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Recurrent optic neuritis as early presentation of idiopathic hypertrophic cranial pachymeningitis

Abstract— A 44-year-old Malay lady presented with drooping of the right eyelid and worsening of left eye vision for one week duration. There was associated headache, periorbital discomfort and diplopia on left gaze. She previously had a history of recurrent optic neuritis affecting both eyes over a period of 12 years. On examination, there was right-sided partial ptosis and left exotropia. The adduction, abduction, elevation and depression of the right eye was limited. Left eye extraocular movements were full. The right eye visual acuity was 6/9, while the left eye visual acuity was perception to light, with a positive relative afferent papillary defect and a pale optic disc. The right optic disc was normal. There was reduced sensation in the trigeminal nerve distribution over the right side of the face. Neurological examination was otherwise normal. Magnetic resonance imaging of the brain and orbit revealed meningeal thickening with involvement of the right orbital apex and cavernous sinus. Blood investigations for infectious and autoimmune causes were unremarkable. She was diagnosed to have idiopathic hypertrophic cranial pachymeningitis and treated with systemic corticosteroids. The right eye extraocular motility improved, while the left eye visual acuity improved to counting finger. This case demonstrates that idiopathic hypertrophic cranial pachymeningitis may present as recurrent optic neuritis in the early phase, before radiological evidence of the disease is present. A high index of suspicion for the underlying cause is essential to prevent irreversible optic nerve damage due to recurrent optic neuritis.

Keywords — Hypertrophic pachymeningitis, optic neuritis, ophthalmoplegia

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1 CASE REPORT

Idiopathic hypertrophic cranial pachymeningitis (IHCP) is a chronic inflammatory disease of unknown origin, characterized by dural thickening and compression of adjacent structures, resulting in neurological deficits [1]. Clinical features include chronic headache, ataxia, progressive multiple cranial nerve palsies and visual field defects [1-3]. To the best of our knowledge, there have been no reported cases of IHCP presenting with recurrent optic neuritis. We present this case to illustrate that recurrent optic neuritis is an early presentation of IHCP and may precede the development of radiological evidence of the disease by up to 7 years.

A 44-year-old Malay woman was first seen in August 2001 when she presented with a history of reduced vision and central scotoma of the left eye. It was associated with headache, but no weakness or numbness of the limbs. There were also no nasal or ear complaints. Visual acuity (VA) was 1/60 in the left eye with a positive relative afferent pupillary defect (RAPD), but a normal optic disc. The right eye findings were unremarkable. Other cranial nerves were not involved. Magnetic resonance imaging (MRI) of the brain and optic nerves were normal (Figure 1A). She was diagnosed with left retrobulbar optic neuritis and treated with intravenous methylprednisolone for three days, followed by

oral prednisolone for eleven days as per the Optic Neuritis Treatment Trials (ONTT) regime [4]. Her visual acuity in the left eye improved to 6/6.

The second episode of optic neuritis occurred in January 2002. The patient was pregnant at 20 weeks of gestation when she experienced visual blurring, with a central scotoma in the right eye. The right eye VA was 6/36 with a positive RAPD and a swollen optic disc (Figure 2). She was managed conservatively in view of her pregnancy. Her right eye vision spontaneously improved to 6/9 after two weeks. A third episode of optic neuritis occurred in June 2003, when the left eye VA dropped to 1/60, with a swollen left optic disc. There was no other cranial nerve involvement. MRI of the brain and optic nerves were normal (Figure 1B). There was mucosal thickening of the sphenoid sinus suggestive of sinusitis, for which she was treated with oral antibiotics. The left optic neuritis was treated according to the ONTT regime, after which her left eye VA improved to 6/12.

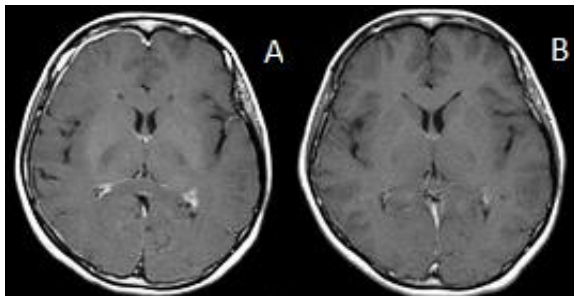


Figure 1: Axial images of MRI brain done in 2001 (A) and 2003 (B) were normal, with no pachymeningeal thickening.



Figure 2: Bilateral fundus photos taken in 2002 showing right eye optic disc swelling.

Patient subsequently developed a fourth attack of optic neuritis in November 2008, again in the left eye. This time, the left eye VA was hand movement, with a positive RAPD and a swollen optic disc. MRI brain and orbit (Figure 3) now showed pachymeningeal enhancement

involving the interhemispheric fissure, tentorium cerebelli and right occipital region. Optic nerve thickness and signal intensity was normal. There was also mucosal thickening in the right mastoid air cells, sphenoid sinuses and ethmoid sinuses. She was again treated with corticosteroids as in the ONTT regime, after which her visual acuity improved.

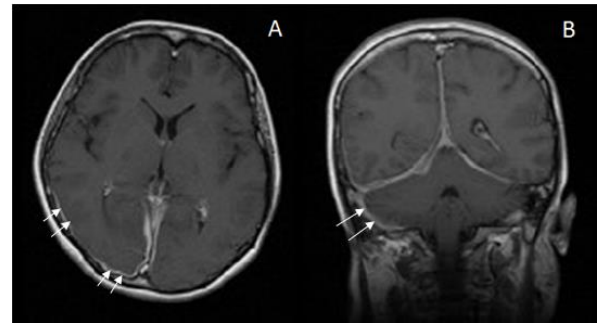


Figure 3: Images of MRI done in 2008. Axial (A) and coronal (B) images of the brain showed pachymeningeal thickening (white arrows).

Her last attack was in December 2012, when she complained of right eyelid droopiness for one week duration and worsening of left eye vision associated with headache, periorbital discomfort and diplopia on left gaze. On examination, there was right-sided partial ptosis and left exotropia. The right eye VA was 6/9, while the left eye VA was perception to light. The left eye RAPD was positive and the left optic disc was pale. The right optic disc was normal. There was limited adduction, abduction, elevation and depression of the right eye. The extraocular movements of the left eye were full. There was reduced sensation in the trigeminal nerve distribution over the right side of the face. Neurological examination was otherwise normal. She had no clinical features suggestive of connective tissue disease.

MRI brain and orbit revealed thickened meninges which enhanced along the tentorium cerebelli, falx cerebri, base of both temporal lobes and along the cavernous sinus bilaterally (Figure 4). The thickened meninges in the right temporal lobe involved the right orbital apex (Figure 5). There was sclerosis of the right mastoid bone, sphenoid and clivus secondary to chronic mastoiditis and sinusitis. Infectious and inflammatory screen was negative. Screening for potential associated auto-immune diseases (antinuclear antibody, rheumatoid factor) was likewise

negative. Cerebrospinal fluid studies revealed normal protein level with no white cell and negative stain for *Cryptococcus*. Stains and cultures for bacteria, fungi and tuberculosis were also negative. Patient refused meningeal biopsy. She was diagnosed with IHCP on the basis of the pachymeningeal thickening noted on neuroimaging and the lack of any identifiable etiology.

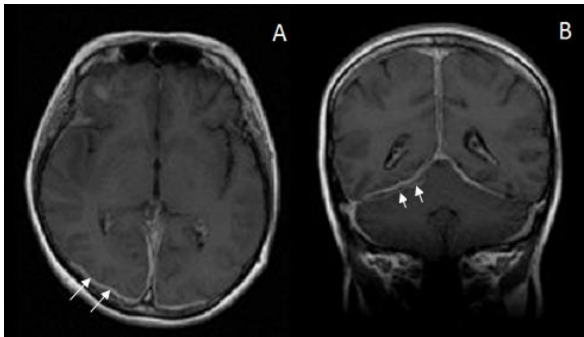


Figure 4: Axial (A) and coronal (B) images of the MRI brain done in 2012 showed progression of the pachymeningeal thickening (white arrows).

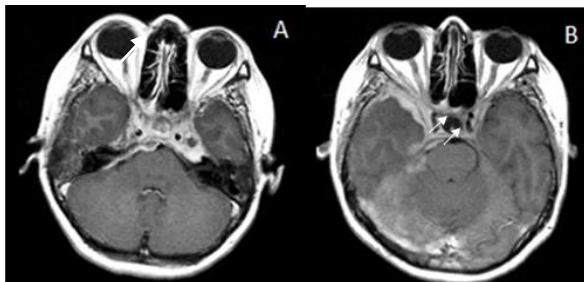


Figure 5: Axial images of the MRI done in 2012 (B) showed right orbital apex meningeal thickening (white arrows), compared to 2008 (A).

After a course of intravenous methylprednisolone followed by oral prednisolone 1mg/kg/day with gradual tapering, vision improved to counting finger in the left eye, although the left optic disc remained pale. Her right eye vision was maintained at 6/9, with improvement in extraocular motility. Oral corticosteroids were maintained at low dose in view of her relapses. Her condition remains stable up to 4 years after the last attack, and she continues follow up under the neuroophthalmology and neurology team.

2 DISCUSSION

Hypertrophic cranial pachymeningitis is an uncommon autoimmune condition and its

pathogenesis remains unclear. It causes a chronic inflammatory process which results in thickening of the dura mater [1]. The underlying causes include autoimmune disorders such as Wegener granulomatosis, systemic lupus erythematosus, rheumatoid arthritis; infections such as tuberculosis and syphilis; and neoplasms [1,3,5,6]. It is a diagnosis of exclusion, when no obvious etiology is discovered [6, 7]. This case serves as a reminder that this diagnosis should be considered in patients with recurrent optic neuritis, as autoimmune diseases may co-exist in a single patient.

Clinical manifestations of hypertrophic cranial pachymeningitis are related to its location. Mass effect of the thickened dura mater leads to compression of adjacent structures. Common presenting symptoms include headache, multiple cranial neuropathies and cerebellar dysfunction [1, 2]. The headache seen in our patient is most likely due to dural inflammation [8]. The distribution of multiple cranial nerve palsies is related to two areas: the cavernous sinus and superior orbital fissure; and falcatentorial due to posterior fossa dural involvement [6]. Cranial nerve II, III, IV, V, and VI palsies are associated with involvement of cavernous sinuses, superior orbital fissure and optic canal [7]. Neuro-ophthalmic findings include optic neuropathy, visual field defect, ophthalmoplegia and retro-orbital pain [3, 5]. Cranial nerve V, VII, VIII, IX and X neuropathy are usually due to falcatentorial dural involvement [7]. Other less frequent symptoms are seizures, hypopituitarism, diabetes insipidus and psychotic manifestations [2].

Our patient presented with recurrent optic neuritis, later developing cranial nerve involvement. Meningeal thickening in the right cavernous sinus with compression of cranial nerves III, IV, V and VI explains the ptosis and limitation of extraocular muscle movements in the right eye. In the left eye, recurrent attacks of optic neuritis resulted in optic atrophy. This is similar to a series of 14 patients with IHCP, in which two patients had visual loss due to recurrent optic neuritis [6]. There was no significant mass to suggest compressive optic neuropathy of the left optic nerve on MRI, unlike in some other reported cases, where visual loss and ophthalmoplegia has been attributed to mass effect in the parasellar and superior orbital fissure regions [8].

Imaging is crucial in the evaluation of hypertrophic cranial pachymeningitis. MRI is the

preferred choice of imaging to diagnose and monitor the disease [6]. The thickened dura is iso-intense to hypo-intense on T1-weighted images, hypo-intense on T2-weighted images, and enhances with gadolinium [1, 5, 7]. Neuroimaging studies may remain negative for two years before significant findings are detectable in IHCP [1]. This is well-illustrated in our case; the initial MRI failed to explain the recurrent optic neuritis, with the patient's imaging studies showing no pachymeningeal thickening during the early episodes of optic neuritis. In our patient, the delay between initial symptoms and diagnosis was far longer than two years, with the MRI showing pachymeningeal enhancement only 7 years after the initial presentation.

Although histopathological examination (HPE) is useful to confirm the diagnosis of IHCP, pathologic findings can be nonspecific, with HPE showing a chronic inflammatory cell infiltrate [3, 9]. This inflammatory process may explain why conditions like chronic sinusitis, otitis media and mastoiditis are well recognized associations of IHCP [9].

IHCP has a chronic and relapsing clinical course [3, 6] and requires prolonged treatment [2]. Unfortunately, there is still no consensus on the management of IHCP. Based on the available literature, this condition usually responds to corticosteroids [1, 6]. Immunosuppressions with azathioprine, methotrexate, cyclophosphamide or chloroquine are steroid-sparing alternatives, especially in cases of relapse [5-7]. Other treatment modalities include radiotherapy, ventriculoperitoneal shunts, antiepileptic drugs, surgery and observation [9].

3 CONCLUSIONS

IHCP is a rare condition which may present as recurrent optic neuritis in the early phase. MRI may remain normal for some years, despite clinical sequelae of the disease. A high index of suspicion for the underlying cause is essential to prevent irreversible optic nerve damage in recurrent optic neuritis. Systemic corticosteroids are the mainstay of treatment for idiopathic hypertrophic cranial pachymeningitis, and a prolonged slow tapering may be required to reduce the risk of relapse.

CONFLICTS OF INTEREST

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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NS, ETLM and CCY wrote the manuscript. WMS and SSK interpreted the neuroimaging results and prepared the images. LK, AY, AH, JT and WHWH reviewed the manuscript.

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