Idiopathic hypertrophic cranial pachymeningitis: Three biopsy-proven cases including one case with abdominal pseudotumor and review of the literature

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Abstract

Hypertrophic pachymeningitis (HP) is a rare disorder of diverse etiology. It presents with headaches, cranial neuropathies and ataxia occurring alone or in combination. Dural biopsy is essential to exclude secondary causes of pachymeningitis. There is paucity of data on biopsied cases of HP. We report three biopsy-proven cases of idiopathic hypertrophic cranial pachymeningitis. All our patients had headaches and multiple cranial neuropathies; ataxia was seen in one patient. One patient had recurrent anterior and posterior cranial neuropathies, while one each had recurrent anterior and posterior cranial neuropathies. Two patients had profound irreversible monocular visual loss. All of them showed prominent pachymeningeal thickening on imaging. Infarcts were seen in one patient, which have rarely been documented. All patients showed biopsy evidence of meningeal thickening and nonspecific chronic inflammation of the dura. The disease may have a remitting and relapsing course, and usually responds to steroids. Clinical improvement was excellent in two patients and modest in one on steroid therapy. All our patients required azathioprine during the course of therapy. Early institution and long-term maintenance of steroid therapy prevents neurologic sequelae. Occurrence of abdominal inflammatory pseudotumor in a patient of HP possibly as part of multifocal fibrosclerosis has not been described earlier.

Key Words

Abdominal pseudotumor, chronic headache, dural biopsy, idiopathic hypertrophic pachymeningitis, infarcts, multifocal fibrosclerosis

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Ann Indian Acad Neurol 2011;14:189-93

Introduction

Hypertrophic pachymeningitis (HP) is a rare disorder of diverse etiology, characterized by fibrosing inflammatory process that thickens the dura mater.[1] Common clinical features include headaches, cranial neuropathies and ataxia.[2] Dural biopsy is essential to exclude secondary causes of pachymeningitis.[3] Until 2008, 60 treated cases of HP have been reported in the English literature.[4] Three more cases were reported from India in 2009.[5,6] There is paucity of data on biopsied cases of HP. From 1997 to 2008, Goyal *et al*.,[7] Sylaja *et al*.[3] and Shobha *et al*.[8] have documented, respectively, two, four and five cases of biopsy-confirmed "idiopathic" hypertrophic cranial pachymeningitis (IHCPM) from India. We report three biopsy-proven cases of IHCPM from West-Central India. We also document one case of IHCPM possibly associated with inflammatory pseudotumor (IPT) of the omentum.

Access this article online	
Quick Response Code:	Website: www.annalsofian.org
	DOI: 10.4103/0972-2327.85891

Case Reports

Case 1

A 24-year-old lady presented in August 2006 with generalized throbbing headache, horizontal diplopias, dysphagia, nasal regurgitation, hoarseness of voice and numbness over cheeks developing over 2 months. There were no constitutional symptoms. She had three episodes of diplopias, headaches and fever in the past 9 months followed by spontaneous recovery after the first two episodes. She had bilateral VI nerve palsy. Sensation in V nerves distribution and gag reflex were decreased. Rest of the examination was normal.

The erythrocyte sedimentation rate (ESR) was 50 mm/h. Except hemoglobin of 7.8 gm/dl, the rest of the hemogram and metabolic parameters were normal. Cerebrospinal fluid (CSF) had WBCs 100/cmm (lymphocytes), proteins 30 mg/dl,

sugar 62 mg/dl and ADA 3 IU/L and Gram's, Ziehl Neelson and India Ink stains were negative; no malignant cell was seen. Serology for human immunodeficiency syndrome (HIV), venereal diseases research laboratory (VDRL) and hepatitis B surface antigen was negative. Tests for anti-nuclear antibody, anti-neutrophil cytoplasmic antibody (c-ANCA & p-ANCA) and rheumatoid factor were negative. Serum angiotensin converting enzyme (ACE) level was 34 U/L (8–65 U/L). Contrast-enhanced computerized tomography (CECT) chest was normal. Contrast magnetic resonance imaging (MRI) brain and spine showed pachymeningial thickening in the parasellar region [Figure 1a], middle cranial fossae and region of clivus, extending into the spinal canal up to the C3 level.

She received anti-tubercular therapy (ATT) with streptomycin, isoniazid, rifampicin and pyrazinamide (SHRZ) and prednisolone tapered over 2 months. Diplopia improved over 2 months and dysphagia after 5 months. Six months later, she developed diffuse pain abdomen with vomiting, but no jaundice. ATT was stopped. After a further 6 months, she had recurrence of diplopia with right ptosis. Pain abdomen persisted.

Laboratory investigations as in the initial presentation were normal. CSF for mycobacterium tuberculosis by polymerase chain reaction and TORCH (toxoplasmosis, rubella, cytomegalovirus, herpes group) antibody titers titers were negative. CECT abdomen showed a 4.5 cm x 2.4 cm x 3 cm ill-defined heterogenously enhancing soft tissue mass with enhancing septae in the right adnexa [Figure 1b].

Laparotomy with excision biopsy of the mass showed omental tissue with dense inflammatory infiltrate with congested vessels and foreign body-type giant cells; no area of necrosis, epitheloid granuloma or acid fast bacilli was seen [Figure 2a]. She was restarted on ATT and prednisolone for 2 months with which she improved over 1 month.

One year later, she developed right III, IV and left VI cranial nerve palsies with decreased sensation in the right V cranial nerve distribution. CSF analysis revealed eight lymphocytes. She received oral prednisolone 60 mg/day, propranolol 80 mg/day and nortryptiline 50 mg/day. ATT was stopped. Azathioprine 100 mg/day was added for its steroid-sparing effect. She suffered acute-onset painful loss of vision from right eye on steroid taper at 4 months. Dural biopsy, through right frontal craniotomy, revealed, on histopathological examination, thickened meninges with fibrocollagenous tissue along with focal mild chronic nonspecific inflammation, consisting predominantly of CD-20-immunopositive lymphocytes, without evidence of granuloma or vasculitis [Figure 2b].

She was restarted on a therapeutic dose of prednisolone followed by slow taper over 1 year. She is headache-free and has not had recurrence of cranial neuropathies on the maintenance dose of prednisolone and azathioprine over 18 months.

Case 2

A 56-year-old lady, known diabetic and hypertensive, presented in May 2009 with recurrent bilateral throbbing periorbital pain for 4 years and worsening right-sided hemicranial headache for 3 months. She had diplopia and

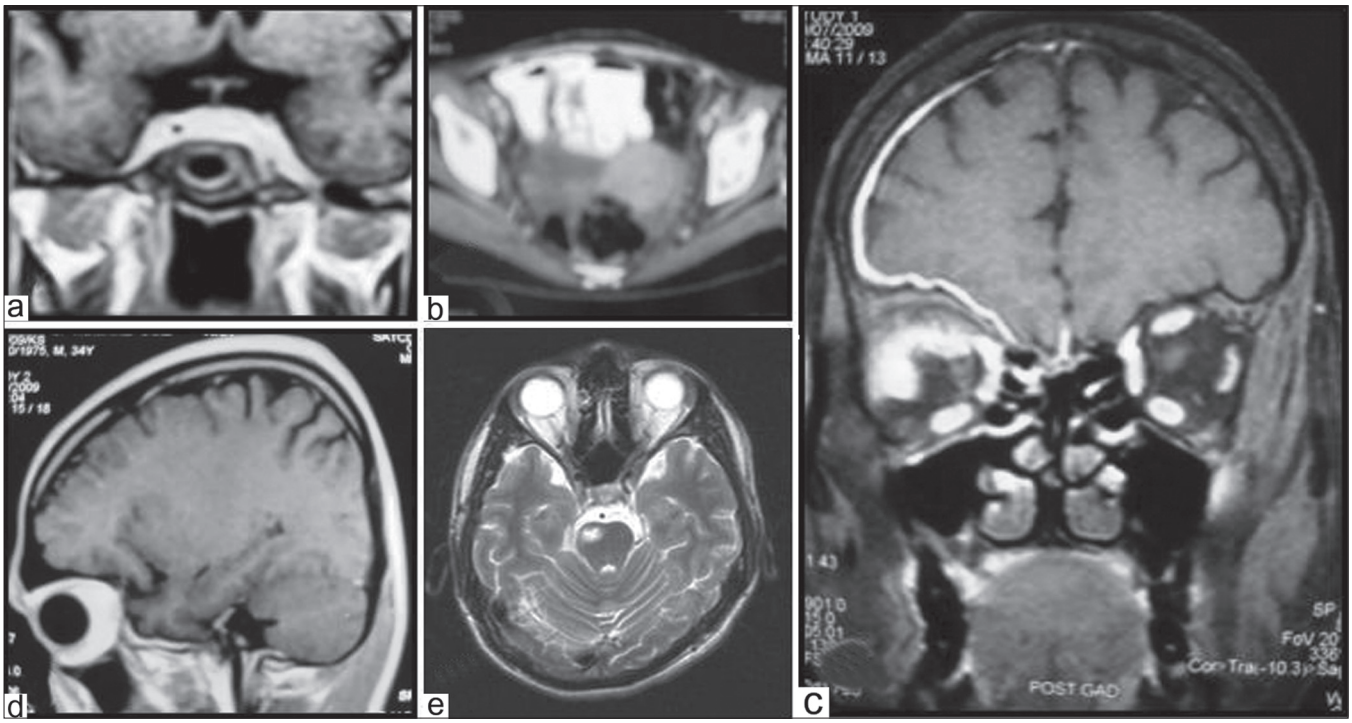

Figure 1: Magnetic resonance imaging (MRI) coronal gadolinium-enhanced T1WI showing thick meningeal enhancement of the dura mater in the parasellar region (a). Contrast-enhanced computerized tomography of the abdomen showing enhancing omental mass (b). MRI coronal gadolinium-enhanced T1WI showing thick meningeal enhancement of the right frontal dura mater and bulky superior and lateral rectii (c). MRI sagittal gadolinium-enhanced T1WI showing thick meningeal enhancement of the left temporal dura mater (d). MRI axial T2WI showing infarct in the right pons (e)

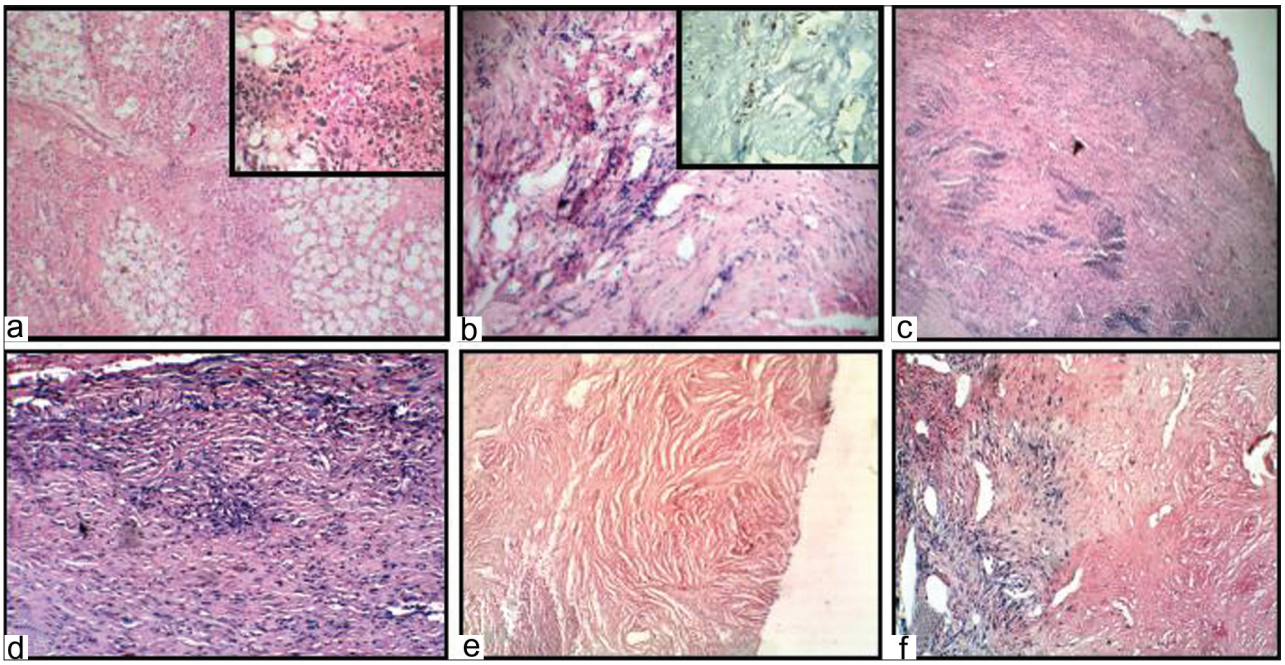

Figure 2: Photomicrograph of case 1: Omental biopsy showing acute on chronic inflammation with foreign body type of giant cell reaction (a: Hematoxylin and eosin [H and E], ×100) (a inset: H and E, ×200). Dural biopsy showing meningeal thickening composed of fibrocollagenous tissue (b: H and E, ×100) with mild CD20-immunopositive lymphocytic inflammatory infiltrates (b inset: CD20, ×200). Cases 2 (c, e) and 3 (d, f): Meningeal biopsy showing meningeal thickening composed of fibrocollagenous tissue (c, e: H and E, ×100) with mild to moderate lymphomonocytic inflammatory infiltrates (d, f: H and E, ×200)

gradually progressive diminution of vision from her right eye. She had received suboptimal doses of prednisolone in the past. She had perception of light on the right and visual acuity of 6/9 on the left eye; bilateral ophthalmoplegia with ptosis (right > left).

Hemogram and metabolic parameters were normal. CSF study was normal. Serology for HIV, VDRL and vasculitis workup was negative. Serum ACE level was 20 U/L (8–52 U/L). CECT chest was normal. MRI brain revealed thickened enhancing right superior and lateral rectii with enhancing dura along the right cerebral convexity and base of the skull [Figure 1c]. Dural biopsy, through right frontal craniotomy, showed evidence of pachymeningitis [Figures 2c and e].

She received prednisolone and azathioprine with which the headache decreased and ophthalmoplegia improved. MRI brain after 6 months did not show any significant change in size of the right orbital lesion; thick pachymeningeal enhancement was not seen. She has moderate relief of her headaches but has not had recurrence of ophthalmoplegia over 1 year of follow-up.

Case 3

A 24-year-old farmer presented with subacute-onset slowly progressive weakness of all limbs, diplopia, dysarthria and nasal regurgitation over 3 weeks. He had right VI and lower motor VII nerves palsies, left-sided nystagmus, diminished gag reflex and right-sided hemiparesis.

ESR was 130 mm/1h. CSF was normal. Serology for HIV, VDRL and vasculitis workup was negative. MRI brain showed lacunar infarcts in the bilateral frontal paramedian regions (left > right) and in the right occipital lobe.

He received ATT and prednisolone. Four weeks later, dysphagia recovered and he was ambulant without support. On tapering steroids, he developed headache, diplopia and left-sided weakness. He had right VI and left upper motor VII cranial nerves palsies, dysarthria, hypophonia and left hemiparesis with left cerebellar signs. CSF was normal. MRI revealed hyperintense lesions on T2WI in the right midbrain and pons, left cerebellar hemisphere and thickened enhancing dura in the parasellar region and at the left temporal pole [Figures 1d and e]. Dural biopsy, through left temporal craniotomy, showed evidence of pachymeningitis [Figures 2d and f]. On prednisolone and azathioprine, he remained symptom-free over 9 months of follow-up.

Discussion

IHCPM is a poorly understood inflammatory disease involving the dura mater of the skull base, tentorium and falx cerebrii.[9] HP may be "idiopathic" or "secondary," where identifiable causes coexist, although their definite relationship may be debatable.[1,10]

Etiopathogenesis

The exact etiopathogenesis is unknown. It may be an autoimmune disorder or occurring as a direct result of infectious or infiltrative pathology.[7,11] Rossi *et al.* demonstrated fibrosis and prominent CD4+ T-cell inflammatory infiltrate on dural biopsy in HP, suggesting a probable pathogenetic role for cell-mediated immunity.[9] Riku *et al.* have shown that HP may be a dural lesion of IgG4-related systemic disease.[12] Tolosa-Hunt Syndrome (THS) may be a focal manifestation of pachymeningitis involving the walls of cavernous sinuses,

and IHCPM may be a localized manifestation of multifocal fibrosclerosis (MF).[3]

Clinical features

IHCPM affects males predominantly.[4,13] The age ranges from 20 to 78 years (mean, 51 years).[14] Two of our three patients (mean age, 35 years) were female. The main clinical features are headache, progressive cranial nerve palsies and cerebellar dysfunction,[9,15] resulting from compression of adjacent structures by hypertrophied pachymeninges.[13,16] All our patients had headaches and multiple cranial neuropathies, while one had ataxia.

Chronic daily headache, often resembling chronic migraine, is the most common manifestation.[2] Headache can be the only symptom for years before other symptoms manifest.[17]

Riku and Kato have described two patterns of cranial nerve involvement based on site of dural inflammation: Cavernous sinus to superior orbital fissure and falcotentorial to posterior fossa dural involvements.[11,15] Cranial neuropathies were observed in all cases. The first patient had recurrent anterior and posterior cranial neuropathies while the second had recurrent anterior cranial neuropathies. The third patient had posterior cranial neuropathies. Two patients had profound irreversible mono-ocular visual loss. However, occurrence of this phenomenon is uncommon.[13,16,17]

Presentation with ataxia is less common. Diffuse ischemia, venous sinus congestion and mass effect of thickened tentorium have been incriminated.[11] Symptomatic spinal pachymeningitis either occurs alone or as a craniospinal form.[10] Our first case had asymptomatic cervical spinal pachymeningitis.

Rare association

MF and HP are both rare disorders of an unknown etiology, characterized by chronic inflammation leading to dense fibrosis. MF can occur at different sites.[2,3,11,12] Our first patient had an IPT of the omentum. IPT has been described in multiple sites.[18] However, the rate of prevalence of mesenteric IPT is not known.[19]

Occurrence of abdominal IPT with IHCPM has not been described earlier. Propensity to myofibroblastic proliferation at two distant sites in the first patient raises the possibility of hitherto unidentified inciting factors in genetically predisposed individuals to MF.

Investigation

IHCPM is a diagnosis of exclusion.[3,7] A thorough workup includes search for infectious, autoimmune and neoplastic diseases.[10]

An overwhelming majority have elevation of ESR.[14] Two of our patients had ESR over 50 mm/h and the third patient had ESR of 130 mm/h. CSF in most cases shows variable lymphocytic pleocytosis.[1,11,15,17] Protein levels are moderately elevated. CSF may be normal in one-fourth of the patients.[17] The first patient showed lymphocytic pleocytosis.

IHCPM is being increasingly recognized with advent of CT and MRI. CT shows thickened enhancing dura.[3] MRI is the most useful radiological method that reveals diffuse or localized thickening of dura.[15,20] Thickened dura appears isointense to hypotense on both T1 and T2W images, with uniform dense enhancement on contrast study.[7] Dural thickening is better appreciated on coronal and sagittal images in the interhemispheric fissure, tentorium and basal dura.[2,3] All three patients showed prominent pachymeningeal changes on imaging. Tentorial and posterior falx involvement was seen in the first and third patients. The area of involvement correlated with the clinical picture in all patients. Cerebral and cerebellar infarcts, as noted in the third patient, in association with IHCPM are seldom documented in the literature.[11,21]

Dural biopsy is essential to establish the diagnosis of IHCPM and to exclude other causes of pachymeningitis.[1,8,13,15] Biopsy from an accessible site with CT or MRI documented enhancing and thickened dura mater is more likely to yield a positive etiological diagnosis.[3,8,15] Pathological findings consist of thick fibrous dura often associated with chronic inflammatory cell infiltrate comprising lymphocytes and plasma cells.[8,9,13,15] Giant cells, caseation necrosis or epitheloid granuloma or evidence of vasculitis are usually not seen.[15] Shobha *et al.* in a recent study of 11 cases of HP found specific etiology in only six cases, while the other five cases were of an idiopathic variety.[8] Dural biopsy in all our patients was consistent with IHCPM.

Differential diagnosis

Differential diagnoses are extensive. Tubercular meningitis needs careful exclusion.[22] In developing countries, a majority of the patients presenting with features of IHCPM will receive a trial of ATT before alternative diagnoses are considered. Syphilitic pachymeningitis,[2,11] neurosarcoidosis,[2] Wegener's granulomatosis,[23] meningeal carcinomatosis,[2,24] en-plaque meningiomas[2] and intracranial hypotension[2] need exclusion. The second patient had recurrent episodes of THS[14] but, on evaluation, had imaging and histopathological evidence of pachymeningitis over the cerebral convexity and base of the skull.

Clinical symptomatology, imaging characteristics, absence of abnormal laboratory and CSF studies, histopathological basis and long course of disease and responsiveness to steroid strongly favor the diagnoses of IHCPM in all our cases.

Treatment

The optimal treatment of IHCPM is unknown.[10,25] Untreated, the clinical course is usually marked by severe headache and progressive neurologic deterioration and vision loss.[20] Steroid is the mainstay of therapy and is often effective in arresting disease progression.[6,9,10,15,21,25] Serial imaging studies may show reduction in thickness and degree of enhancement of meninges.[2] This was seen in the second patient. However, symptoms may become steroid-dependent as observed in our patients.[9,21,17,25] Clinical improvement was excellent in the first and third patients, both of whom relapsed on steroid withdrawal with complete remission of symptoms on steroid reinstitution. Response was modest in the second patient. Addition of immunosuppressive agents like azathioprine and cyclophosphamide is required in steroid-dependent cases.[2,13,20,21,25] All our patients received azathioprine for steroid-sparing effect in the first and third cases and for suboptimal response to steroid in the second case. Empirical ATT has been advocated.[8,14] There was no response to ATT in our study.

Conclusions

HP is an important cause of recurrent cranial neuropathies and headaches. Early institution and long-term maintenance of steroid therapy along with azathioprine may prevent neurologic sequelae. HP and abdominal IPT may represent manifestations of MF in response to unknown immune-mediated mechanisms.

References

1. Masson C, Boukriche Y, Colombani JM. Inflammatory hypertrophic cranial pachymeningitis. Presse Med 2001;95:65-70.
2. Prabhakar S, Bhatia R, Lal V, Singh P. Hypertrophic pachymeningitis: Varied manifestations of a single disease entity. Neurol India 2002;50:45-52.
3. Sylaja PN, Cherian PJ, Das CK, Radhakrishnan VV, Radhakrishnan K. Idiopathic hypertrophic cranial pachymeningitis. Neurol India 2002;50:53-9.
4. Bosman T, Simonin C, Launay D, Caron S, Destée A, Defebvre L. Idiopathic hypertrophic cranial pachymeningitis treated by oral methotrexate: A case report and review of literature. Rheumatol Intl 2008;28:713-8.
5. Ashraf VV, Bhasi R, Kumar RP, Girija AS. Primary Sjogren's syndrome manifesting as multiple cranial neuropathies: MRI findings. Ann Indian Acad Neurol 2009;12:124-6.
6. Bhatia R, Tripathi M, Srivastava A, Garg A, Singh MB, Nanda A, *et al.* Idiopathic hypertrophic cranial pachymeningitis and dural sinus occlusion: Two patients with long-term follow up. J Clin Neurosci 2009;16:937-42.
7. Goyal M, Malik A, Mishra NK, Gaikwad SB. Idiopathic hypertrophic pachymeningitis: Spectrum of the disease. Neuroradiology 1997;39:619-23.
8. Shobha N, Mahadevan A, Taly AB, Sinha S, Srikanth SG, Satish S, *et al.* Hypertrophic cranial pachymeningitis in countries endemic for tuberculosis: Diagnostic and therapeutic dilemmas. J Clin Neurosci 2008;15:418-27.
9. Rossi S, Giannini F, Cerase A, Bartalini S, Tripodi S, Volpi N, *et al.* Uncommon findings in idiopathic hypertrophic cranial pachymeningitis. J Neurol 2004;251:548-55.
10. Jimenez-Caballero PE, Diamantopoulos-Fernandez J, Camacho-Castaneda I. Hypertrophic cranial and spinal pachymeningitis: A description of four new cases and a review of the literature. Rev Neurol 2006;43:470-5.
11. Mamelak AN, Kelly WM, Davis RL, Rosenblum ML. Idiopathic hypertrophic cranial pachymeningitis: Report of three cases. J Neurosurg 1993;79:270-6.
12. Riku S, Hashizume Y, Yoshida M, Riku Y. Is hypertrophic pachymeningitis a dural lesion of IgG4-related systemic disease? Rinsho Shinkeigaku 2009;49:594-6.
13. Rojana-udomsart A, Pulkes T, Viranuwatti K, Laothamatas J, Phudhichareonrat S, Witoonpanich R. Idiopathic hypertrophic cranial pachymeningitis. J Clin Neurosci 2008;15:465-9.
14. Parney IF, Johnson ES, Allen PB. Idiopathic cranial hypertrophic pachymeningitis responsive to antituberculous therapy: A case report. Neurosurgery 1997;41:965-71.
15. Riku S, Kato S. Idiopathic hypertrophic pachymeningitis. Neurolpathology 2003;23:335-44.
16. Lizarazo J, Parra E, Gutiérrez P, Mora C, Vargas J. Idiopathic hypertrophic cranial pachymeningitis. Biomedica 2004;24:125-32.
17. Hatano N, Behari S, Nagatani T, Kimura M, Ooka K, Saito K, *et al.* Idiopathic hypertrophic pachymeningitis: Clinicoradiological spectrum and therapeutic options. Neurosurgery 1999;45:1336-44.
18. Gunny RS, Akhbar N, Connor SEJ. CT and MRI appearances of inflammatory pseudotumour of the cervical lymph nodes. Br J Radiol 2005;78:651-4.
19. Shetty RB. Inflammatory pseudotumour of the mesentery. Indian J Surg 2007;69:108-9.
20. Kupersmith MJ, Martin V, Heller G, Shah A, Mitnick HJ. Idiopathic hypertrophic pachymeningitis. Neurology 2004;62:686-94.
21. Masson C, Henin D, Hauw JJ, Rey A, Raverdy P, Masson M. Cranial pachymeningitis of unknown origin: A study of seven cases. Neurology 1993;43:1329-34.
22. Goyal M, Sharma A, Mishra NK, Gaikwad SB, Sharma MC. Imaging appearance of pachymeningeal tuberculosis. AJR Am J Roentgenol 1997;1169:1421-4.
23. Nagashima T, Maguchi S, Terayama Y, Horimoto M, Nemoto M, Nunomura M, *et al.* P-ANCA positive Wegener's granulomatosis presenting with hypertrophic pachymeningitis and multiple cranial neuropathies: Case report and review of literature. Neuropathology 2000;20:23-30.
24. Saremi F, Helmy M, Farzin S, Zee CS, Go JL. MRI of cranial nerve enhancement. AJR Am J Roentgenol 2005;185:1487-97.
25. Choi S, Park SC, Jung YK, Lee SS. Combined therapy of corticosteroid and azathioprine in hypertrophic cranial pachymeningitis. Eur Neurol 2000;44:193-8.

How to cite this article: Hassan KM, Deb P, Bhatoe HS. Idiopathic hypertrophic cranial pachymeningitis: Three biopsy-proven cases including one case with abdominal pseudotumor and review of the literature. Ann Indian Acad Neurol 2011;14:189-93.

Received: 07-09-10, **Revised:** 05-11-10, **Accepted:** 18-12-10

Source of Support: Nil, **Conflict of Interest:** Nil