Primary Central Nervous System Vasculitis Presenting with Isolated Headache

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Primary central nervous system vasculitis (PCNSV) is an uncommon inflammatory disorder affecting small-to-medium–sized vessels of the central nervous system.[1] Patients present with multiple symptoms of varying duration, severity and progression, headache, and cognitive dysfunction being the commonest followed by focal deficits, seizures, and ataxia.[1] We present a PCNSV patient presenting with isolated headache.

A 22-year-old male, presented with progressively increasing, intermittent, holocranial headache, of moderate intensity, lasting for 2 to 4 hours, twice to thrice per week for past 2 years. This was not associated with photophobia/phonophobia/nausea/vomiting/chemosis/lacrimation/nasal congestion/variation with postural change. He had no other symptoms and mild responsive to nonsteroidal anti-inflammatory drugs. Clinical examination was normal.

Routine investigations, vasculitic profile, viral markers, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were normal. Magnetic resonance imaging (MRI) with MR angiography brain (with contrast) revealed T2-FLAIR (fluid-attenuated inversion recovery) hyperintensities in left frontal lobe with susceptibility-weighted imaging (SWI) sequence showing multiple microbleeds (►**Fig. 1A, B**). PCNSV was considered in view of cortical-subcortical microbleeds. Cerebrospinal fluid (CSF) examination showed five cells (100% lymphocytes), 52 mg/dL glucose (random blood sugar: 76 mg/dL) and 35 mg/dL protein. CSF cultures, malignant cytology and oligoclonal bands were negative. Cerebromeningeal biopsy was performed from the right temporal pole for tissue diagnosis, revealing findings suggestive of granulomatous type PCNSV (►**Fig. 2A, B**).

He was treated with intravenous methylprednisolone pulse (1g/day for 5 days), followed by monthly cyclophosphamide infusions (750mg/m^2) for six doses and maintenance therapy with azathioprine (100 mg/day). His headache improved and is asymptomatic at 2-year follow-up.

Diagnosis of PCNSV requires development of neurologic deficit unexplained by other processes, along with characteristic findings on angiogram, or CNS biopsy showing vasculitis.[2] Our patient did not fulfil this criteria, but brain biopsy was diagnostic. Approximately 10% PCNSV patients are biopsy positive and angiography negative.[1]

PCNSV presentation with isolated headache (classified as 6.4.2 under the International Classification of Headache Disorders-3rd edition [ICHD-3] nomenclature[3]) has not been reported. Headache results from inflammation of vessels, leading to inflammatory cytokine release, which is relayed to the thalamus and limbic-parietal cortex leading to pain sensation.[4]

Presence of localized cortical–subcortical microbleeds, in absence of vascular risk factors, should raise suspicion of PCNSV.[5] These are missed on routine MRI sequences, thereby highlighting the importance of SWI.[5]

Constitutional symptoms are usually absent and CSF examination is abnormal in 93% cases.[1] ESR and CRP are elevated in 17.5 and 33% patients, respectively.[1] Both were normal in our patient. MRI brain is abnormal in 96% cases[1]; infarcts being more common, unlike our patient.

We seek to highlight the importance of neuroimaging which led to the consideration of PCNSV as a differential diagnosis and the importance of achieving a tissue diagnosis via cerebromeningeal biopsy.

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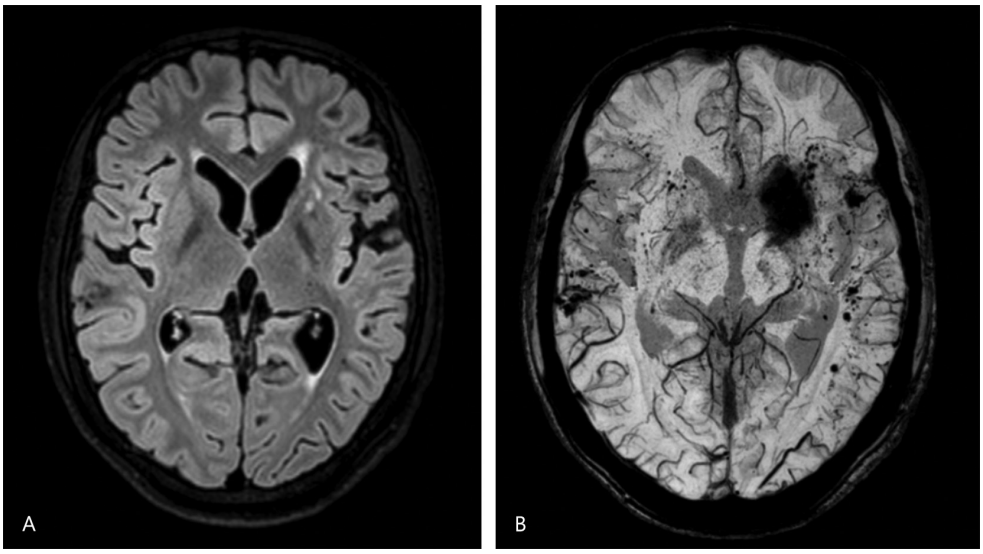

Fig. 1 (**A**) Magnetic resonance imaging (MRI) brain revealing T2-FLAIR (fluid-attenuated inversion recovery) hyperintensities in the left frontal lobe. (**B**) Susceptibility-weighted imaging sequence of MRI brain showing multiple microbleeds.

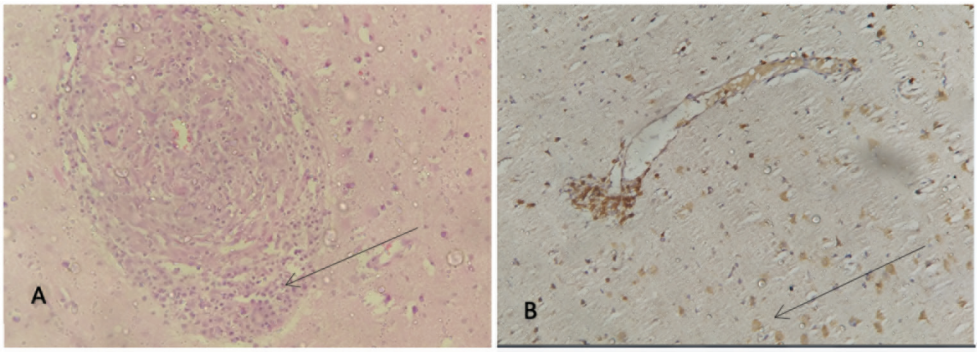

Fig. 2 Right temporal cerebromeningeal biopsy showing chronic perivascular inflammation with predominant CD3+ T-cells with evidence of old hemorrhage, suggestive of granulomatous type primary central nervous system vasculitis on hematoxylin and eosin (**A**) and immunohistochemistry (**B**) stains.

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Conflict of Interest
None declared.

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References

1 Salvarani C, Brown RD Jr., Christianson T, et al. An update of the Mayo Clinic cohort of patients with adult primary central nervous system vasculitis: description of 163 patients. Medicine (Baltimore) 2015;94(21):e738
2 Calabrese LH, Mallek JA. Primary angiitis of the central nervous system. Report of 8 new cases, review of the literature, and proposal for diagnostic criteria. Medicine (Baltimore) 1988; 67(1):20–39
3 Headache Classification Committee of the International Headache Society (IHS) The international classification of headache disorders, 3rd edition. Cephalalgia2018;38(1):1:211
4 Goadsby PJ, Lipton RB, Ferrari MD. Migraine–current understanding and treatment. N Engl J Med 2002;346(4):257–270
5 Boulouis G, de Boysson H, Zuber M, et al; French Vasculitis Group. Primary angiitis of the central nervous system: magnetic resonance imaging spectrum of parenchymal, meningeal, and vascular lesions at baseline. Stroke 2017;48(5):1248–1255