Case Report

Hypertrophic Pachymeningitis from Neuro-Behçet's Disease: A Case Report

Suntaree Thitiwichienlert[1*], Dussadee Sakonlaya[2], Panlop Chakkavittumrong[3], Punchong Hanvivadhanakul[4], Supinda Leeamornsiri[1], Wimolwan Tangpagasit[1], Thanapat Dechasasawat[5]

Abstract

A 26-year-old female presented with visual loss for 10 days from optic neuritis, which had recurred in the fellow eye one year apart. Neuroimaging, Pathergy test and skin biopsy results supported the diagnosis of neuro-Behçet's disease. The patient was successfully treated with pulse methylprednisolone followed by prednisolone and immunosuppressive agents.

Keywords: Optic Neuritis, Pachymeningitis, Behçet's Disease

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[1] Department of Ophthalmology, Faculty of Medicine, Thammasat University
[2] Department of Pathology and Forensic Medicine, Faculty of Medicine, Thammasat University
[3] Department of Dermatology, Faculty of Medicine, Thammasat University
[4] Department of Rheumatology, Faculty of Medicine, Thammasat University
[5] Department of Radiology, Faculty of Medicine, Thammasat University
[*] **Corresponding Author:** Suntaree Thitiwichienlert, Department of Ophthalmology, Faculty of Medicine, Thammasat University, Khlong Luang, Pathum Thani 12130, Thailand, Tel: +66 2926 9957, +669 8059 9191 Fax: +66 2986 9212, Email: punoipunoi@hotmail.com

Introduction

Hypertrophic pachymeningitis is a rare inflammatory meningeal process, which involves the dura mater and causes diffuse or local dura thickening. It can be caused by various etiologies such as infection, neoplasm, inflammation, or idiopathic. Clinical features include headache, optic neuropathy, cranial nerve palsy, stroke, seizure, and intracranial hypertension.[1] Behçet's disease is a chronic recurrent multiple-organ inflammatory disorder. Neuro-Behçet's disease is caused by vasculitis-induced thrombosis, while hypertrophic pachymeningitis is rare.[2] Behçet's disease is a rare disease, and hypertrophic pachymeningitis from presumed Behçet's disease is a very rare condition. Previous studies reported cases of hypertrophic pachymeningitis from Neuro-Behçet's disease with bilateral anterior uveitis, benign intracranial hypertension with papilledema, and cranial nerve palsies.[3-5] Opticneuropathy is an uncommon ocular involvement in Behçet's disease and optic neuritis has rarely been reported in Behçet's disease. The authors report an unusual case of unilateral optic neuritis from hypertrophic pachymeningitis with sequential involvement of the other is in accordance with fellow eye one year later. This study followed the tenets of the Declaration of Helsinki for research involving human subjects in all subjects. The study protocol was approved by our Institutional Ethics Committee (approval number MTU-EC-OP-0-074/66). Informed consent was obtained from the patient.

Case Report

A 26-year-old female presented with acute headache and progressive visual loss in the right eye for 10 days. The initial best corrected visual acuity (BCVA) was 10/200 OD and 20/30 OS. The intraocular pressure was 16, 19 mm Hg. Ocular examinations were normal OU. Pupils test revealed a relative afferent pupillary defect (RAPD) positive grade I in the right eye. The fundus examination revealed normal background fundus and the optic disc appeared pink with sharp margins and a cup-to-disc ratio of taken at 0.3 in both eyes (fundus photo was not done in the first visit). The color vision was normal and the visual field revealed a right central scotoma and a left normal left visual field. We suspected retrobulbaroptic neuropathy and we performed Optical coherence tomography (OCT) for a baseline to assess the retinal nerve fiber layer (RNFL) the loss of time. OCT showed a normal average peripapillary RNFL thickness in both eyes. Neurological examinations revealed no focal deficits. Other systemic symptoms were negative.

The following laboratory analyses were unremarkable: complete blood count, fasting blood sugar, lipid profiles, coagulation assay, venereal disease research laboratory (VDRL), treponema pallidum hemagglutination assay (TPHA), hepatitis panel, anti-HIV test, thyroid function test (TFT), rheumatoid factor (RF), antinuclear antibody (ANA), anti-double-stranded DNA (anti-dsDNA), antineutrophil cytoplasmic antibodies (ANCA), and antibodies to aquaporin-4 (AQP4-IgG). However, anti-aquaporin-4 high levels of blood tests showed high erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) levels (20 mm/hr and 26.69 mg/dL). Contrast-enhanced magnetic resonance imaging (MRI) of the brain and orbit showed faint hyperintensity with focal enhancement at the right intracanalicular optic nerve with a relative enhancement of the adjacent optic nerve sheath complex at the right optic canal, and thin dural thickening along the right anterior clinoid process. MRI of the brain also showed multifocal dural thickening along bilateral parietooccipitotemporal convexities, bilateral tentorium cerebelli, and posterior fossae, up to 0.5 cm in maximal thickness, indicating possible idiopathic pachymeningitis or IgG-4 related disease (Figure 1). Lumbar puncture revealed normal cerebrospinal fluid (CSF) pressure, protein, sugar, cell count, gram stain and culture. Additional serum IgG-4 testing was normal. While waiting for laboratory and MRI results and before starting steroids, her right visual acuity was improved to 20/30 at one month following after the initial visit. Repeat visual field testing revealed an improvement of the right central scotoma and resolution of the right central scotoma in the third clinical visit. We suggested steroid treatment, but the patient had spontaneous resolution without treatment, and then she was lost to follow-up during the coronavirus pandemic.

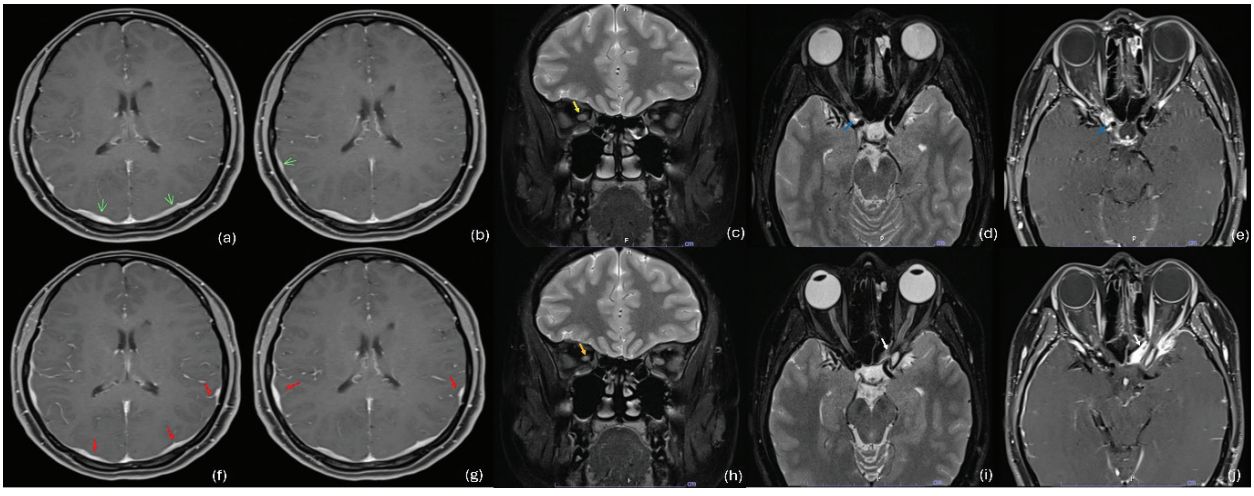

Figure 1 Contrast-enhanced MRI brain and orbit with comparison between the 1st episode (a-e) and 2nd episode (f-j): (a,b) axial view T1FS shows multifocal dural thickening along bilateral parietooccipitotemporal convexities (green arrow), (c) coronal view T2FS shows the right optic nerve (yellow arrow), (d) axial view T2FS shows a faint hyperintense right optic nerve (blue arrow), (e) axial view T1 FS with gadolinium shows focal enhancement at the right intracanalicular optic nerve with an enhancement of the optic nerve sheath and thin dural thickening along the right anterior clinoid process (blue arrow), (f, g) progression of multifocal dural thickening (red arrow), (h) a decrease in size of the right optic nerve (orange arrow), (i) a faint hyperintense left optic nerve (white arrow), (j) focal enhancement is noted at the left intracanalicular optic nerve with an enhancement of the optic nerve sheath, and thin dural thickening along the left anterior clinoid process (white arrow).

One year later, she experienced of acute headaches and visual loss in the left eye for one day. She was earlier vaccinated with an inactivated coronavirus vaccine one week prior. BCVA was 20/20 OD and 5/200 OS. Slit-lamp examinations revealed a normal anterior segment with RAPD positive grade I OS. Fundus examination showed temporal pallor of the right optic disc and mild swelling hyperemic left optic disc. OCT optic nerve head images show thinning of the temporal RNFL in the right eye and increased peripapillary RNFL thickness of the left eye (Figure 2). She had dyschromatopsia OS and visual field evaluation revealed a right normal central visual field and a left generalized depression. Left optic neuritis was diagnosed. MRI of the brain and orbit showed faint hyperintensity with focal enhancement at the left intracanalicular optic nerve in with a relative enhancement of adjacent optic nerve in the sheath complex at the left optic canal, and thin dural thickening along the left anterior clinoid process involving left orbital apex and anterior aspect of the left cavernous sinus. It also showed multifocal dural thickening along bilateral cerebral convexities, bilateral tentorium cerebelli, and posterior fossa (Figure 1). The overall progression of these lesions probably suggested an IgG4-related disease or other inflammatory diseases. Lumbar puncture revealed normal CSF profiles.

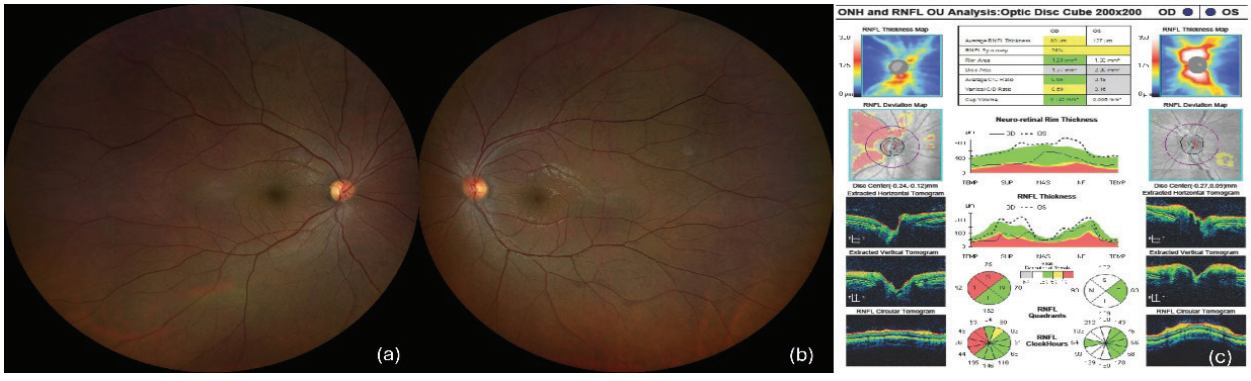

Figure 2 Optic disc photographs show temporal pallor of the right optic disc (a) and mild swelling hyperemic left optic disc (b), OCT optic nerve head images show thinning of the temporal RNFL in the right eye and increased peripapillary RNFL thickness of the left eye (c).

She had papulopustules on the extremities and vulva. We consulted a dermatologist, and rheumatologist. Repeat laboratory analyses before steroid treatment were unremarkable. ESR and CRP were used as markers to monitor the inflammatory levels. The patient still had elevated ESR and CRP (13 mm/hr and 14.26 mg/dL). Her skin pathergy test was positive. We did not send human leukocyte antigen typing B51 (HLA-B51), but we performed a skin biopsy on the forearm and the vulva, in which histopathological findings showed the presence of nuclear dust in the superficial perivascular area and deep perivascular infiltrate of lymphohistiocytes with some polymorphonuclear neutrophils (PMN) (Figure 3). We proposed the diagnosis of neuro-Behçet's disease. The patient received intravenous methylprednisolone (IVMP) for 3 days, followed by 1 mg/kg/day (MKD) of oral prednisolone. One week later, BCVA improved to 20/20 OS. Prednisolone was decreased to a dose of 50 mg/day and tapered off within 8 weeks. The patient received colchicine 0.5-2 mg/day and azathioprine 2-2.5 mg/kg/day to control inflammation and prevent relapse. ESR and CRP decreased to normal levels. Papulopustular skin and vulva lesions improved. Her headache and visual symptoms have not recurred during an 18-month follow-up.

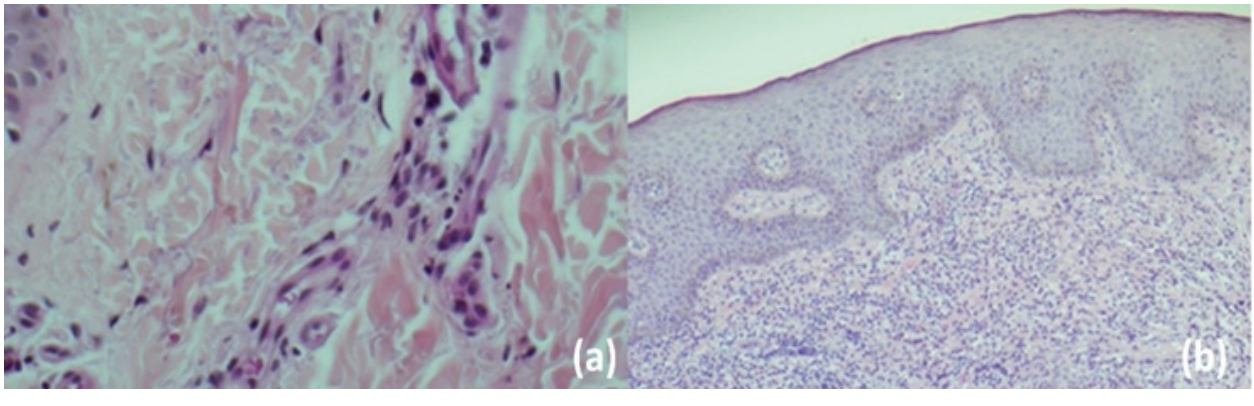

Figure 3 A histopathologic examination reveals (a) the presence of nuclear dust in the superficial perivascular area of the forearm, (b) psoriasiform and spongiotic dermatitis with hypergranulosis; irregular acanthosis; lymphocytic and neutrophilic exocytosis; dense superficial perivascular and interstitial infiltrate with a mildly dense deep perivascular infiltrate of lymphohistiocytes with some PMNs, without demonstrable ulcer or viral cytopathic changes of the vulva.

Discussion

Behçet's disease is an uncommon cause of hypertrophic pachymeningitis. Yoon et al. reported the first case presenting with blurred vision and chronic headaches from hypertrophic pachymeningitis in neuro-Behçet's disease.[3] He had anterior uveitis, skin lesions, recurrent oral ulcers, pachymeningitis, and a positive pathergy test. His patient had a negative HLA-B51 test and did not undergo a dura biopsy, but his patient was diagnosed with Behçet's disease based on the areas of involvement (anterior uveitis, skin lesion, recurrent oral ulcer, pachymeningitis, and positive pathergy test). Previous studies found that HLA-B51 was highly associated with Behçet's disease, especially in the Silk Road countries where reports have found a prevalence of up to 50-80%.[6,7]

In the first episode, the clinical findings of our patient were suggestive of retrobulbar optic neuropathy with headache. An initial differential diagnosis of retrobulbar optic neuritis, or compressive/infiltrative optic neuropathy was made. We evaluated the patient as an atypical optic neuritis and performed neuroimaging to exclude compressive or infiltrative lesions, but the MRI findings suggested inflammatory optic neuropathy from adjacent dural disease. Hypertrophic pachymeningitis can be diagnosed with characteristic the MRI findings, it presents as a localized or diffuse thickening of the dura, where the inflammatory process often causes abnormal enhancement in those areas.[8] Dural biopsy makes a definitive diagnosis, but sometimes there is a limitation to performing dural biopsy, lumbar puncture and blood tests to exclude secondary hypertrophic pachymeningitis may be needed. In this case, we diagnosed hypertrophic pachymeningitis as idiopathic in the first episode because our incomplete investigations could not provide clues to the underlying systemic diseases. Prednisone at a dose 1 mg/kg/day used for often employed as the first-line treatment of idiopathic hypertrophic pachymeningitis. However, our patient had spontaneous improvement, and previous literature has also reported spontaneousresolution of idiopathic hypertrophic pachymeningitis without treatment.[9]

In the second episode, the clinical finding suggest of anterior optic neuropathy. A possible differential diagnosis of post-vaccination optic neuritis or recurrent hypertrophic pachymeningitis was made. Repeated MRI findings suggested optic neuritis from adjacent sinusitis or dural disease in the fellow eye and suspected worsening of the meningeal inflammatory process. Our further investigation included a planned dural biopsy because we suspected a secondary cause. Fortunately, the patient had papulopustular skin lesions on the trunk and extremities which are the most common cutaneous manifestation, and in the common distribution, of Behçet's disease.[10,11] Biopsy of the skin and genitalia is less invasive than a dura biopsy histopathological. A histopathologic examination of the biopsied lesions revealed lymphohistiocytic and neutrophilic inflammatory infiltration at perivascular areas, which had similar features described in the previous histopathological study of Behcet's disease.[12] The pathergy test is one of the diagnostic criteria, and recent studies have revealed a rate of approximately pathergy positivity of about 45%.[13] The majority of patients with neurological symptoms have been reported without ocular involvement. Our case did not have uveitis, retinal vasculitis, or any signs of intraocular inflammation. According to the new international criteria for the diagnosis of Behçet's disease (ICBD),[14] ICBD has a sensitivity of 98.2% and a specificity of 95.6% if the total score is greater than or equal to 4 points. We did not investigate HLA-B51, but we diagnosed neuro-Behçet's disease based on the ICBD score. (genital aphthosis (2 points), skin lesions (1 point), optic neuritis (2 points), neurological manifestations (1 point), and a positive pathergy test (1 point)).

A previous study by the Japanese National Research Committee for Behçet's disease recommended moderate to high dose corticosteroids in acute or subacute attacks of neuro-Behçet's disease. Prednisolone $\geq$ 20 mg/day may be given first and tapered over two to three months. Pulse therapy may be considered if the patient dose not response.[15] Hirohata et al. recommended starting a colchicine dose of 1.0-2.0 mg/day for 5 years to prevent long-term relapse, while prednisolone should be decreased gradually.[16]A previous study by the European League Against Rheumatism (EULAR) Standing Committee for Behçet's disease recommended pulsed IVMP and azathioprine as first-line therapy for neurological involvement, and they considered colchicine as first-line therapy for

oral/genital ulcers, papulopustular, and acne-like lesions.[17] In the present study, combined colchicine and azathioprine are possibly effective in for the prevention of relapse.

In summary, hypertrophic pachymeningitis, resulting in optic neuritis, is a rare presentation of a neuro-Behcet disease. Tissue biopsy is essential for the diagnosis combined with clinical signs and symtoms is essential for diagnosis. High-dose corticosteroids are fundamental in such cases. Our multidisciplinary teamwork demonstrated an uncommon biopsy-proven case of neuro-Behçet's disease, with neuroimaging findings on presentation suggestive of hypertrophic pachymeningitis.

Acknowledgments

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Conflict of Interest: All authors report no conflicts of interest relevant to this article.

References

1. Hatano N, Behari S, Nagatani T, et al. Idiopathic hypertrophic cranial pachymeningitis: clinico-radiological spectrum and therapeutic options. *Neurosurgery.* 1999; 45(6):1336-42.
2. Siva A, Saip S. The spectrum of nervous system involvement in Behcet's syndrome and its differential diagnosis. *J Neurol*. 2009;256(4):513-29.
3. Yoon BN, Kim SJ, Lim MJ, et al. Neuro-Behçet's Disease Presenting as Hypertrophic Pachymeningitis. *Exp Neurobiol*. 2015;24(3):252-5.
4. Alkan G, Kartal A, Emiroğlu M, Paksoy Y. Neuro-Behçet disease presented with pachymeningitis in a child. *Arch Argent Pediatr*. 2019;117(6):e644-e647.
5. Behcet's disease: A report of three clinically distinct cases from North-west India. Indian Journal of Health Sciences and Biomedical Research (KLEU) 11(1): 89-91, Jan-Apr 2018. | DOI: 10.4103/kleuhsj.kleuhsj_150_17
6. Ohno S, Ohguchi M, Hirose S, Matsuda H, Wakisaka A, Aizawa M. Close association of HLA-Bw51 with Behçet's disease. *Arch Ophthalmol.* 1982;100:1455-8.
7. Takeno M. The association of Behçet's syndrome with HLA-B51 as understood in 2021. *Curr Opin Rheumatol*. 2022;34(1):4-9.
8. Karthik SN, Bhanu K, Velayutham S, Jawahar M. Hypertrophic pachymeningitis. *Ann Indian Acad Neurol*. 2011;14(3):203-4.
9. Nishio S, Morioka T, Togawa A, et al. Spontaneous resolution of hypertrophic cranial pachymeningitis. *Neurosurg Rev*. 1995;18(3):201-4.
10. Alpsoy E, Zouboulis C, Ehrlich GE. Mucocutaneous lesions of Behçet's disease. *Yonsei Medical Journal*. 2007;48(4):573-85.
11. Alpsoy E, Dönmez L, Bacanlı A, Apaydin C, Butun B. Review of the chronology of clinical manifestations in 60 patients with Behçet's disease. *Dermatology*. 2003;207(4):354-6.
12. Kalkan G, Karadag AS, Astarci HM, Akbay G, Ustun H, Eksioglu M. A histopathological approach: when papulopustular lesions should be in the diagnostic criteria of Behçet's disease? *Journal of the European Academy of Dermatology and Venereology*. 2009;23(9):1056-60.
13. Kalay Yildizhan İ, Boyvat A. Diagnostic Sensitivity of Different Applications of Pathergy Test for Behçet's Disease. *Arch Rheumatol*. 2019;35(1):29-34.
14. International Team for the Revision of the International Criteria for Behçet's Disease (ITR-ICBD). The International Criteria for Behçet's Disease (ICBD): a collaborative study of 27 countrieson the sensitivity and specificity of the new criteria. *J Eur AcadDermatol Venereol*. 2014;28:338-47.
15. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. *Ann Rheum Dis*. 2018;77(6):808-18.
16. Hirohata S, Kikuchi H, Sawada T, et al. Analysis of various factors on the relapse of acute neurological attacks in Behçet's disease. *Mod Rheumatol*. 2014;24(6):961-5.
17. Hatemi G, Christensen R, Bang D, et al. 2018 update of the EULAR recommendations for the management of Behçet's syndrome. *Ann Rheum Dis*. 2018;77(6):808-18.