CNS Histiocytosis- Rare Disease with An Unusual Manifestation

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Abstract
CNS histiocytosis is a rare and debilitating disease with multiple presentations. We here present a rare case of histiocytosis in a 4 year old child manifesting with diplopia as the sole neurological symptom. The patient had only saccadic abnormalities on examination and lesions in tectal pons and cerebellum. Initially considering the possibility of demyelinating disorder, steroids were given with partial resolution of signs but no improvement in signs or MRI imaging. Biopsy gave the diagnosis. The diagnosis of CNS histiocytosis should be considered even in patients with few symptoms and actively evaluated for.

Case Report
Four year old girl presented with an acute onset of diplopia since one week. On clinical examination, abnormalities of slow ocular saccades and diplopia which was present in both horizontal and vertical direction were seen. There were no evidence of any other cranial nerve palsies. Rest of the neurological examination-cognition, motor and sensory, cerebellar systems assessment was normal. There were no meningeal signs.

MRI Brain revealed patchy enhancing ill-defined lesions in T2/Flair sequences in tectal pons and medial cerebellum. (Fig 1a,b)

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Introduction
Histiocytosis encompasses a group of disorders characterized by uncontrolled clonal proliferation of histiocytes. Prevalence of histiocytosis is 1-2/2,00,000 with most cases presenting with skin, lungs and bone disease. CNS involvement is very rare but can be potentially devastating.¹

Histiocytosis commonly presents in the age group of 5-15 years. Focal granulomatous lesions may present as lesions of craniofacial bone and skull base. Hypothalamic pituitary axis is the commonest intracranial site involved, diabetes insipidus being the most common initial symptom.²³

The other clinical features include (i) bone pains (ii) headache (iii) ataxia (iv) psychomotor retardation. Radiological abnormalities reported are increased T2 weighted signal in basal ganglia, pons and dentate nucleus of cerebellum, thickening of the pituitary stalk, absence of the pituitary bright spot and hypothalamic lesions. Histopathologic studies demonstrated these lesions being dominated by Langerhan cells. We hereby report an unusual case in a younger child.
Low Grade Glioma or demyelinating disorder were considered. MR Spectroscopy showed decreased NAA with increased choline peaks. Blood, CSF and Neurophysiological (VEP) work up was done which was normal except CSF hypo-glycorrhachia (CSF sugar-32). Whole body PET CT was normal.

In cases of brainstem involvement, thepons and midbrain are likely to get involved apart from cerebellum, presenting radiologically as midbrain atrophy and hyperintensities in pons. Most of the cases in literature presented clinically with ataxia, dysarthria, dysmetria, behavioural disturbances along with other constitutional symptoms.

In our patient there was a paucity of clinical symptoms as well as MRI findings. Her symptoms could not be explained based on MRI findings alone. This suggests that the associated pathology is patchy and not interrupting the fibers grossly.

Review of histopathological studies done in Histiocytosis shows that the presence of classical CD1a+ cells is highly variable, it might dominate in some cases, whereas another series demonstrated an absence of CD1a+ cells and histiocytes, presence of inflammation with collection of CD8+ lymphocytes along with neuronal degeneration and extensive demyelination. These studies are consistent with findings in our case demonstrating absence of CD1a+ cells, but presence of leptomeningeal histiocytes and other features suggestive of histicycrosis. Spectroscopy was consistent with neuronal loss and ruled out an infectious lesion1.

In a study by Nicole Grois et al, where 12 children in the age group of 2-15 years, isolated brainstem involvement was not found in any patient. All cases had Hypothalamic/Pituitary lesions, Basal Ganglia, Cerebellar and pontine lesions and absence of the Pituitary bright spot. Ataxia, cognitive decline and bony pains were presenting symptoms in most of the children, unlike our patient.

In a study by Movement Disorder Society a single case of a 58 year old man who presented with isolated cerebellar involvement and ataxia is reported. A Bone scan was done in this case which showed non specific uptake of tracer in the left calvarial bone and was diagnosed as Erdheim Chester(non Langerhan Histiocytosis). Our patient did not show any osteolytic bony lesions.

Demyelinating diseases, Neoplasms, CLIPPERS and isolated Neurosarcoid are possible differential diagnosis. Often biopsy is probably the gold in clinching the diagnosis.

Histiocytosis leads to production of cytokines which results in recruitment of proinflammatory cells from circulation to the brain. This can explain the response to steroids in such cases.

Gold standard for the diagnosis of CNS histiocytosis is CSF levels of Interferon Alpha, Interleukin 1,6, and S-100 levels2. These tests could not be carried out in our patient due to non availability.

Hematologists/ Pediatric Oncologists treat Histiocytosis with chemotherapeutic agents like Vincristine, Vinblastine, Methotrexate, Isotretinoin and newer agents BRAF inhibitor like dabrafenib.4 Considering the age of the patient, side effects and risk of serious complications arising out of chemotherapy regimens is quite high. Whether aggressive treatment is warranted in cases of isolated neuro-histiocytosis, where the involvement is restricted to a particular region and non-disabling symptoms is a matter of further research.

Conclusions
This case is unique due to isolated involvement of brainstem, disproportionate clinical findings with fluctuating course thus causing a diagnostic dilemma. In such situations, young age of the patient, steroid responsive relapsing course and bilateral brainstem involvement on imaging, a possibility of CNS Histiocytosis should be considered along with other diagnosis. Histopathology and Immunohistochemistry confirm the diagnosis of histiocytosis.

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References


