

Granulomatous meningitis

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ABSTRACT

We report idiopathic hypertrophic pachymeningitis in a previously-healthy 34-year-old Filipino man, who presented with third and sixth cranial nerve palsies, headache, vomiting and left proptosis. Magnetic resonance imaging of the brain showed diffuse dural thickening and enhancement, with mild cerebrospinal fluid lymphocytosis and slight protein elevation. The patient was treated with anti-tuberculous medications and steroids, and made good recovery. We discuss the differential diagnoses and various diagnostic tests with respect to granulomatous inflammation of the meninges.

Keywords: granulomatous lesions, idiopathic hypertrophic pachymeningitis, meningeal inflammation, pachymeningitis, sarcoidosis, tuberculosis

Singapore Med J 2009;50(11):e371-e373

INTRODUCTION

Idiopathic hypertrophic pachymeningitis (IHPM) is an uncommon chronic inflammation of the meninges. It shares similarities in clinical presentation and histopathology with other conditions such as tuberculosis (TB) and sarcoidosis. These and other causes of granulomatous meningitis must first be excluded before making the diagnosis of IHPM.

CASE REPORT

A 34-year-old Filipino man, with no significant past medical history, was admitted in March 2007 with a two-day history of headache, vomiting, periorbital pain and diplopia on left gaze (Fig. 1). He was found to have a left sixth cranial nerve palsy, mild left proptosis and mild optic disc swelling bilaterally. Magnetic resonance (MR) imaging showed diffuse dural thickening, and enhancement over the left cerebral convexity and cerebellar hemisphere with extension into the left orbital apex via the superior orbital fissure (Fig. 2). Lumbar puncture done in the lateral decubitus position showed raised cerebrospinal fluid (CSF) pressure (28 cmH₂O) and mildly elevated protein (0.6) with lymphocytosis (100% lymphocytes). CSF was negative for cryptococcal antigens and *Mycobacterium tuberculosis*. The patient

developed a partial left third cranial nerve palsy while in hospital. Histopathological examination of a dural biopsy revealed fibrosis and granulomatous inflammation with foci of dysplastic calcification and necrosis (Fig. 3), but acid-fast bacilli were not identified with Ziehl-Neelson stain. Polymerase chain reaction (PCR) of the dura for TB was negative, and TB culture was negative. Chest radiograph was normal. Mantoux test showed a 3-cm induration (the patient not having been previously immunised against TB). Serum angiotensin-converting enzyme (ACE) was normal, and syphilis studies were negative.

Steroids (prednisolone) and anti-tuberculosis medicine (isoniazid, rifampicin and pyrazinamide) were empirically commenced and given for a course of six months. The patient was discharged 13 days later. He had no diplopia in the primary position, although abduction of the left eye was still limited. The disc swelling had resolved. At the last review in April 2007, his eye movements had returned to normal. The repeat MR images showed that the dural thickening had resolved (Fig. 4). Since then, the patient has returned to the Philippines.

DISCUSSION

The differential diagnoses of thickened meninges are infection (TB, syphilis, Lyme disease, fungal infections), inflammation (Wegener granulomatosis, rheumatoid arthritis, sarcoidosis, IHPM), malignancy and intracranial hypotension (spontaneous, post spinal fluid drainage).⁽¹⁾ Of these, infection (TB, fungal infections, syphilis) and inflammation (sarcoidosis, Tolosa-Hunt Syndrome, IHPM) cause granulomatous pachymeningitis.⁽²⁾ TB and sarcoidosis are more common, but distinguishing between the two can be challenging. Both diseases can affect the same organs and produce granulomas. TB is usually associated with granulomas of epithelioid histiocytes with Langhans-type giant cells, showing central caseous necrosis. The histopathological findings in sarcoidosis are of tight clusters of epithelioid histiocytes, usually without central necrosis and naked granulomas, with a surrounding rim of chronic inflammatory cells. The giant cells may have Asteroid and Schaumann bodies. The presence of necrosis does not, however, exclude sarcoidosis. Moreover, sarcoidosis and TB can occur in the same patient.⁽³⁾ PCR of the dura has a high sensitivity

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Fig. 1 Photographs of nine positions of gaze taken a few days after presentation show limited abduction, adduction, elevation and depression of the left eye.

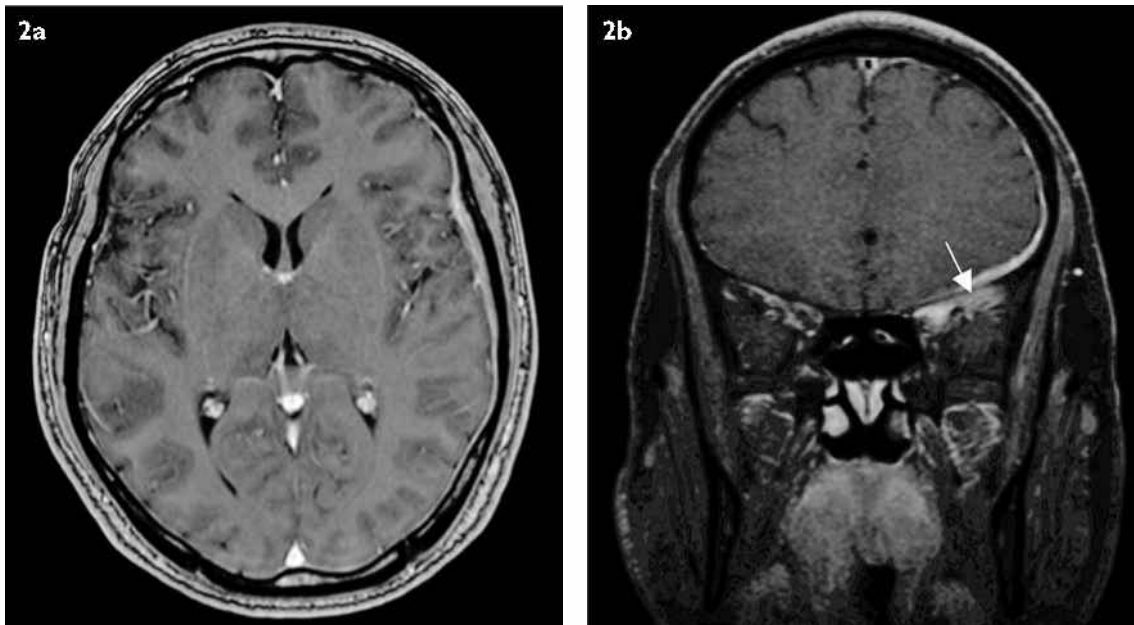


Fig. 2 (a) Axial and (b) coronal gadolinium-enhanced T1-W MR images of the brain and orbits obtained at presentation show diffuse dural thickening and enhancement over the left cerebral convexity. Abnormal enhancing tissue is also noted in the left orbital apex (arrow).

(97%–100%) and specificity (90%–100%) for any form of TB infection.⁽⁴⁾ However, a positive PCR test does not necessarily imply active TB, the specificity for the active form being only 70%. The Mantoux skin test has a low sensitivity and specificity of 94% and 51%, respectively.⁽⁵⁾ False-negative reactions are common in immunosuppressed patients and those with overwhelming TB. It has been shown that chest radiographs show active or previous TB infection in only about 50% of those with TB meningitis, so a negative chest radiograph does not rule out the possibility of TB meningitis.⁽⁶⁾ Steroids also has been shown to improve survival in TB meningitis.⁽⁷⁾

Sarcoidosis is less common than TB, especially in Southeast Asia.⁽⁸⁾ Nervous system disease is an uncommon complication of sarcoidosis, occurring in about 5% of the cases (10% in postmortem series). Cranial nerve palsies occur in about half of the patients with neurosarcoidosis.⁽⁹⁾ Chest radiographs are abnormal

in most patients with neurosarcoidosis at presentation. Intrathoracic lymphadenopathy is the commonest finding (occurring in over 85% of the patients).⁽¹⁰⁾ CSF examination shows abnormalities in about half of all patients with neurosarcoidosis, but the abnormalities (lymphocyte pleocytosis, raised protein concentration, and decreased glucose concentrations) are nonspecific. Testing of serum ACE levels is a good marker for sarcoidosis, as false positive results are unusual (< 5%). However, 25% of untreated patients with sarcoidosis do not have elevated serum ACE levels.⁽¹¹⁾

IHPM is an uncommon chronic inflammatory process of unknown origin that can cause neurological deficits owing to the thickening of the dura. It is characteristically a diagnosis of exclusion.⁽¹²⁾ Patients with this condition commonly present with cranial neuropathies, accompanied by headache. The diagnosis is based on neuroimaging of the thickened and enhancing

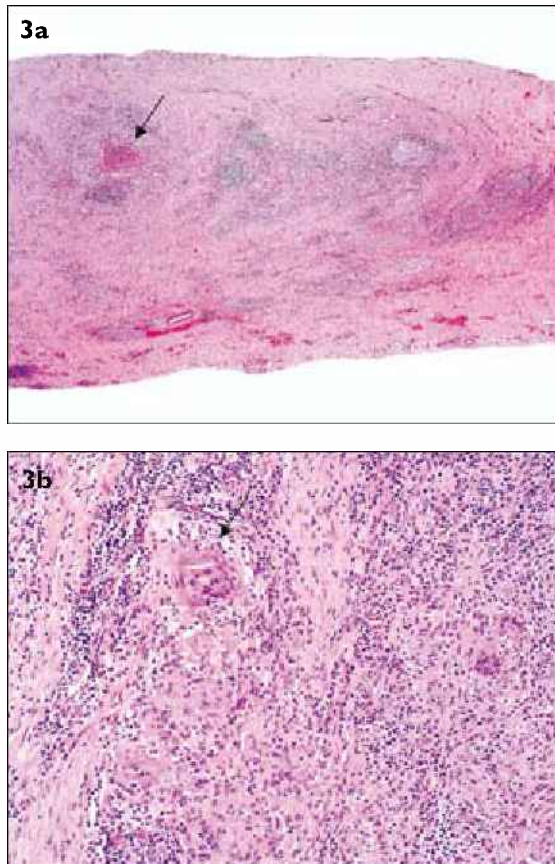


Fig. 3 Photomicrographs of the biopsy of the dura show caseous granulomas with inflammatory cells taken at (a) $\times 20$ and (b) $\times 200$ magnifications (Haematoxylin & eosin).

dura mater.⁽¹³⁾ The CSF chemistry is variable and non-diagnostic, and the opening pressure is occasionally elevated. Histology shows chronic inflammation consisting of lymphocytes, plasma cells, macrophages, epithelioid cells, granulomas, and later on, fibrosis. Treatment is with immunosuppressive agents, beginning with steroids. The course of treatment can be long, and steroid-sparing agents such as methotrexate or azathioprine may be required.⁽¹⁾

In our case, as TB was one of the diagnoses considered before the culture result was out, anti-TB medication was started. Chronic inflammatory disease, such as sarcoidosis, requires steroids as the primary treatment.⁽¹⁴⁾ This patient represents one of those situations where histopathology, while helpful, does not give the final answer, and the treatment decision must still be made clinically.

ACKNOWLEDGEMENTS

The authors are thankful to Dr Ing-Berne Yeh, from the Department of Diagnostic Imaging, National University Hospital, for the description of the radiological images, and Dr Diana Lim, from the Department of Pathology, National University Hospital, for the pathological images.

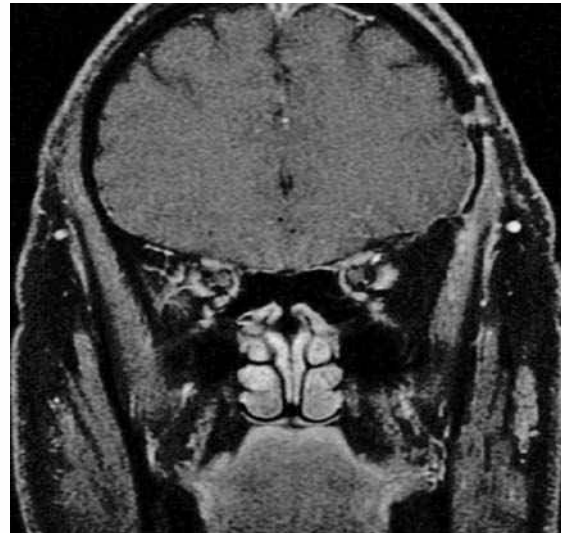


Fig. 4 Repeat coronal gadolinium-enhanced T1-W MR image of the brain and orbits obtained after treatment show that the dural thickening and enhancement over the left cerebral convexity and abnormal enhancing tissue in the left orbital apex have resolved.

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