A Case of Pachymeningitis Presenting as Optic Perineuritis and Multiple Cranial Neuropathies

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ABSTRACT

Objective: To discuss the clinical presentation and management of idiopathic hypertrophic pachymeningitis that presented with multiple cranial neuropathies.

Methods: This is a case report.

Case Presentation: A 37-year-old female presented with right-sided headache and ipsilateral cranial nerve (CN) I, II, III, IV, and V deficits which improved with nonsteroidal anti-inflammatory drugs (NSAIDs). Six months later she developed bilateral blurring of vision with pain on eye movement, which progressed to severe bilateral affectation that prompted admission and treatment with high-dose methylprednisolone therapy followed by prolonged oral steroid treatment which was gradually tapered. Recurrence was treated with oral steroids and azathioprine. Diagnostic modalities included an initial cranial contrast computed tomography (CT) scan which was inconclusive; contrast magnetic resonance imaging (MRI) clinched the diagnosis, as well as demonstrated thickening of the optic nerve perineurium. Visual field analysis 30-2 as well as optic nerve head optical coherence tomography (OCT) were used to support the diagnosis and document optic nerve affectation. Biologic testing was used to rule out tuberculosis, syphilis, fungal infection, granulomatosis with polyangiitis, polyarteritis nodosa, and rheumatoid arthritis. The patient had complete vision recovery in the left eye but only partial vision recovery in the right eye.

Conclusions: Pachymeningitis should be a diagnostic consideration in patients with headache and multiple cranial neuropathies. Clinicians should always perform independent evaluation of diagnostic modalities with the patient's clinical presentation in mind. Pachymeningitis can involve the perineurium through contiguous spread of the lesion and present as optic perineuritis as well, with more insidious progression and lasting deficits than isolated optic perineuritis.

Keywords: Idiopathic Hypertrophic Pachymeningitis, Optic Perineuritis, Multiple Cranial Neuropathies

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Hypertrophic pachymeningitis (HP) is characterized by inflammatory thickening of the dura mater, resulting in focal neurologic deficits, cranial nerve (CN) palsies, and headache. Pachymeningitis itself is a rare disease entity involving inflammation of the cranial meninges, often due to an underlying infectious agent or secondary to a systemic inflammatory disease. In Japan, crude prevalence of HP was reported at 0.949 per 100,000 population.[1] Gender predilection varies among studies, but mean age at presentation is reported to be in the 50s, with an age range between 30 to 80 years old.[2] Headache is almost universally present in 94% of cases, and cranial nerve deficits are present in 50-84%. The most commonly affected cranial nerves are cranial nerves (CNs) are II, IV, V, and VI. Other manifestations include ataxia, cerebellar dysfunction, and seizures. Pachymeningitis may be secondary to an infectious process, commonly due to tuberculosis or syphilis; or primary, also known as idiopathic HP, wherein no underlying cause can be identified[3]. The diagnosis is primarily via brain magnetic resonance imaging (MRI). While dural biopsy remains the gold standard, it is an invasive procedure with inherent risks. Histopathologic studies of the affected dura further subdivides the etiopathogenesis of the disease to being secondary to systemic inflammatory conditions such as granulomatosis with polyangiitis (GPA), rheumatoid arthritis (RA), or more recently, IgG4-Related Disease; if no specific histopathologic subtype is identified on biopsy, the disease is classified as undifferentiated HP. Histopathologic studies reveal fibrosis of the dura; depending on the subtype, more specific characteristics such as infiltration with CD4+ T-Cells in IgG4-Related Disease, or necrosis either within microabscesses or in large, "geographic" regions with granulomatous inflammation such as in GPA, may be found. The most commonly involved site of inflammation is the tentorium cerebelli (80% of cases)[4]. Symptoms are the result of mass effect, nerve compression, or vascular compromise[2,5].

CASE PRESENTATION

A 37-year-old female consulted for headache and rapid loss of vision.

History of present illness began six months prior to admission when the patient developed new-onset right-sided headache that was partially responsive to NSAIDs, accompanied with diplopia on downgaze. She consulted at our outpatient department, where multiple CN deficits involving the right CNs I, III, IV and V-1 were found. Optic nerve involvement of the right eye was also considered, evidenced by temporal pallor of the right optic disc; visual acuity remained 20/20 and color vision was intact in both eyes (Figure 1). The rest of the neuro-ophthalmic exam was unremarkable.

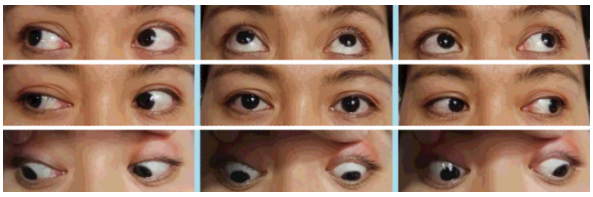


Figure 1: Adnexa and versions of patient GA. Figure 1a (right): Nine-gaze pictures of the patient showing slight ptosis on right gaze, subtle hypertropia of the right eye and -1 adduction deficit in left gaze, and exotropia on downgaze.

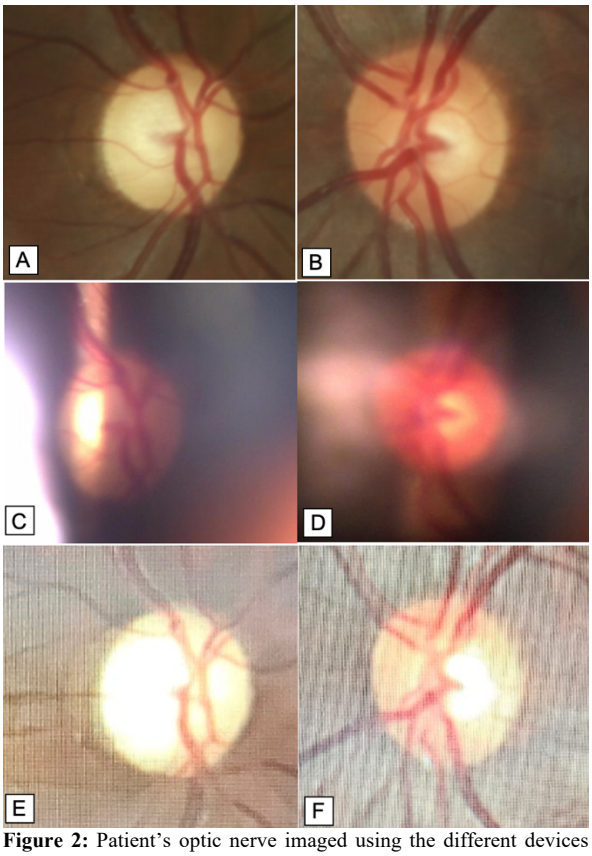


Figure 2: Patient's optic nerve imaged using the different devices available in our institution at different points in time, OD (right) and OS (left) from 6 months prior to admission (a,b); note the temporal pallor OD. During admission (c,d), there was initial hyperemia of the left optic disc noted (d). At three months post-high-dose methylprednisolone treatment, we note progression of disc pallor OD (e), as well as resolution of the hyperemia noted during admission (f).

The patient underwent optical coherence tomography of the optic nerve head (OCT-ONH) using the Optovue OCT machine, with note of severe generalized peripapillary RNFL thinning with effacement of the double-hump pattern inferiorly but the general impression of the double-hump pattern intact. The left OCT-ONH was essentially unremarkable (Figure 3a-b).

Visual field analysis was done with the Frey machine using the 30-2 Swedish Interactive Threshold Algorithm (SITA) Standard Threshold testing strategy. Results for the right eye showed a superior peripheral/superotemporal hemiarcuate scotoma, an inferior hemiarcuate-to-arcuate scotoma, and blind spot enlargement (Figure 4a). Visual field analysis of the left eye showed significant inferior arcuate scotoma crossing vertical midline and horizontal raphe, and blind spot enlargement (Figure 4e).

A bilateral optic neuropathy was considered accompanied by other cranial neuropathies of the right side. A contrast-enhanced MRI of the brain and orbits was advised; however the patient's orthodontic devices precluded neuroimaging at this time. Cranial and orbital CT scan with contrast was performed. The imaging results showed what in retrospect can be identified as hyperdensity with enhancement in the right medial temporal lobe adjacent to the sellar region near the clivus and chiasm, as well as hyperdensity and thickening of the right tentorium cerebelli. At the time, however, the radiology service did not confirm the hyperdensity as definitively significant, and the sign out official reading of an unremarkable brain and orbits CT scan with a mucus retention cyst in the right maxilla was made (Figure 5).

The patient sought a second medical opinion with an internist who made a diagnosis of cluster headache and prescribed mefenamic acid 500mg and verapamil 240mg 2x/day, which provided near-complete relief of symptoms. The patient was lost to follow-up in the interim.

Two weeks prior to consult, the patient noted rapidly progressive dimming of vision on the right eye associated with right-sided headache and bilateral orbital pain, worse with eye movement. The patient consulted at our institution. Examination revealed visual acuities of poor light projection in the right eye and 5/200 in the left eye. Brain MRI with contrast was performed. The patient also underwent serial VFA 30-2, which showed rapid progression of right eye dimming of vision (Figure 4b) to the floor of detectable stimuli on the Frey machine (Figure 4c); the left eye initially showed minimal peripheral scotomata (Figure 4b). Onset of dimming of vision of the left eye, which presented on admission as scotoma in the temporal hemifield and inferonasal quadrant prompted admission (Figure 4e).

Upon admission, the patient was noted with poor light projection of the right eye and 5/200 distance visual acuity of the left eye. The right eye was unable to identify colored lights. The left eye was unable to identify Ishihara plates and only identified ⅔ colored lights correctly. A grade III relative afferent pupillary defect (RAPD) of the right eye was noted; the right pupil measured 4mm on direct illumination and 2mm with consensual response while the left pupil measured 2mm on direct illumination and 4mm on consensual response (Figure 5a-b). The patient had adequate levator function with intact lid crease and no ptosis of both eyes. Slit-lamp examination showed a normal conjunctiva and cornea with +2 cells in the anterior chamber in both eyes. The fundus was devoid of lesions. The rest of the cranial nerve and systemic neurologic examinations were unremarkable, with resolution of the other baseline cranial nerve deficits noted.

The patient underwent cranial MRI with contrast which showed focal dural enhancement of the right medial temporal lobe, adjacent to the sellar and chiasmal areas with extension of the dural inflammation into the optic nerve perineurium; as well as enhancement of the right tentorium cerebelli (Figure 6). The patient's OCT-ONH OD showed thinning in the temporal quadrant and inferotemporal and superonasal RNFL sectors; the topographic scans show focal superotemporal thickening compared to baseline. The patient's OCT-ONH OS showed subtle focal thickening in the superotemporal and nasal lower peripapillary RNFL areas (Figure 3c-d).

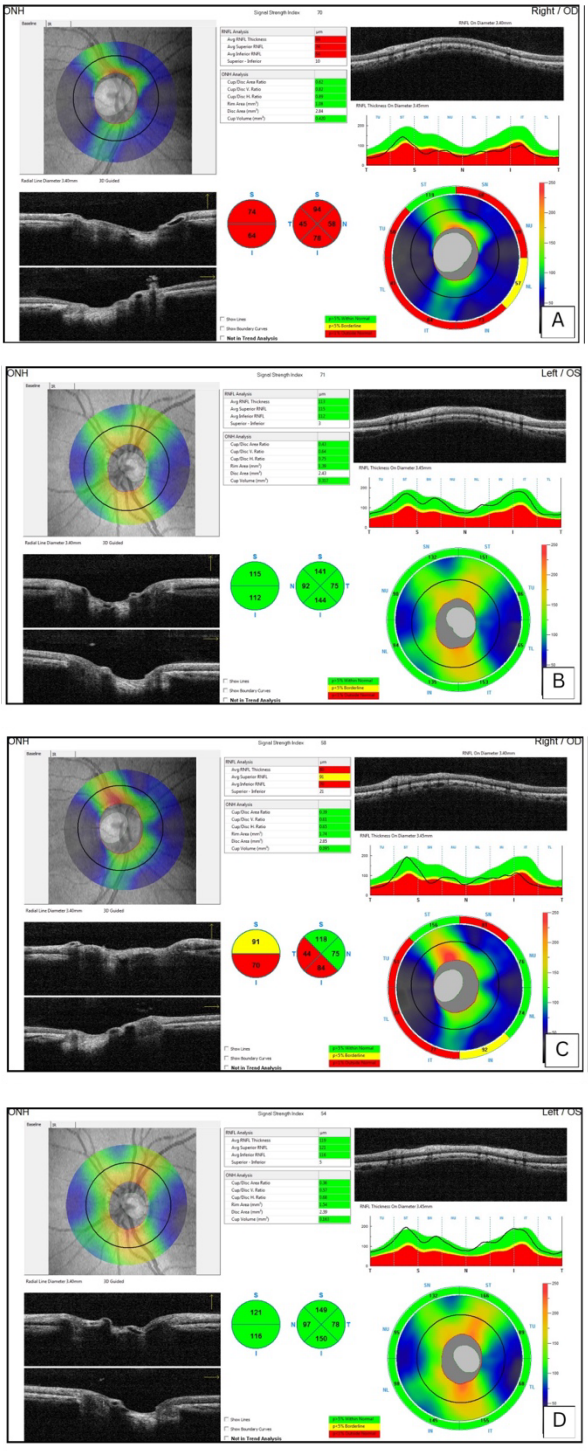
Comprehensive diagnostic evaluation showed elevated erythrocyte sedimentation rate (indicate

level and normal values), C-reactive protein (indicate leval and normal values). Serum c-ANCA, p-ANCA, C3 complement protein, rheumatoid factor, anti-nuclear antibody, anti-ds-DNA, chest x-ray, serum VDRL, HBsAg, and anti-HCV and thyroid panel were all within normal limits. ESR and CRP were both elevated at 85 and 6.43 , respectively. Lumbar puncture was done which showed cerebrospinal fluid (CSF) with pleocytosis (18.1 WBCs/uL) with lymphocytic predominance (84.4%). CSF protein count was elevated (80.2mg/dL) however glucose was within normal range (63.7mg/dL). Cell block cytology of CSF showed scant lymphocytes with no malignant cells noted; KOH, India ink, and AFB staining were all negative (Table 1).

The patient was started on IV methylprednisolone 250mg IVTT q6h for 3 days, brimonidine eye drops 2x/day to both eyes for optic nerve and retinal cell neuroprotection, prednisolone eye drops 3x/day to both eyes, and alpha-lipoic acid 300mg cap once a day. She was also started on mecobalamine 500mg tab once a day and vitamin D + Calcium tab once a day.

Repeat eye examination revealed vision improved to 10/200 on the left eye, while there was note of robust fair light perception in 1 quadrant of the right eye. Both anterior chambers were quiet. The rest of the ophthalmologic exam was unremarkable. The patient was shifted oral prednisone at 50mg/day). Vision recovered OS to 20/40 improved to 20/20 with corrective lenses (Table 2). The patient was discharged on the 7th hospital day. Repeat of OCT-ONH OU was done prior to discharge, with note of interval reduction in thickening of the peripapillary RNFL OD, as well as resolution of the focal thickening areas OS (Figure 3e-f).

The patient was maintained on oral prednisone which was gradually tapered; recurrence of headache upon discontinuation of steroid prompted a restart of oral treatment with addition of azathioprine 500mg tab 2x/day. She achieved robust remission of blurred vision in the left eye, achieving a best corrected visual acuity (BCVA) of 20/20 on latest follow-up. The right eye achieved a final BCVA of 15/200 with partial recovery of vision in the superonasal visual field (Figure 4d & h). Repeat cranial MRI with contrast and fat suppression 6 months post-induction of treatment showed marked decrease in all areas of leptomeningeal thickening noted on baseline study, with no new lesions noted (Figure 7). The patient remained on azathioprine tab 2x/day and prednisone 20mg tab daily.



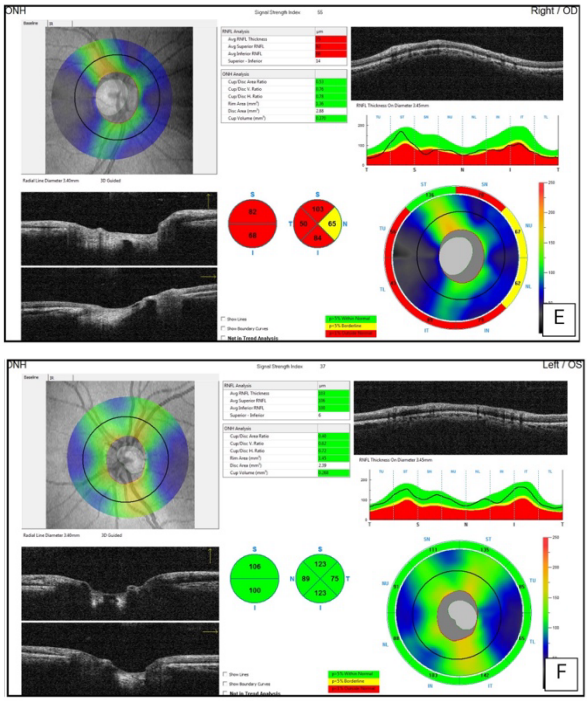
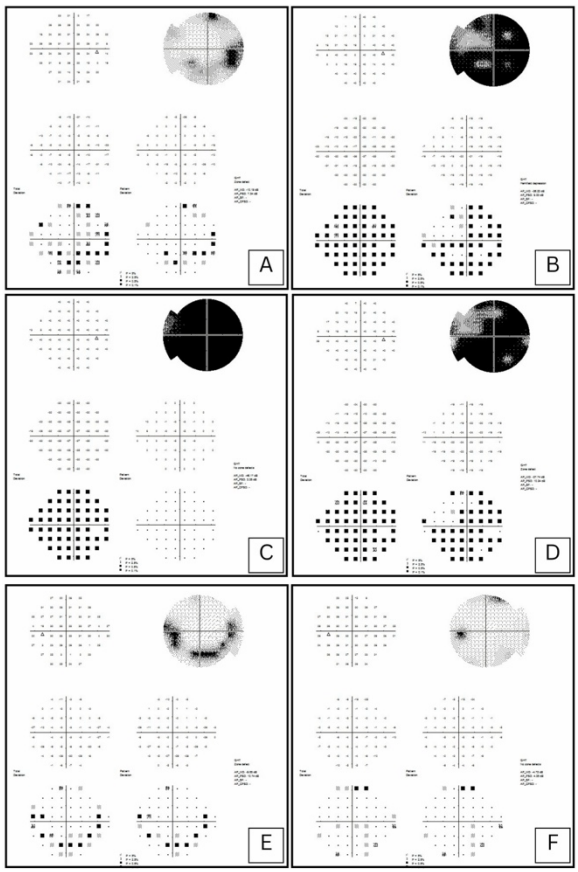


Figure 3: OCT-ONH of the patient throughout the course of the disease. 3a-b: patient's OCT-ONH OD and OS respectively, 6 months prior to admission; 3c-d: OCT-ONH OD and OS on admission; 3e-f: on discharge.



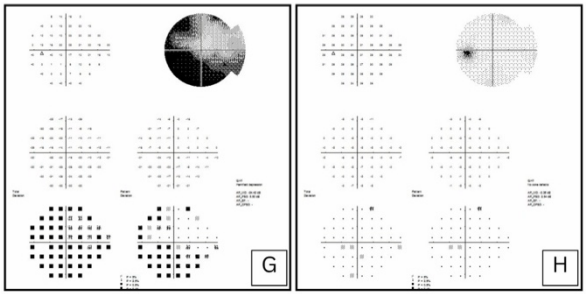


Figure 4: Patient's VFA OD (first row) and OS (second row) six months prior to admission (a,e), two weeks prior to admission (b,f), prior to admission (c,g), and on follow-up (d,h).

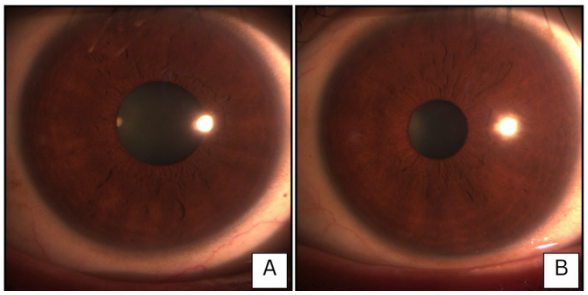


Figure 5: Patient's pupil OD (a) and OS (b) on admission, demonstrating right pupil size larger than left under similar light conditions.

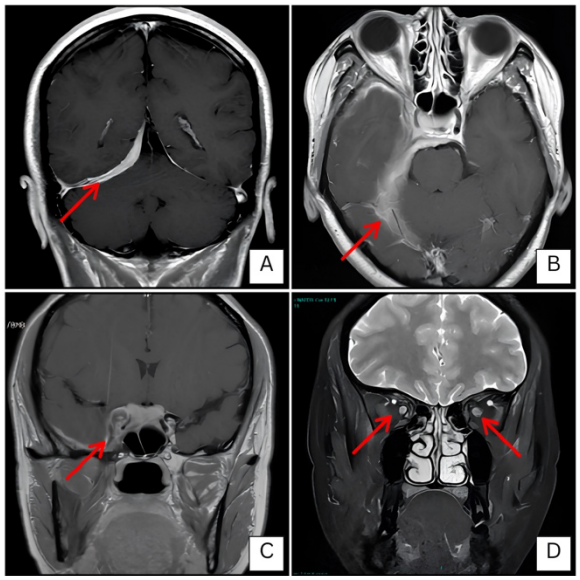


Figure 6: MRI done 10/24/25. Arrows show the areas of leptomeningeal enhancement, evident on T1 and T2-weighted images with contrast (a, b arrows). The right cavernous sinus (c, arrow) and the perineurium of both optic nerves show contrast enhancement (d, arrows).

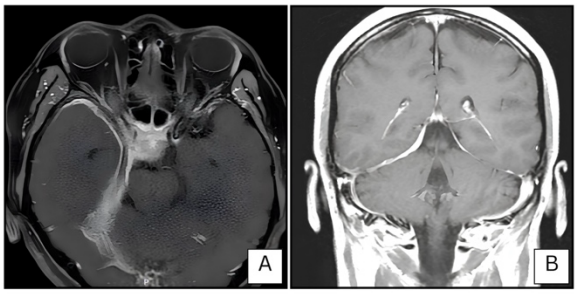


Figure 7: Interval decrease in hyperintensity of the right tentorium and anterior temporal lobe on contrast MRI.

DISCUSSION

In literature, gender preponderance of idiopathic hypertrophic pachymeningitis varies between studies, but mean age is commonly at the 50s, with an age range between 30 and 60, up to 80 years old, placing our patient at the younger end of the range[1,2]. Headache is almost universally present (94%); CN deficits were present in 50-84% of patients in existing studies. The most commonly-affected cranial nerves included CNs II, VI, IV, and V, of which only CN VI was not affected in our patient.

Diagnosis involves a combination of identifying the disease entity as well as its possible underlying etiologies using neuroimaging and biomarkers. In literature, CT scan is cited to be less likely to positively identify lesions; however, lesions may be visible as contrast-enhancing areas of dura, as was the case in our patient. MRI with contrast is the imaging modality of choice; lesions present as hypointense signals on T1- and T2-weighted sequences and enhance significantly on post-contrast T1 sequences after gadolinium injection. In T2 sequences, the hypointense signal related to the density of fibrous tissue may be bordered by a thin peripheral strip of hypersignal indicating the hypervascularization of the injured dura mater[6].

A comprehensive clinical assessment of HP involves ruling out infectious causes and identifying possible underlying systemic conditions. Infectious etiologies include tuberculosis, syphilis, fungal infections, and infectious complications arising from sinusitis. Non-infectious inflammatory causes can include Sarcoidosis, GPA, RA, IgG4-Related Disease, Systemic Lupus Erythematosus (SLE), Sjogren Syndrome, Giant Cell Arteritis, Behcet's Disease, and Relapsing Polychondritis[2]. A diagnosis of idiopathic HP is made when no underlying disease can be identified. The following table details several diagnostic tests included in the workup of HP. Other diagnostics not requested in our case due to lack of accessibility or availability, but ideally included in the workup are serum IgG4, anti-NMO & anti AQP4 antibodies, serum ACE & Lysozyme, serum TB Quantiferon, and chest CT-scan. A biopsy was advised for the patient's cranial lesions but the patient did not consent at this time, which would ideally definitively rule out such etiologies as fungal infection and malignant processes prior to starting steroids (Table 3).

Table 3: Workup of Hypertrophic Pachymeningitis[6].

Imaging Evaluation	Etiology Investigations
• MRI of the brain with contrast • Sinus CT (Aspergillus sinusitis) • Thorax CT (Sarcoidosis) • Cervical US	• Serum IgG4 • ANCA • ANA • Serum VDRL • HIV Serology • Rheumatoid Factor • Galactomannan (Aspergillosis) • Long bones radiography • Hypophysis Survey

Optic perineuritis is commonly considered a variant of orbital inflammatory disease. The optic nerve sheath is contiguous with the brain meninges; in this case, the inflamed intracranial dura is in close proximity and may have had contiguous spread towards the optic perineurium. We came across one case report where c-ANCA-associated pachymeningitis also presented with optic perineuritis[7]. Another study cites the identification of 37 cases of orbital inflammatory disease with associated idiopathic hypertrophic pachymeningitis[8].

The assessment of response to treatment involves both clinical assessment of the reversal and/or abrogation of progression of neurologic deficits, as well as monitoring inflammatory and disease-specific biomarkers relevant to the underlying disease. Neurologic damage may be severe and irreversible, thus making the timely diagnosis of the condition imperative. Unfortunately, a non-response to treatment is the more likely outcome rather than complete or partial response. Furthermore, long-term corticosteroid and disease-modifying antirheumatic drug (DMARD) treatment is both expected and

necessary to prevent relapse; however, disease flare may occur even while on long-term suppressive treatment. Involvement of the optic nerve in the disease allows for non-invasive monitoring of response to disease treatment through the patient's visual function and optic nerve status. This may involve color vision testing, optical coherence tomography, visual field analysis, and other measures of visual function. A gradual tapering of treatment is necessary, as recurrence is more common with rapid discontinuation of treatment[9].

CONCLUSION

This is the case of clinically-diagnosed hypertrophic pachymeningitis with optic perineuritis which responded to intensive steroid treatment, with recovery of vision in one eye and partial recovery in the more severely-affected eye; robust disease remission was achieved however recurrence is currently being treated. Pachymeningitis should be a differential diagnosis in any patient with headache and multiple cranial nerve palsies with diffuse neurologic topographic distribution. MRI with contrast remains the most sensitive and specific non-invasive diagnostic imaging modality of choice for neurologic conditions, and an invaluable tool in vision loss due to optic nerve and neurologic conditions, although a careful examination of CT scan results may yield suggestive findings. Ophthalmology and neurology services should work in close coordination to detect, treat, and monitor patients with this disease.

ACKNOWLEDGEMENTS

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ETHICS COMPLIANCE STATEMENT

The authors affirm that this case report was prepared in accordance with the ethical standards of the *Philippine Journal of Ophthalmology*, the principles outlined in the Declaration of Helsinki, and applicable institutional and national guidelines on research involving human participants.

Written informed consent for publication of clinical details and accompanying images were obtained from the patient prior to manuscript submission. The authors confirm that all identifying information has been removed or anonymized to protect patient privacy.

The authors declare that the case report did not require formal institutional review board (IRB) approval, as per the policies of the authors' institution, because it describes a single clinical case without experimental intervention.

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