

Primary central nervous system anaplastic large cell lymphoma presenting initially with meningitis

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Primary or secondary anaplastic large-cell lymphoma (ALCL) is an uncommon type of T-cell lymphoma and is extremely rare.¹⁻³ It was said that only 15-20 cases of primary CNS-ALCLs have been reported in the literature.³ ALCL may present with a variety of symptoms and MRI findings. We report a case of a 10-year-old girl who presented with meningitis and later developed optic neuritis. She was initially diagnosed as tuberculosis meningitis after a positive interferon- γ test. Clinicians should be aware of the unusual clinical behavior of primary central nervous system lymphomas (PCNSL).

CASE REPORT

A 10-year-old girl presented with fever, headache, and vomiting for 7 days. A lumbar puncture revealed 26 white blood cells, 8 red blood cells, protein 45 mg/dl, and glucose 67 mg/dL. The initial computed tomography (CT) scan was normal and she was diagnosed with viral meningitis. However, after discharge, symptoms recurred and a repeat cerebrospinal fluid analysis showed 41 white blood cells. Despite treatment with antibiotics, intermittent fever lasted for 15

days. The patient was transferred to our hospital for evaluation of possible tuberculosis meningitis as there was a history of contact with a tuberculosis patient. Initial brain MRI showed leptomeningeal enhancement, consistent with leptomeningitis due to an infectious etiology. (Figure 1A) There was no lymphadenopathy or organomegaly. The laboratory findings revealed an elevated serum white blood cell count of 15,360/mm³ and positive interferon- γ (IGRA). Although the Mantoux test, sputum mycobacterium cultures, CSF, and

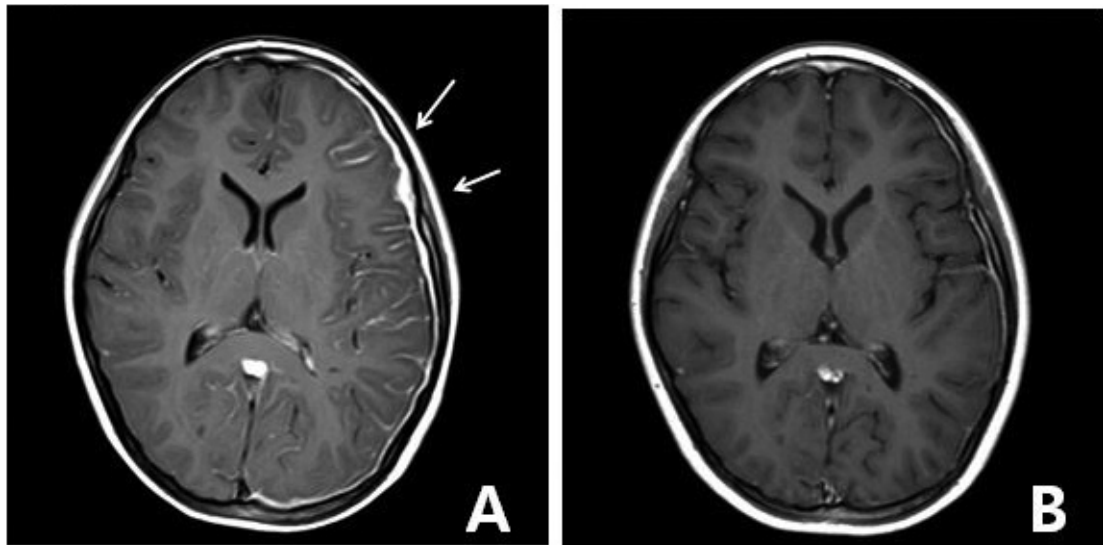


Figure 1. A). Brain MRI in March 2013, enhanced T1 series showed leptomeningeal enhancement in the left hemisphere. B). Brain MRI in April 2013, enhanced T1 series revealed improved leptomeningeal enhancement.

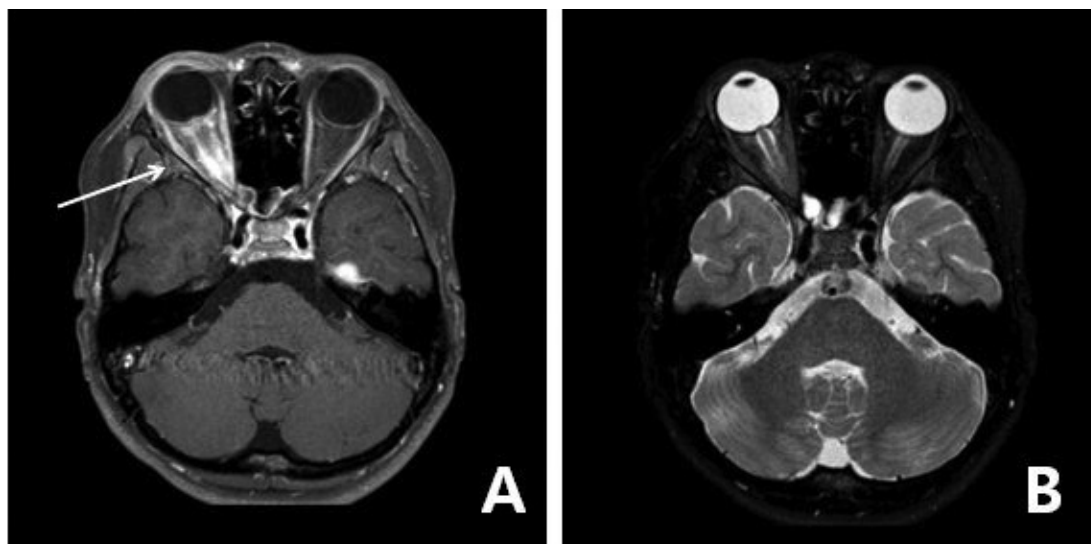


Figure 2. A). Brain MRI in April 2013, enhanced T1 series showed the enhanced sheath of the right optic nerve. B). Brain MRI in May 2013, T2 series demonstrated improved inflammatory changes in the right optic nerve.

acid fast bacilli (AFB) stain were all negative, a presumptive diagnosis of tuberculosis meningitis was made and empiric treatment of tuberculosis meningitis was started with the following 4-drug regimen: isoniazid, rifampin, pyrazinamide, and ethambutol.

One month later in April 2013, the patient presented to the emergency room with pain of the right eye. There was eye pain that worsened with eye movement. An orbital MRI showed evidence of right optic nerve enhancement (Figure 2A). On ophthalmologic examination, the anterior segment of the right eye was unremarkable, but an infiltrative optic neuropathy was suspected. The optic neuritis was presumed to be associated with tuberculosis, and thus all medications were continued except ethambutol due to the possibility of ethambutol-induced optic neuritis.

Two weeks after discharge in May 2013, she developed morning headaches with vomiting and complex partial seizures with right facial and lip twitching. Repeat MRI showed an enhancing, homogenous lesion in the left parietal area. (Figure 3B) An excisional biopsy of the lesion revealed large lymphoma cells with vesicular nuclei and prominent nucleoli. And It was Ki-1 and anaplastic lymphoma kinase (ALK) positive and highlighted by positive staining for CD30 and CD45. (Figure 4) The patient was treated with chemotherapy including high dose methotrexate. After chemotherapy, optic neuropathy, headache, and fever improved.

DISCUSSION

According to the literature, the usual interval between initial presentation and final diagnosis of PCNSL is approximately 3 months.⁴ The patients may present with a wide variety of symptoms and radiologic findings may be confused with other lesions.⁵ Our patient was first diagnosed with tuberculosis meningitis due to the presence of fever, vomiting, headache, leptomeningeal enhancement on MRI, and positive interferon-. The majority (60%-85%) of ALCLs are ALK positive lymphomas that exhibit the characteristic t(2;5)(p23;q23) translocation to produce the ALK protein. ALK expression is considered to be a primary oncogenic event in ALCL.⁶

On the second admission, the patient presented with optic neuritis. Although there are case reports of ALCL involving the ocular adnexa⁷ and optic nerve⁸, they are exceptionally rare. Other than direct lymphomatous infiltration of the optic nerve, there was also report of possible epidemiologic association between multiple sclerosis (MS) and lymphoma.⁹

In our patient, the initial MRI scan showed optic nerve enhancement. The symptoms improved on follow-up MRI after steroid therapy. (Figure 2B) We also considered the possibility of ethambutol-induced ocular toxicity. But, the optic nerve enhancement in MRI was not consistent with the diagnosis.

According to the literature¹⁰, PCNSL on MRI usually appear as hypointense (53%) or isointense

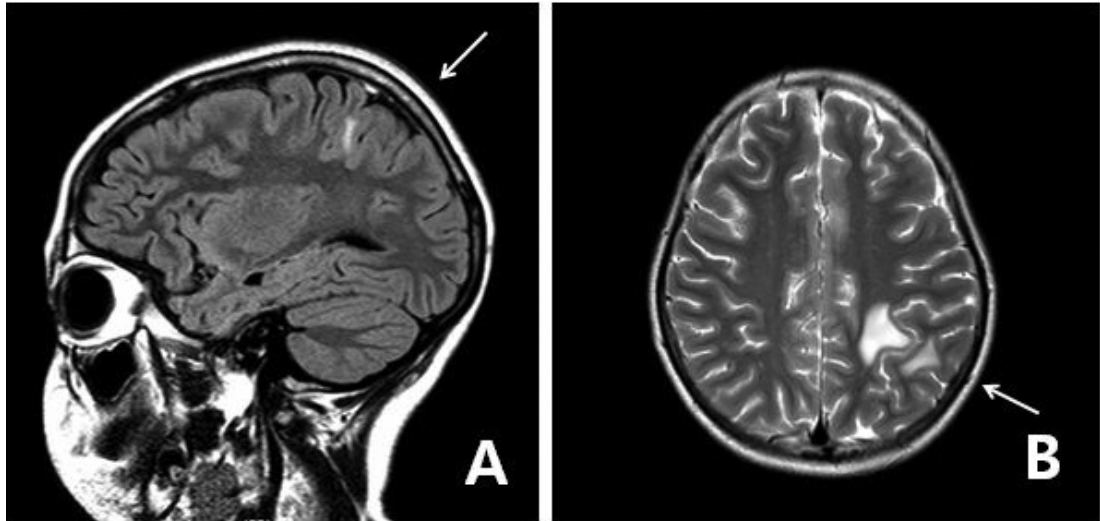


Figure 3. A). Brain MRI in April 2013, T1 series showed a lesion on the location where a mass lesion would later be found. B). Brain MRI in May 2013, T2 series revealed a well-circumscribed homogeneous hyperintense lesion in the parietal area.

(37%) lesions on T1-weighted images and more commonly as hyperintense (42%) or isointense (37%) lesions on T2-weighted images. Meningeal enhancement without an associated intracranial mass is rare in PCNSL. In our patient, the initial MRI findings included leptomeningeal enhancement and repeat MRI showed a well-circumscribed homogeneous enhancing lesion in

the parietal area. (Figure 3B) Upon further review of the earlier MRI, there was a lesion where the mass lesion was later found. (Figure 3A)

In summary, ALCL is an uncommon lymphoma with a variety of different symptoms and MRI findings. Clinicians should be aware of the unusual clinical behavior of PCNSL.

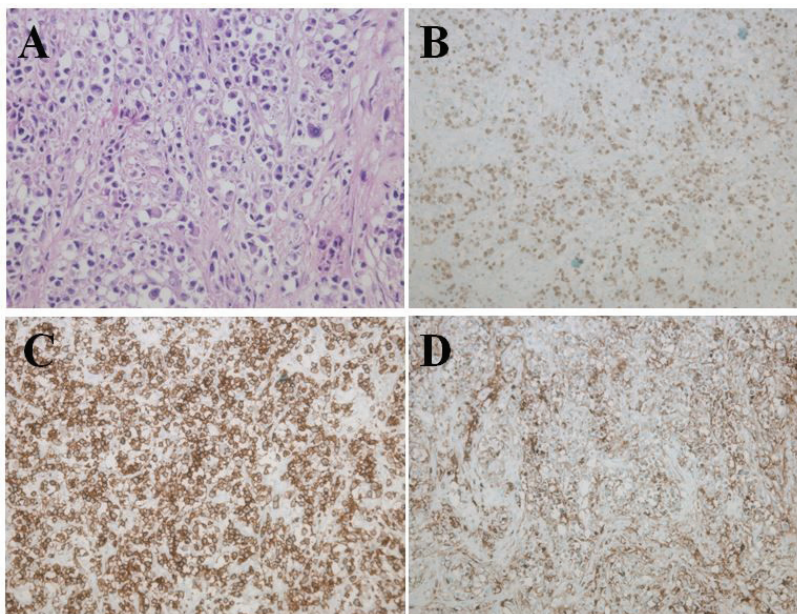


Figure 4. These figures showed large pleomorphic cells with pleomorphic nuclei in stained with hematoxylin and eosin stain (X 200, A) and immunohistochemical stain (B: ALK stain; C: CD30; D: CD45)

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REFERENCES

1. Bhagavathi S, Wilson JD. Primary central nervous system lymphoma. *Arch Pathol Lab Med* 2008; 132:1830-4.
2. Stein H, Foss HD, Durkop H, *et al.* CD30(+) anaplastic large cell lymphoma: a review of its histopathologic, genetic, and clinical features. *Blood* 2000; 96:3681-95.
3. Rupani A, Modi C, Desai S, Rege J. Primary anaplastic large cell lymphoma of central nervous system--a case report. *J Postgrad Med* 2005; 51:326-7.
4. O'Neill BP, Illig JJ. Primary central nervous system lymphoma. *Mayo Clin Proc* 1989; 64:1005-20.
5. Sasani M, Bayhan M, Sasani H, *et al.* Primary central nervous system lymphoma presenting as a pure third ventricular lesion: a case report. *Journal of Medical Case Reports* 2011; 5:213.
6. Ait-Tahar K, Barnardo MC, Pulford K. CD4 T-helper responses to the anaplastic lymphoma kinase (ALK) protein in patients with ALK-positive anaplastic large-cell lymphoma. *Cancer Research* 2007; 67:1898-901.
7. Davis EJ, Rathinam SR, Okada AA, *et al.* Clinical spectrum of tuberculous optic neuropathy. *J Ophth Inflamm Infect* 2012; 2:183-9.
8. Clarke B, Legodi E, Chrystal V, Govender D. Systemic anaplastic large cell lymphoma presenting with conjunctival involvement. *Arch Ophthalmol* 2003; 121:568-70.
9. Yang JH, Wu SL. Multiple sclerosis preceding CNS lymphoma: a case report. *Acta Neurol Taiwanica* 2007; 16:92-7.
10. Zhang D, Hu LB, Henning TD, Ravarani EM, Zou LG, Feng XY, *et al.* MRI findings of primary CNS lymphoma in 26 immunocompetent patients. *Korean Journal of Radiology* 2010; 11:269-77.