. Pituiter stalkı tutan lezyonun radyolojik görünümü sarkoidoz, sifilis, tüberküloz ve yabancı cisim granülamatozu için patognomik olan inflamatuar infiltrasyon görüntüsündeydi. Laboratuar testleri ile sifilis ve tüberküloz tanıları ekarte edildi. Olası tanı sarkoidozdu. Diğer sistemleri araştırdığımızda akciğerler, lenf nodları, deri ve gözlerde sarkoidoz tutulumu gözlenmedi. Transkranyal insizyonel biyopsi histopatolojik incelemesi makrofaj, epiteloid hücreler, sitokin salgılayan multinükleer dev hücrelerden oluşan kazeifiye olmayan granülom göstermekteydi. Santral korda CD4 ve CD8 lenfositler, B lenfositler, plazma hücreleri ve fibroblastlar gözlendi. Tanı nörosarkoidozdu. Bu olguyu pituiter lezyonların ayırıcı tanısında izole nörosarkoidozun da yeri olduğunu hatırlatmak ve bu durumun tanı ve tedavisinde son bilgileri gözden geçirmek için sunmaktayız. *(Marmara Üniversitesi Tıp Fakültesi Dergisi 2011;24:196-9)*

Anahtar Kelimeler: Pituiter lezyonlar, Sarkoidoz, Nörosarkoidoz, Kazeifiye olmayan granülomlar

Introduction

Sarcoidosis is a multisystem granulomatous disorder, with an unknown etiology, commonly affecting young adults and usually presenting with bilateral hilar lymphadenopathy, pulmonary infiltration and skin or eye lesions[1]. Although involvement of the central nervous system (CNS) is rare (5%), the disease can lead to severe neurological problems[2]. Patients with sarcoidosis rarely present with sellar mass[3].

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Intracranial masses as a manifestation of neurosarcoidosis are occasionally seen. In this article, we present a case of neurosarcoidosis, pituitary sarcaidosis and discuss the relevant literature.

Case Report

A 30-year-old woman was referred to our clinic with an intracranial lesion, that was presented with amenorrhea and polyuria. Laboratory blood analysis for complete blood count, urea, serum electrolytes, liver function, thyroid function, immunoglobulin electrophoresis, serum angiotensin converting enzyme (ACE), prothrombin time, partial thromboplastin time, autoimmune profile including anti-neutrophil cytoplasmic antibodies, cardiolipin and phospholipid antibodies were within the normal range. The only abnormality was hyponatremia (116mEq/L –normal range 137-143 mEq/L-) due to diabetes insipidus. A cerebrospinal fluid (CSF) cell count was normal, but the protein level was elevated to 0.89 g/dl, and there were identical oligoclonal bands in the CSF and in the blood pointing to a systemic disorder with CNS involvement rather than a pure CNS disorder. The chest x-ray, lung function tests and neurological examination were within normal ranges.

Magnetic resonance imaging (MRI) showed a heterogeneously enhanced intrasellar and suprasellar dumbbell shaped mass and thickening of the pituitary stalk. After injection of a contrast medium, we detected dynamic images at the coronal plane at spin echo T1 (Figure 1). In both T1 and T2 sequences gray matter signal voiding was equal to hypophysis. A sagittal T1-weighted image of the pituitary shows a large low intensity mass in the sellar and suprasellar area with irregular thickening of the wall and extension into the infundibulum (Figure 2). The diaphragma sellae was more convex than normal. A pituitary enlargement with thickening of the pituitary stalk was detected by MRI with gadolinium enhancement and attenuation in the intensity of the pituitary. The lesion involving the pituitary stalk showed inflammatory infiltration that is pathognomic for sarcoidosis, syphilis, tuberculosis and foreign body granulomatosis. In order to rule out syphilis and tuberculosis, venereal disease research laboratory studies, fluorescent treponemal antibody-absorption and tuberculin tests were done, and all were negative. The case was evaluated as "probable" neurosarcoidosis depending on the clinical picture, laboratory investigations such as cerebrospinal fluid lymphocyte sub-populations and MRI findings.

A pterioneal craniotomy was performed and the stalk was totally excised (Figure 3). Histopathological analysis of the lesion revealed a non-caseating granuloma, consisting of macrophages, macrophage-derived epithelioid cells, and multinucleated giant cells that secrete cytokines verified the diagnosis of neurosarcoidosis (Figure 4). Around the central core, CD4 and CD8 lymphocytes, B lymphocytes, plasma cells, and fibroblasts were detected. The diagnosis was neurosarcoidosis.

Corticosteroid therapy resulted in the initial improvement of the symptoms, but failed to cure the polyuria related to the diabetes insipidus. She had medication after operation due to panhypopituitarism. She was under medication with Dostinex (cabergoline, Pharmacia, Italy) for two months, Deltacortil (prednisolone, Pfizer, USA) for one year and Levotiron (Liothyronine, Cytomel, U.S.A.) for one year. She also used Minirin (desmopressin, Aventis, France) for one year. All drugs were stopped and by a close endocrinology follow up the patient's medical status improved. The patient reported no further progression.

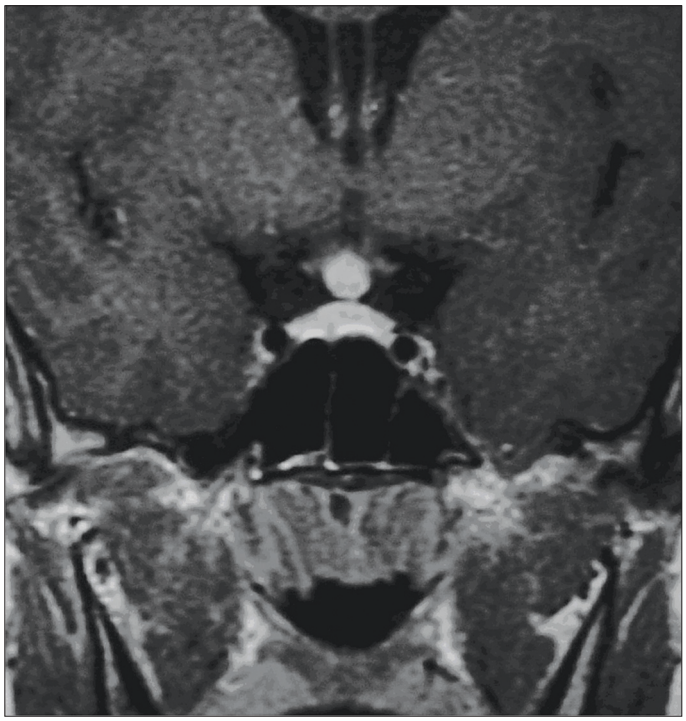

Figure 1. Coronal brain T1-weighted MR image after i.v. gadolinium demonstrates an enhanced mass of the pituitary and stalk.

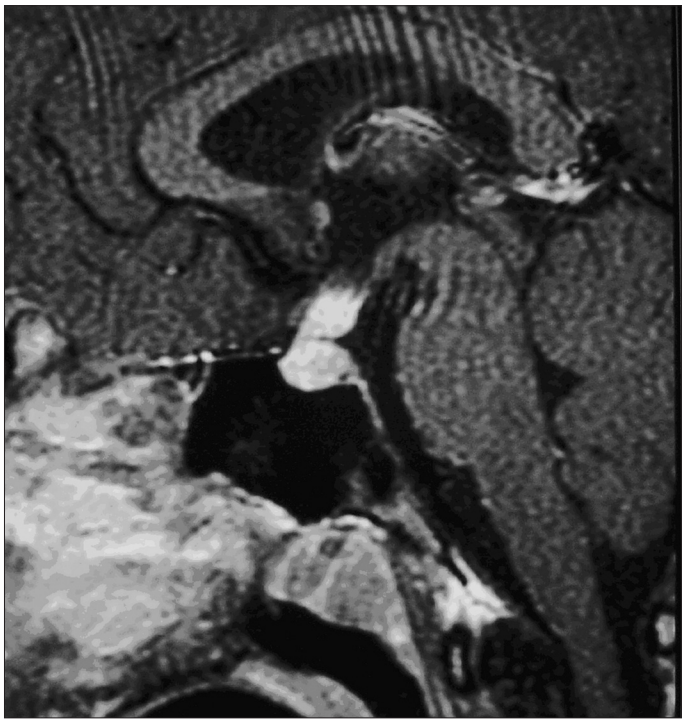

Figure 2. Sagittal brain T1-weighted MR image after i.v. gadolinium demonstrates an enhanced mass of the pituitary.

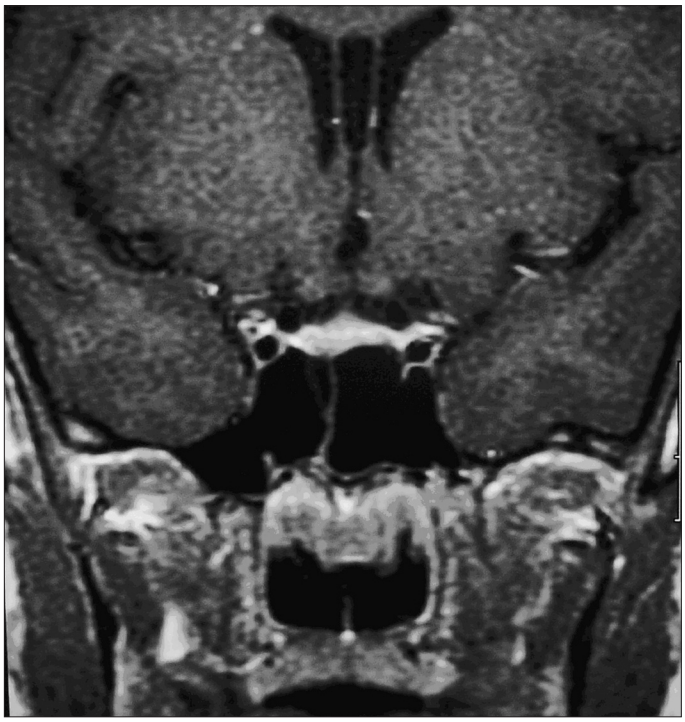

Figure 3. Coronal section T1-weighted MR postoperative image after i.v gadolinium demonstrates no enhancing mass or pituitary stalk.

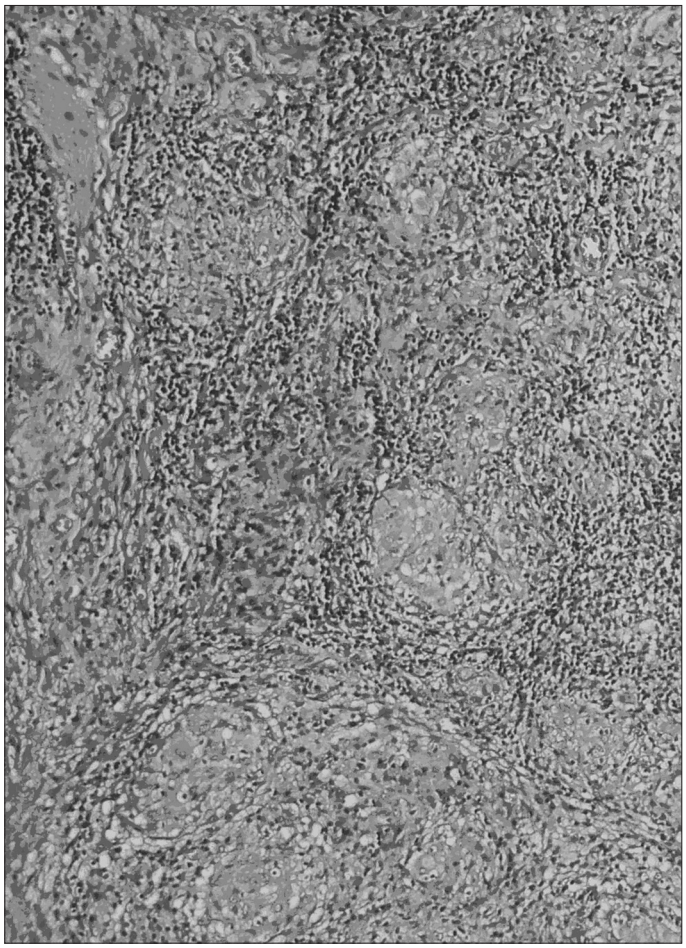

Figure 4. Granulomas in typical position within central collections of epithelioid cells and the encircling rim of lymphocytes.

Discussion

The incidence of sarcoidosis varies from 1 to 40 cases per 100,000 population with a peak in the 3rd and 4th decades of life[2,4]. Although the cause is unknown, a defective immune system, environmental factors such as heavy metals, organic/inorganic dusts, inherited/genetic factors and infections caused by various microorganisms are thought to be the possible causative agents[4]. In symptomatic patients, sarcoidosis can involve one or more organ systems and present with a wide variety of signs and symptoms which can be constitutional: fatigue, weight loss, fever or malaise; generalized, or focused on a single organ. The onset of the disease is usually insidious, but can be acute also. Respiratory symptoms are most common and include cough and chest discomfort, and dyspnea. Following the lung, lymph nodes, skin and the eyes are most often the organ involved. Despite the fact that there are granulomas on histological examination of many organs in the majority of patients, these much less often produce signs and symptoms. Primary CNS involvement alone is a rare condition. In most of the cases with primary CNS involvement the disease occurs in the hypothalamus alone or in both the hypothalamus and pituitary, but rarely in the pituitary alone[1]. This case is a good example of extreme neurosarcoidosis presentation.

The clinical presentation of neurosarcoidosis is widely variable, it can be manifested in a maltitude of ways including cranial neuropathy, aseptic meningitis, encephalopathy, vasculopathy, seizures, psychiatric manifestations, hydrocephalus, hypothalamic pituitary disorders, myelopathy and peripheral neuropathy[1,4-7]. The disease has a predilection to spread from the leptomeninges to the Virchow-Robin spaces leading to invasion and thrombosis of associated blood vessels resulting in granulomatous angitis. In our case, the patient presented with a chief complaint of dysmenorrhea.

It must be kept in mind that the Kveim test has a low sensitivity in neurosarcoidosis and thus is of limited use. Gallium uptake may demonstrate an extracranial granuloma available for biopsy[8]. A whole-body gallium scan shows increased uptake related to CNS disease in less than 5% of patients with this condition but may give evidence of the presence of systemic disease in 45% of patients with CNS involvement[9]. However, in selected cases of isolated CNS disorders, a meningeal or cerebral biopsy may be required if standard investigations are not conclusive in order to exclude other causes such as tumor metastasis, lymphoma, vasculitis and remaining granulomatous disorders. ACE levels in the serum and cerebrospinal fluid may be increased, decreased or normal[2]. Serum or CSF ACE levels are found to be elevated in approximately 70-80% of patients with sarcoidosis, hypercalcemia may be found in 2-15% of the patients due to enhanced sensitivity to vitamin D, however the diagnosis of sarcoidosis is confirmed by histopathological examination[5,10,11]. In our case the CSF cell count was normal but the protein was slightly elevated to 0.89 gm/dL and there were identical oligoclonal bands in CSF and in blood pointing to a systemic disorder with CNS involvement rather than a pure CNS disorder.

Both computed tomography and MRI scans are helpful in disease evaluation; however MRI scan is the modality of choice[5,12]. MRIs show a wide range of CNS abnormalities including hypothalamic-pituitary infiltrating lesions, cerebral parenchyme masses, leptomeningeal lesions, and focal white-matter lesions [5,13]. The use of gadolinium improves the sensitivity of detecting leptomeningeal lesions. Additional MRI findings include white matter and periventricular hyperintensity mimicking multiple sclerosis, hydrocephalus, atrophy, periventricular enhancement, chiasmal edema, extra-axial masses, and parenchymal or spinal cord masses[7]. Neurosarcoidosis is usually a diagnosis of exclusion. However, the radiographic features are suggestive. There are classically two radiographic patterns described for neurosarcoidosis: 1) Chronic basilar leptomeningitis with involvement of the hypothalamus, pituitary stalk, optic nerve, and chiasm; 2) Parenchymal sarcoid nodules, which occasionally calcify[10,11]. Differential diagnosis ofcentral diabetes insipidus should be considered by an endocrinologist. The disease is associated with intrathoracic lesions in about 70% of cases; therefore, an intensive search for enlarged pulmonary lymph nodes should be performed[14]. MRI is the modality of choice in neurosarcoidosis evaluation[5,12] and although any technique can be used to diagnose suprasellar lesions, tissue biopsy taken from the lesion is required for definitive diagnosis and to exclude other cerebral pathologies.

Corticosteroids are the mainstay of neurosarcoidosis treatment, alleviating symptoms and potentially slowing disease progression; however there is no known cure. Aggressive disease or frequent recurrence may require other immunosuppressive drugs such as methotrexate or cyclophosphamide. Approximately two thirds of patients with neurosarcoidosis have a self-limited illness, while the remainder have a chronic remitting and relapsing course[15]. Neurological deficits have been reported to respond to corticosteroids in contrast to hormonal abnormalities that generally persist despite therapy[16]. However, in our case the patient was totally cured in her close endocrinology follow-up even after the medication was stopped one year later. The prognosis of chronic neurosarcoidosis is poor. The mortality rate of sarcoidosis is 1-6%15. Severe involvement of lung parenchyme leading to pulmonary fibrosis and respiratory failure and myocardial involvement leading to arhythmias and cardiac failure are the most common causes of death in sarcoidosis[15].

In conclusion, sarcoidosis is associated with diverse neurological manifestations and neuroimaging findings. The diagnosis of neurosarcoidosis can reasonably be supported in many patients by MRI findings although the definite diagnosis of isolated CNS sarcoidosis requires a biopsy to exclude neoplasms and other granulomatous diseases. The optimum management of patients with neurosarcoidosis relies on the ability of clinicians to recognize the broad spectrum of clinical and neuroimaging manifestations of the disorder and the final neuropathological confirmation. This disease needs multidiciplinary treatment due to systemic involvement.

References

1. Stern BJ, Krumholz A, Johns C, Scott P. Nissim J. Sarcoidosis and its neurological manifestations. Arch Neurol 1985;42:909-17.
2. Sharma OP. Neurosarcoidosis: a personal perspective based on the study of 37 patients. Chest 1997;112:220-8. doi: 10.1378/chest.112.1.220
3. Sato N, Sze G, Kim JH. Cystic pituitary mass in neurosarcoidosis. AJNR 1997;18:1182-5.
4. Pentland B, Mitchell JD, Cull RE, Ford MJ. Central nervous system sarcoidosis. Q J Med 1985;56:457-65.
5. Fels C, Riegel A, Javaheripour-Otto K, Obenauer S. Neurosarcoidosis findings in MRI. Clin Imaging 2004;28:166-9. doi: 10.1007/s11060-008-9687-1
6. Wiederholt WC, Siekert RG. Neurological manifestations of sarcoidosis. Neurology 1965;15:1147-54.
7. Younger DS, Hayo AP, Brust JC, Rawland LP. Granulomatous angiitis of the brain. An inflammatory reaction of diverse etiology. Arch Neurol 1988;45:514-8.
8. Pickuth D, Heywang-Kobrunner SH. Neurosarcoidosis: evaluation with MRI. J Neuroradiol 2000;27:185-8.
9. Zajicek JP, Scolding NJ, Foster O, et al. Central nervous system sarcoidosis: diagnosis and management. Q J Med 1999;92:103-17.
10. Christoforidis GA, Spickler EM, Recio MV, Mehta BM. MR of CNS sarcoidosis: correlation of imaging features to clinical symptoms and response to treatment. AJNR Am J Neuroradiol 1999;20:655-69.
11. Osborn AG, Blaser SI, Salzman KL, et al. Diagnostic Imaging: Brain. 1st edition. Altona:Amirsys Inc., 2004: II 4:52-5.
12. Smith JK, Matheus MG, Castillo M. Imaging manifestations of neurosarcoidosis. AJR Am J Roentgenol 2004;182:289-95.
13. Wolfsberger S, Ba-Ssalamah A, Pinker K, et al. Application of three-tesla magnetic resonance imaging for diagnosis and surgery of sellar lesions. J Neurosurg 2004;100:278-86. doi: 10.3171/jns.200.100.2.0278
14. Chapelon C, Ziza JM, Piette JC, et al. Neurosarcoidosis: signs, course and treatment in 35 confirmed cases. Medicine 1990;69:261-76.
15. Luke RA, Stern BJ, Krumholz A, Johns CJ. Neurosarcoidosis: The long term clinical course. Neurology 1987;37:461-3.
16. Freda PU, Silverberg SJ, Post KD, Wardlaw SL. Hypothalamic-pituitary sarcoidosis. Trends Endocrinol Metab 1992;3:321-5. doi:10.1016/1043-2760(92)90110-M