Hypertrophic multiple cranial neuropathies: An unusual presentation of primary CNS lymphoma

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Mrs. G.S., a 45-year-old lady, presented with 3 month history of throbbing, continuous bilateral headaches. She developed double vision and drooping of left eyelid 15 days after the headache and went on to have numbness on left side of face, facial asymmetry, intermittent spinning sensation and imbalance. There were no constitutional features. She did not have neck stiffness, pallor, lymphadenopathy, rash or sternal tenderness. Cranial nerve examination showed left third, fifth, sixth nerves and bilateral seventh nerve deficits. Vision, optic fundus and rest of the cranial nerves were normal. Motor and sensory examination of limbs was normal and there were no long tract signs. Review of other systems was unremarkable.

Complete blood count (CBC), biochemistry and blood sugars were normal. Erythrocyte sedimentation rate (ESR) was 10 mm at 1 hour. Cranial nerves were studied using T1, T2, FLAIR, CISS, DWI, ADC map, SWI and contrast enhanced T1 weighted MRI sequences which showed thickening of cisternal segments of left third [Figure 1a and b], left fifth, [Figure 1c] and right seventh to eighth cranial nerve complex [Figure 1d]. The nerves were isointense on T1, T2 and FLAIR sequences and the affected nerves did not show restricted diffusion. On gadolinium enhanced study the thickened nerves showed uniform enhancement. There was neither parenchymal lesion nor any meningeal enhancement. Cerebro spinal fluid (CSF) examination showed 52 cells/mm^3 with 70% lymphocytes and 30% neutrophills. CSF sugar was 83 mg%, against simultaneous blood sugar of 123 mg% and protein was mildly elevated to 63 mg%. No malignant or atypical cells could be detected. Bacterial, acid fast bacillus (AFB) and fungal cultures were negative.

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Various possible causes of polyneuritis cranialis, such as immunological diseases, (Sarcoidosis, chronic inflammatory demyelinating polyneuropathy or CIDP), both malignant (Lymphoma, Carcinomatous) and infectious (tuberculosis, fungal, HIV) were considered and patient was further investigated. Serum angiotensin-converting enzyme (ACE) level was 8 units/L (normal 8-52 units/L) and calcium was 9.1 mg%. Antinuclear antibody test (ANA) and ANA blot test was negative. Human immunodeficiency virus (HIV), hepatitis B antigen (HBsAg), veneral disease research laboratory (VDRL) and hepatitis C virus (HCV) serological tests were also negative. A computed tomography (CT) scan of paranasal sinuses, skull base, chest, abdomen and pelvis with contrast was normal.

At this stage, the patient developed dysphagia, decreased hearing, tinnitus and worsening of bifacial weakness. Her CSF was studied again on two occasions to look for malignant cells, wherein 15 cc samples were taken each time and immediately centrifuged for analysis. Both the samples were negative for malignant cells. Positron emission tomography-CT (PET-CT) also was normal. She was empirically started on injection methyl prednisolone 1 g for 5 days with partial response, followed by oral prednisolone. Antitubercular therapy was also used. Her headaches subsided completely. Her condition was assumed to be immune mediated and injectable Cyclophosphamide was added. The initial response to immunosuppression proved short lasting and she had to be readmitted with dysphagia, right third nerve palsy, hearing loss in both ears and right arm pain. Repeat imaging showed newfound involvement of right 3rd nerve which was thickened, enhancing and also showed restricted diffusion with corresponding low signals on ADC. [Figure 2a-c]. This finding favored lymphoma. Right anterior cervical rootlet was thickened.

In pursuit of a tissue diagnosis, the patient underwent left fifth nerve fascicular biopsy which was suggestive of high grade

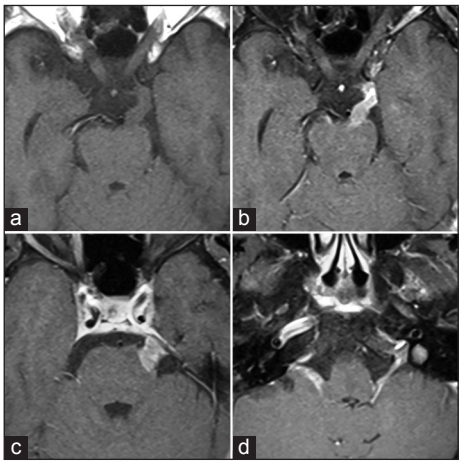

Figure 1: (a) Axial T1 weighted image showing thickened isointense Cisternal portion of left occulomotor nerve (b) Contrast- enhanced axial T1 weighted image with fat suppression showing homogenously enhancing cisternal portion of left occulomotor nerve (c) Contrast- enhanced axial T1 weighted image with fat suppression showing thickened, homogenously enhancing, cisternal portion of left trigeminal nerve. (d) Contrast-enhanced axial T1 weighted image with fat suppression showing thickened and enhancing right facial and vestibulocochlear nerve complex

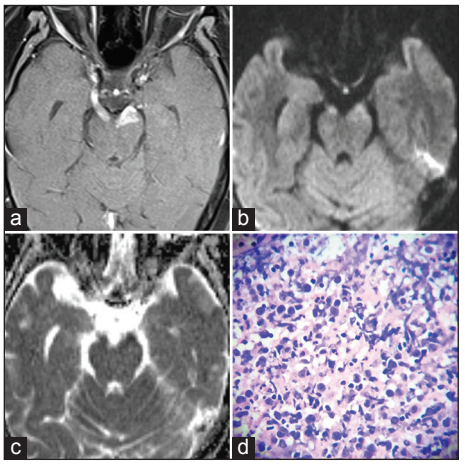

Figure 2: (a) Contrast- enhanced axial T1 weighted image with fat suppression showing thickened and enhancing cisternal portions of bilateral occulomotor nerves (b) Axial DWI (diffusion weighted image) showing restricted diffusion with increased signal intensity in both occulomotor nerves as they are exiting from midbrain. (c) Axial ADC (Apparent diffusion coefficient) map MRI image showing decreased signal intensity in both occulomotor nerves as they are exiting from midbrain. (d) H&E section (40×) of biopsy from left 5th nerve lesion showing tumor comprising of highly pleomorphic large round cells s/o high grade Non Hodgkin's lymphoma. Tumor cells have Hyperchromatic nuclei with scant to moderate eosinophilic cytoplasm

non Hodgkin's lymphoma. [Figure 2d] Immunophenotyping showed CD20 and Bcl-2 positivity and the tissue was negative for CD10 and CD3.

Discussion

Multiple cranial neuropathies have diverse etiologies.[1] Hypertrophy of the cranial nerves on the MRI can be an important clue to the differential diagnosis. In particular, the preferential affection of cisternal segment can help narrow down the etiologies. MR enhancement and thickening of cisternal portions of the cranial nerves denotes diseases like intrinsic tumors of the nerves, infiltrative malignancies, inflammatory and infectious diseases [Table 1].[2-8] As can be seen from Table 1, when the nerves are significantly thickened, neoplasms (Primary/metastatic) dominate the etiologies followed by conditions like sarcoidosis, CIDP, and at times chronic infections like syphilis, schistosomiasis, chronic meningitis.

In the present case the nerve thickening was due to lymphomatous infiltration. As such, primary CNS lymphomas (PCNSL) account for only 1-5% of all brain tumors.[9] Our patient is further unusual in that she developed isolated hypertrophic cranial neuropathies without parenchymal or meningeal lesions or any systemic involvement. This is extremely uncommon in PCNSL as patients usually present with single or multiple periventricular homogenously enhancing lesions.[10] The second MRI study favored lymphoma by showing some degree of restricted diffusion and lower ADC values. Diffusion restriction of lesions on DWI sequences with corresponding lower ADC values, if present, has been shown to be associated with lymphoma more consistently than other inflammatory lesions, tumors and metastatic lesions, but tissue diagnosis is mandatory.[10]

Table 1: Cranial neuropathies affecting cisternal portion of cranial nerves and Imaging characteristics

Causes	Enhancement of cisternal portion	Thickening
Neoplastic		
Lymphoma	+	+
Leukemia	+	+
Meningeal carcinomatosis	+	+
Melanomatosis	+	+
Schwannomas	+	+
Neurofibromas	+	+
Meningiomas	+	+
Inflammatory		
Sarcoidosis	+	+
Inflammatory demyelinating polyneuropathy	±	+
Vasculitis	±	±
Infectious		
Bacterial, viral, fungal	+	±
Tuberculous meningitis	+	±
Syphilis	+	±
Schistosomiasis	+	±
HIV	+	+
Lyme disease	±	±

In conclusion, Lymphoma can mimic inflammatory/infectious diseases and an occasional case of multiple cranial neuropathies showing thickened and enhancing cisternal segments of the cranial nerves may be in fact, a case of PCNSL even in the absence of more typical parenchymal/meningeal lesions and early tissue diagnosis should be considered.

References

1. Keane JR. Multiple cranial nerve palsies: Analysis of 979 cases. Arch Neurol 2005;62:1714-7.
2. Saremi F, Helmy M, Farzin S, Zee CS, Go JL. MRI of cranial nerve enhancement. AJR Am J Roentgenol 2005;185:1487-97.
3. Mark AS, Blake P, Atlas SW, Ross M, Brown D, Kolsky M. Gd-DTPA enhancement of the cisternal portion of the oculomotor nerve on MR imaging. AJNR Am J Neuroradiol 1992;13:1463-70.
4. Khadilkar SV, Visana DR, Huchche AM, Shah N, Gupta N, Bharucha NE. Hypertrophic trigeminal nerves: Moustache sign. Neurol India 2013;61:566-7.
5. Khadilkar SV, Harish AH, Prasad PB, Sunila J, Muzumdar G, Smruti BK, *et al*. Adult male with multiple cranial nerve palsies. Ann Indian Acad Neurol 2012;15:96-100.
6. Iplikcioglu AC, Dinc C, Bikmaz K, Ozcan D. Primary lymphoma of the trigeminal nerve. Br J Neurosurg 2006;20:103-5.
7. Rose O, Ahmad Z, Snow B. Multiple cranial nerve palsies as the first presentation of sarcoidosis. Case Rep Otolaryngol 2014;2014:592510.
8. VandeVyver V, Lemmerling M, Van Hecke W, Verstraete K. MRI findings of the normal and diseased trigeminal nerve ganglion and branches: A pictorial review. JBR–BTR 2007;90:272-7.
9. Sierra del Rio M, Rousseau A, Soussain C, Ricard D, Hoang-Xuan K. Primary CNS lymphoma in immunocompetent patients. Oncologist 2009;14:526-39.
10. Haldorsen IS, Espeland A, Larsson EM. Central nervous system lymphoma: Characteristic findings on traditional and advanced imaging. AJNR Am J Neuroradiol 2011;32:984-92.

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