Cerebellar syndromes as a late presentation of Langerhans cell histiocytosis

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ABSTRACT

We report a patient with late onset ataxia who was initially labeled as idiopathic diabetes insipidus for many years. Pathological and radiological investigations revealed Langerhans cell histiocytosis. This case report aims to draw the attention of physicians to this delayed and rare presentation.

Neurosciences 2004; Vol. 9 (4): 309-311

Langerhans cell histiocytosis (LCH) is a rare disorder in adults with variable clinical expression from benign often self-limiting, to aggressive potentially fatal multisystem disease. The basic disease process has been classified as non-malignant, but clonal proliferation of a subgroup of histiocytes has been identified.[1] The CNS involvement usually affects the hypothalamic pituitary region resulting in diabetes insipidus (DI) in 22-50% of LCH patients whereas other brain lesions are less common.[2,3]

Case Report. A 49-year-old female presented to our hospital with left hand unilateral ataxia of gradual onset for 3 weeks with also tendency to fall to the left. She has been suffering from polyuria and polydipsia for the past 8 years and was hence diagnosed at another hospital as idiopathic diabetes insipidus. Her brain CT Scan was normal at the time of the initial evaluation. On examination the left eye was blind due to trauma and she had cataract of the right eye. She was also found to have gingival ulcer. On neurological assessment she had dysarthria with left ataxic hemiparesis. The rest of the systemic examination was normal.

Laboratory investigations showed normal blood count, and normal liver function enzymes. Cerebrospinal fluid protein was slightly elevated 660 mg/L; (normal range 150 mg/L-450mg/L). The MRI study of the brain showed multiple solid lesions, with increased signal intensity on the FLAIR sequence images, which enhanced after contrast injection. They involved the left middle cerebellar peduncle extending to the left side of the pons and to the mesencephalon **(Figure 1a & b)**. There was a similar lesion involving hypothalamus and medulla on MRI (not shown). In addition, a lesion was noted in the right mastoid bone which was osteolytic in nature on CT scan (not shown). A bone scan, single phase, static images showed increased uptake in the right mastoid. Biopsy of the gingival ulcer and mastoid bone revealed sheets and aggregates of Langerhans type histiocytes mixed with abundant eosinophils, lymphocytes and plasma cells **(Figure 2a)**. Immunochemistry showed histiocytes to be S100 positive **(Figure 2b)**. She was diagnosed as a case of LCH and was started on high dose prednisolone (60 mg). An MRI carried out 6 weeks later showed mild regression in the size of the left middle cerebellar peduncle and left superior

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Received 29th February 2004. Accepted for publication in final form 25th May 2004.

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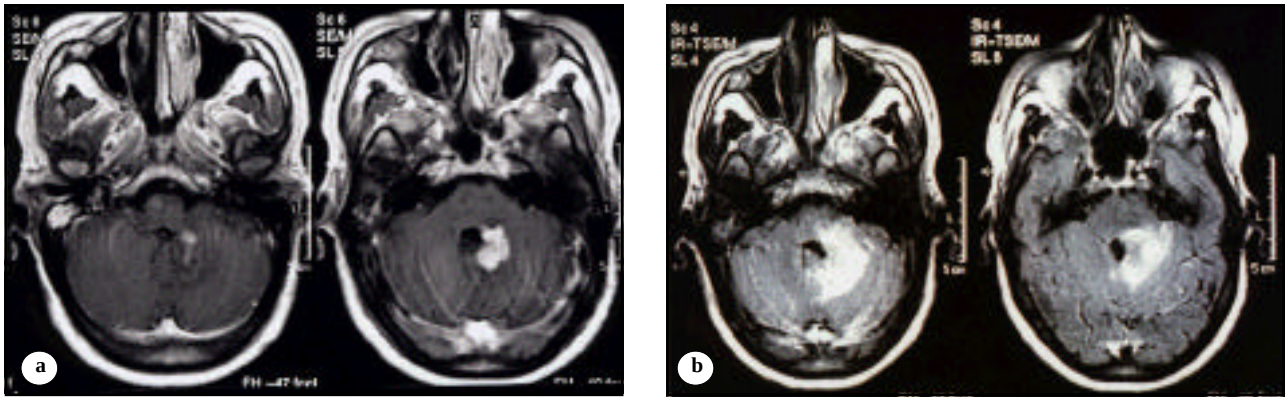

Figure 1 - Magnetic resonance imaging of brain showing **a)** Axial fast flair sequence showing increased signal intensity involving the left middle cerebellar peduncle, extending to the left side of the pons. High signal in the right mastoid bone. **b)** Axial T1 post contrast injection, demonstrating enhancing lesions in the same areas.

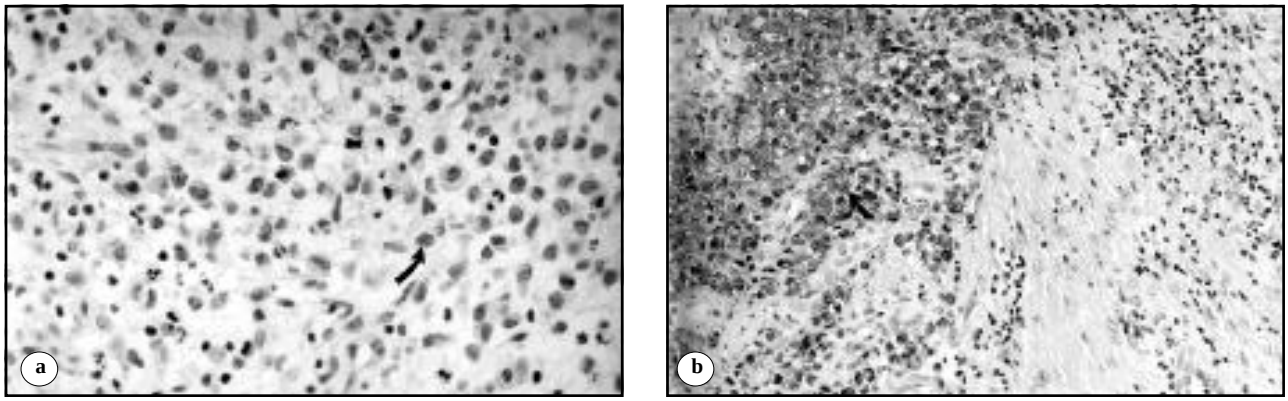

Figure 2 - Pathology showing **a)** High power view showing proliferation of Langerhans cells intermixed with polymorphs and eosinophils. The nuclei of the Langerhans cells are irregular and elongated with prominent grooves and folds with abundant cytoplasm. **b)** Intermediate power view showing S100 positivity in the Langerhan's cells by immunohistochemistry.

cerebellar peduncle lesions, but her neurological status was the same. On subsequent follow up the patient continued to deteriorate and expired within one year.

Discussion. Langerhans cell histiocytosis is a rare disease, which affects children and adults to a lesser degree with the peak incidence being 1-15 years. The CNS involvement in LCH is quoted as 10-50% of cases.[4] Our patient was labeled as idiopathic DI for 7 years as brain CT was normal at the time of presentation. Later she developed unilateral ataxia of gradual onset. However, the most common neurological manifestation is DI (22-50%) caused by hypothalamic infiltration, which may precede other brain lesions.[2,3] The CNS finding on imaging appeared several years later on CT and MRI.[5]

Diabetes insipidus preceding other manifestations of LCH has been well documented in the literature, and CNS involvement may antedate full expression of LCH by several years.[6,7] Cerebellar involvement was reported with some authors suggesting an immunologically mediated remote effect in CNS compatible with the concept of paraneoplastic syndrome.[8-10] Another suggestion was excessive activation of glutamate by neurotoxins or cytokines leading to neuronal injury cell death, which is the common final pathway for many non-neurological disorders.[11,12] In our patient, cerebellar involvement is related directly to infiltration of the cerebellum parenchymal by the LCH.

In conclusion, we recommend that patients known to have DI in the absence of other associations to suggest an overt cause, should be investigated and followed up including repeating MRI for detection of any evolving CNS lesion particularly in the hypothalamus and pituitary as early treatment might have an influence on prognosis.

References

1. Yu RC, Chu C, Buluwela L, Chu AC. Clonal proliferation of Langerhans cells in Langerhans cell histiocytosis. ***Lancet*** 1994; 343: 767-768.
2. Berry DH, Becton DL. Natural history of histiocytosis X. ***Hematol Oncol Clin North Am*** 1987; 1: 23-32.
3. Magnie M, Arico M, Villa A, Genovese E, Beluffi G, Severi F. MR of the hypothalamic-pituitary axis in Langerhans cell histiocytosis. ***Am J Neuro Radiol AJNR*** 1992; 13: 1365-1371.
4. POE LB, Dubowy RL, Hochhauswr L, Collins GH. Demyelinating and gliotic cerebellar lesion in langerhans cell histiocytosis. ***Am J Neuro Radiol AJNR*** 1994; 15: 1921-1928 .
5. Tien RD, Newton HT, McDermott MW, Dillon WP, Kucharczyk J et al. Thickened pituitary stalk on MR images in patients with diabetes insipidus and Langerhans cell histiocytosis. ***Am J Neuro Radiol AJNR*** 1990; 11: 703-708.
6. Grois N, Barkovich AJ, Rosenau W, Ablin AR. Central Nervous System Disease associated with Langerhans Cell Histiocytosis. ***Am J Pediatr Hematol Oncol*** 1993; 15: 245-254.
7. Schmitts S, Wichmann W. Pituitary stalk thickening with diabetes insipidus preceding typical manifestations of Langerhans cell histiocytosis in children. ***Eur J Ped*** 1993; 152: 399-401.
8. Goldberg-Stern H, Weitz R, Zaizov R, Gornish M, Gadoth N. Progressive spinocerebellar degeneration "plus" associated with Langerhans cell histiocytosis: a new paraneoplastic syndrome? ***J Neurol Neurosurg Psychiatry*** 1995; 58: 180-183.
9. Favara BE. Langerhans cell histiocytosis pathology and pathogenesis. ***Semin Oncol*** 1991; 18: 3-7.
10. Vital A, Loiseau H, Kantor G, Vital C, Cohadon F. Primary Langerhans' cell histiocytosis of the central nervous system with fatal outcome. Case report. ***J Neurosurg*** 1996; 85: 1156-1160.
11. Grois N, Favara BE, Mostbeck GH. Central nervous system disease in Langerhans cell histiocytosis. ***Hematol Oncol Clin North Am*** 1998; 2: 287-305.
12. Kepes JJ. Histiocytosis-X. In: Vinken JH, Bruyn GW, editors. Handbook of Clinical Neurology. Vol 38 Part 1. Amsterdam (NE): Elsevier; 1997. p. 93-117.