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Case Report

Hypertrophic Cranial Pachymeningitis After Mollaret's Meningitis: Case Report and Review of The Literature

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Abstract

A 52-year-old woman was referred to Pamukkale University Hospital with the diagnosis of left temporal intracranial epidermoid cyst. Clinical manifestations of her presentation included chronic headache, right sided hemiparesia and epileptic seizures. She was operated and the tumor was resected. Two months after discharge she suffered from fever, nuchal rigidity, and progressive hemiparesia. Although she received steroid treatment with diagnosis of Mollaret's Meningitis (MM), hydrocephalus developed and ventriculo peritoneal shunt was implanted. At follow-up, lower cranial nerve paralysis and quadriparesia developed. Magnetic resonance imaging (MRI) with gadolinium revealed diffuse enhancement of the dura, tentorium, falx and basal cisterns. The diagnosis was accepted as hypertrophic cranial pachymeningitis caused by MM. Clinical presentation, radiological features, etiology, diagnosis, and management options of MM and hypertrophic pachymeningitis are discussed, and the relevant literature is reviewed. As far as we know, this is the first report of hypertrophic cranial pachymeningitis development after MM in the literature.

Keywords: Hypertrophic Pachymeningitis, Mollaret's Meningitis

Mollaret Menenjiti Sonrası Gelişen Hipertrofik Kranial Pakimenenjit, Olgu Sunumu ve Literatür Derlemesi

Özet

52 yaşında bayan hasta, Pamukkale Üniversitesi, Nöroşirürji departmanına sol temporal intrakraniyal epidermoid kist öntanısı ile yatırılmıştır. Klinik bulgularını kronik başağrısı, sağ hemiparezi ve nöbet oluşturmaktadır. Opere edilmiş ve tümör eksize edilmiştir. Taburcu edildikten 2 ay sonra ateş, ense sertliği ve ilerleyici hemiparezi ile başvurmuştur. Mollaret menenjiti tanısı ile steroid tedavisi uygulanan hastada, hidrosefali gelişmiş, şant takılmış, klinik takibinde alt kraniyal sinirlerde parezi ve quadriparezi gelişmiştir. Gadolinium kontrastlı MR tetkikinde dura, tentorium, falx ve bazal sisternlerde yaygın kontrast tutulumu görülmüştür. Tanı, Mollaret menenjiti(MM) sonrasında gelişen hipertrofik pakimenejit olarak konulmuştur. Klinik prezentasyonu, radyolojik bulguları, etyolojisi, teşhisi ve tedavi olanakları tartışılmış, literatür gözden geçirilmiştir. Bildiğimiz kadarıyla, bu çalışma, MM sonrası hipertrofik kraniyal pakimenenjit gelişimini bildiren ilk çalışmadır.

Anahtar Kelimeler: Hipertrofik Pakimenenjit, Mollaret Menenjiti

INTRODUCTION

Intracranial epidermoid tumors constitute about 1% of brain tumors and are considered to be congenital in origin. Epidermoid cysts are benign, slow growing tumors, which require surgical treatment[2,13]. Their diagnosis became easier, especially with the development of diffusion sequences of MRI[13]. The tumor contains cholesterol crystals, keratin, epithelial debris. The contents of tumor may spreads to subarachnoid space by surgical manipulation, which cause meningeal irritation and chemical

meningitis. Aseptic meningitis is the most common cause of postoperative morbidity (22.7%)[13]. Mollaretes recurrent aseptic meningitis is a rare disease, characterized by short attacks of meningeal irritation signs, fever and exellent prognosis [1,20].

Hypertrophic craniospinal pachymeningitis (HCP), was first described by Charcot and Joffroy in 1869 as an extremely rare condition and characterized by diffuse thickening of dura mater, tentorium, falx and cisterns[15,17,21]. Resultant nerve encasement and ischemia produce multiple cranial neuropathies and headache. The etiology of HCP is unclear but may be in association with several disorders, including trauma, infections, tumors, autoimmune diseases or idiopathic. As far as we know, this is the first report of HCP development after MM in the literature.

CASE PRESENTATION

A 52-year-old female patient was admitted with complaints of headache, hemiparesia, dysphasia and epileptic attacks. Neurological examination revealed right hemihypoestesia and hemiparesia. MRI showed a lesion hyperintense on T2 weighted, and hypointense on T1-weighted images at the left temporal region.

She was operated through a pterional craniotomy and epidermoid tumor was completely removed using microsurgical techniques. Intraoperative observation and histological analysis confirmed the diagnosis of epidermoid cysts. Postoperative MRI revealed no residual tumor and small contusions on temporal area secondary to surgery. Fever started at the tenth day postoperatively. Evaluation of cerebrospinal fluid (CSF) indicated no signs of infection. We could not find any microbiological or biochemical evidence of infective or inflammatory condition on CSF. She was put on antibiotic treatment since urine culture showed staphylococcus aureus growth and then she was discharged.

Two months after discharge she presented with fever, nuchal rigidity and dysphasia. Cranial tomography (CT) demonstrated ventricular dilatation. Erythrocyte sedimentation rate was high. Lumbar puncture showed increased CSF pressure with xsantochromic appearance and high protein content. There was pleocytosis with lymphocyte predominance (220 lymphocytes/mm3). Large cells like macrophages namely Mollaret cells were seen in the CSF. She demonstrated negative Gram stains and bacterial culture of CSF. No precise cause for these signs and symptoms were found. Corticosteroid in the form of dexamethason 16 mg/day was started with the diagnosis of MM. Ventriculomegaly did not resolve with daily lumbar punctures. Steroid treatment was gradually tapered and stopped. A ventriculoperitoneal shunt was implanted after the clearance of CSF and the cessation of fever and nuchal rigidity. On 15th day of V/P shunt operation, she demonstrated shunt dysfunction symptoms and signs. She showed somnolence, vomiting, fatigue, and ventricular dilatation on CT and the shunt was removed consequently. A yellowish wax-form material lined within the catheters and valve. An external ventricular drain has was implanted and Corticosteroid was readministered. CSF analysis demonstrated high protein content and pleocytosis. Corticosteroid treatment was discontinued because of the development of diabetic ketoacidosis. A new V/P shunt was remplanted after the clearance of CSF. The patient's complaints of hemiparesia, dysphasia and somnolence showed clinical improvement. However, two months later, she complained of fever and nuchal rigidity. On the first week of readmission consciousness detoriated and decortication rigidity developed. The V/P shunt was functional and CSF examination disclosed pleocytosis. MRI of the brain revealed a diffuse thickening and enhancement after contrast administration of the dura mater of the convexity, falx, tentorium, around the

middle cerebral artery, around the brain stem and basal cisterns (Figure 1,2). MRI also revealed bilateral cerebellar infarction. Exhaustive bacteriological studies failed to identify a specific cause for this situation. The diagnosis of a pachymeningitis was confirmed after CSF analysis, negative bacterial, fungal, tuberculosis cultures and MRI examinations. Although indomethacin has been instituted, she developed quadriparesia, palsies of bilateral IX, X and XII cranial nerves. During treatment, fever and nuchal rigidity disappeared, quadriparesia improved moderately, but lower cranial nerve palsies persisted. Cerebral digital substration angiography showed no abnormality. The dura mater lesions did not regress on MRI. At 4 years follow-up, she suffered from vocal cord paralysis, she had difficulty of swallowing, and was able to use her right hand. She also had trachetomy and gastrostomy, and was mobilized with wheelchair. The lesions on MRI have not changed during the last 6 years.

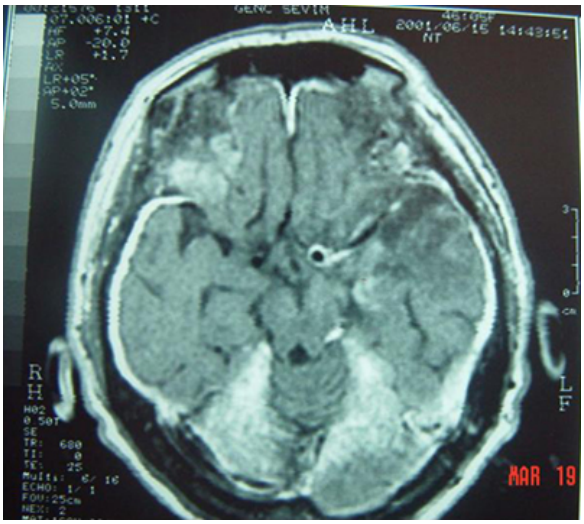

Figure 1: *Contrast-enhanced T1-weighted axial MR image reveals diffuse thickening and contrast enhancement of dura mater and tentorium.*

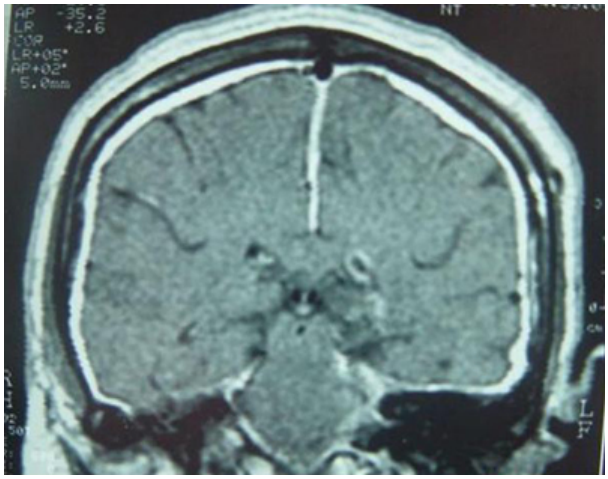

Figure 2: *Contrast-enhanced T1-weighted coronal MR image shows diffuse thickening and contrast enhancement of dura mater*

DISCUSSION

Epidermoid tumors originate from inclusion of epithelial elements within neural groove at the time of its closure to form the neural tube, between the 3rd and 5th weeks of embryonic life[3]. According to one theory, epithelial deposits are trapped in mesoderm. Epidermoid is a slowly growing tumor desquamating normal cells into a cyst. Brain and vessels can adapt slowly to the compression. It is well known that the capsule of an epidermoid cyst is the living portion of the tumor. Viable portions of capsule that remain after surgical excision will likely regrow and continue to make up the breakdown products of epithelial desquamation, rich in cholesterol and fat tissue. This material is known to be irritant to the meninges and cause meningial irritation. This irritation is usually transient but partially uncapsulated tumor is fragile and these materials may come out to subarachnoid space. It can also settle down to perivascular space.

The primary surgical objective is to decompress the mass by evacuating the cyst contents and removing nonadherent

portions of the tumor capsule; portions of the capsule adherent to vital structures should be left undisturbed[3]. Complete removal of the capsule can be very dangerous, in which an aggressive surgical technique may produce extremely highly morbidity and mortality rates[13]. The responsible factor for adherence may be spontaneous rupture during tumor growth. This rupture occurs during operation as well as spontaneously and then its content may spread along the subarachnoid space. The presence of tumor content in the subarachnoid space may induce different type of complications, caused mainly by the inflammatory effects of the cholesterol breakdown products. This can lead to a meningeal inflammatory reaction, obstruction of CSF flow, or irritation of vascular and neural structures. Aseptic meningitis is the most frequent complication caused by the meningeal inflammatory reaction, which also may lead to fibrosis around the cranial nerves and spinal nerve roots. Martin et al suggested that occlusion of the dural sinuses lead to dural thickening[15]. Granulamatous aseptic meningitis can also impair normal CSF flow and causes hydrocephalus. The inflammatory effect of fat on cerebral vessel walls may induce vasospasm and produce transient cerebral ischemia. In one study, with a case of meningitis three phases of cerebral arteriopathy respectively vasospasm, vasodilatation, and organic stenosis were found[19]. One another study showed that contact of craniopharyngioma fluid to arteries leads to vasospasm, and spillage during surgical excision may contribute to vascular complications encountered in the post-operative period[9]. In order to explain this situation, we carry out cerebral angiography at lhe late period and it showed normal vascular structures (no obstruction and narrowing).

Mollaretes recurrent aseptic meningitis is characterized by short attacks of meningeal irritation and fever. The course of MM is self-limiting[1,9,20]. Symptomatic recurrences that occur many years after surgery should be managed with conservative treatment[3]. The attacks resolve spontaneously and without any sequellea[20]. Between attacks, patients areasymptomatic. Symptom-free intervals can be as brief as few days or as long as several years[1]. CSF examination remains the sole diagnostic modality of MM[19]. The CSF shows markedly increased cellularity with pleocytosis with first polymorphonuclear, then mononuclear predominance[1,2,9]. CSF examination of MM presents a spectrum of cytomorphologic features[20]. Large endothelial cells with indistinct cytoplasm (Mollaret's cells) are typically present in the CSF. Mollaret originally described the large mononuclear cells so-called Mollaret cells seen in the CSF. Subsequent ultrastructural and immunocytochemical studies support a monocyte/macrophage lineage for these cells[5,21]. It is suggested that cholesterol-containing debris entering the subarachnoid space from the tumor cysts provoke an aseptic “chemical” meningitis of short course[2,22].

The only criterion facilitating a differentiation between acute bacterial meningitis and CNS dissemination is CSF culture. Neuroimaging plays a limited role in the diagnosis of meningitis. CT and MRI studies are performed to confirm the diagnosis of meningitis, to identify possible sources, to exclude other intracranial diseases and mass lesions, and also to discover any complication of meningitis[6,15,17].

Chronic meningitis is very uncommon and account for less than 10% of all meningitis cases. Nevertheless, although extensive investigations, 30% of the etiologies remain undetermined[4]. Hypertrophic cranial pachymeningitis is a rare form of fibrosing chronic inflammatory process of unknown etiology, which causes localized or diffuse thickening of the intracranial dura mater, tentorium, falx and arachnoid and compressing neural structures, which

cause potentially persistent neurological deficits[12,14,21]. Headache and multiple cranial nerve palsies are the most frequent manifestations. Because no evidence of raised intracranial pressure or hydrocephalus was present, headache could be attributed to focal dural inflammation.

The chronologic imaging findings with progressive intracranial involvement included dural thickening, dural mass, sinus thrombosis, and venous congestion constituted comprehensive pictures of hypertrophic cranial pachymeningitis[11]. There are several reports of pachymeningitis with normal angiogram[16]. Most of the reports about pachymeningitis do not include precise descriptions of intraparenchymal inflammation; however, Kadoya et al recently reported a patient with pachymeningoencephalitis involving the cerebral parenchyma as well as the tentorium[8]. Their case suggest that inflammatory cells can infiltrate the brain parenchyma after invading the subarachnoid and Virchow-Robin spaces[8]. These lesions typically cause progressive cranial nerve palsies, headaches, hydrocephalus and cerebellar dysfunction[23]. The hydrocephalus results from the hypertrophic dura blocking CSF flow in the subarachnoid space and perhaps decreased CSF absorption into the venous system[23]. We found only two cases of cranial CHPM-related hydrocephalus in the literature: one reported by Kadoya et al in the Japanese literature, and one of the three cases reported by Masson et al[8,16]. The complications of IHCP include hydrocephalus and occlusion of the intracranial vasculature that is probably secondary to angiitis.

MRI best identifies hypertrophic cranial pachymeningitis. The thickened dura mater appears isointense or hypointense on T1 and T2WI, associated with a thin rim of hyperintensity in some patients on MRI of hypertrophic pachymeningitis[15]. Thickening is better appreciated in the coronal and sagittal images. Contrast administration reveals uniform intense enhancement of thickened meninges. The low MRI signals probably represent dense fibrosis with decrease in interstitial space and paucity of image able free water, and the enhancement suggests inflammation. The characteristic MR imaging (MRI) appearance of pachymeningitis has been reported to be a hypointense area surrounded by a thin hyperintense margin of the T2-weighted image. This finding is useful for distinguishing hypertrophic pachymeningitis from neoplastic diseases associated with dural thickening, such as meningioma, lymphoma, dural carcinomatosis, and fibroma. Dural carcinoma usually produces intermediate signals on both T1- and T2-weighted sequences, and fibromatous disease has never been reported to show such a high-density peripheral MRI signal as those observed for patients with pachymeningitis. Precise details of the MRI findings for patients with pachymeningoencephalitis, with the exception of postoperative MRI, have not been reported. For our patient, the thickened dura mater was visualized on the preoperative T2-weighted image as a hypointense area, which seemed to reflect the abundant fibrosis observed histologically in the dura mater and seemed to be similar to the images obtained from previously reported patients with pachymeningitis. The iso-and hyperintense areas in the white matter seen in our patient may have been associated with a degree of brain edema causing long relaxation times, resulting in hyperintensity on the T2-weighted image.The thickened dura may also at times mimic dural masses, such as en plaque meningioma. A dura biopsy is essential to confirm the diagnosis[21].The differential diagnosis is established by excluding all other granulomatous (tuberculosis and

sarcoidosis) and infectious diseases, syphillis, lyme disease, and lymphoma[6].

The main goal for treatment of MM is protection[1]. The escape of cystic content into surrounding tissue and CSF may result in localized inflammation and chemical meningitis. Protection of neighboring structures with cotton strips to avoid this complication is a standard method. However, despite profuse saline irrigation during surgery may develop aseptic meningitis during the postoperative course. Furthermore high dose steroids treatment should be started before operation. Therapeutic options consist of long-term immune-suppression with corticosteroid, aspirin, colchicine, indometasine and azathioprine, radiotherapy and/or azathioprine[9,11,12,16,17,21]. Corticosteroid therapy is effective in all cases inducing a complete or partial remission of the neurological symptoms and signs. Some authors stress that radical tumor removal and profuse irrigation of the operative field with hydrocortisone before the dura is closed may wash out tumor debris and avoid postoperative aseptic meningitis. As steroid irrigation significantly decreased the peroperative morbidity of epidermoid tumor resection, indications for intravenous steroids may become more limited, thereby reducing cost[3,10]. The use of cerebral vasodilators to prevent ischemic complications after surgery sometimes may need due to the suggestion of vasospasm on the etiology.

The medical treatment of HCP is almost same with MM. The natural course of HCP is poorly understood, and its management is not well defined. High-dose corticosteroid therapy should be the first choice, and immunosuppressive agents should be the second[18]. Clinical course of HCP is variable; the symptoms may respond well to corticosteroid, but in most cases it recurs or progresses despite treatment. Mamelak et al. also reported progression of symptoms despite corticosteroid therapy[14]. Moreover, patients may become corticosteroid dependent and experience frequent relapses with corticosteroid therapy tapering. The abnormal enhancement on MRI can persist despite good clinical response to steroid treatment. Immunomodulators such as azathioprine and cyclophosphamide have been used, on the basis of the idea that the pathogenetic mechanism of IHCP is autoimmune and is related to that of other fibrosclerotic disorders[7]. However, the efficacy of immunotherapy or radiotherapy has not been proven.The long-term outcome remains uncertain for most patients, but progressive disease could be fatal owing to cranial neuropathies. To improvement of neuropathy, decompressive surgery with removal of the hypertrophic dura is occasionally necessary to alleviate a mass effect but it usually leads to temporary relief[21].

As far as we know, this is the first report of Hypertrophic Cranial Pachymeningitis development after MM in literature.

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