Langerhans Cell Histiocytosis Presenting as Diabetes Insipidus.

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ABSTRACT

Diabetes insipidus (DI) associated with a thickened pituitary stalk is an uncommon disease and its diagnosis is challenging in the paediatric population.

A 3-year-old male child presented with polyuria and polydipsia. Investigations revealed low urine osmolarity & normal serum osmolarity with normal RBS & serum electrolytes. Water deprivation test was suggestive of Diabetes insipidus. MRI brain revealed a thickened pituitary stalk consistent with LCH/Germinoma. Serum and CSF tumour markers for germinoma were negative. Skeletal survey and skin examination revealed no evidence of LCH. On follow-up, child had seborrheic dermatitis, ear discharge and palpable cervical lymph node. Repeat MRI brain showing bulky pituitary stalk. Skin biopsy was suggestive of Langerhans cell Histiocytosis. Chemotherapy was planned according to LCH protocol. The present case highlights the need for serial follow-up and magnetic resonance imaging to diagnose LCH.

Introduction:

The common etiologies presenting with central diabetes insipidus (DI) associated with a thickened pituitary stalk in the paediatric population are Langerhans Cell Histiocytosis (LCH), central nervous system tumours such as germinoma and craniopharyngioma, granulomatous lesions like tuberculosis and sarcoidosis and autoimmune disorders like lymphocytic infundibuloneurohypophysitis.[1] LCH is characterised by clonal proliferation & excess accumulation of pathologic Langerhans cells. Annual incidence of LCH is 0.5 to 5.4 cases per million persons per year. DI is the earliest and principal manifestation of central nervous system involvement, and neuroradiology demonstrates a thickened infundibular stalk. [1]

Case Report:

A 4-year-old male child presented with polyuria, polydipsia with nocturnal enuresis for the last 6 months. Urine osmolality of the child was 51 mosm/kg and serum osmolality was 286 mosm/kg. Diagnosis of Central DI was confirmed by water deprivation test and vasopressin challenge test. After vasopressin challenge urine osmolality increased from 51 to 121 mosm/kg. Magnetic resonance imaging (MRI) showed a thickened pituitary stalk consistent with LCH/Germinoma (Figure 1). The anti-diuretic hormone (ADH) level was <0.50 pg/mL (normal range 0-13) and was in the subnormal range. As serum human chorionic gonadotropin (hCG) and CSF hCG levels were in normal range, germinoma was ruled out. Serum cortisol levels and thyroid function tests were normal. Whole body PET scan was normal. In spite of extensive investigations, no definitive etiology for the central DI and thickened infundibulum could be established, and hence the patient was kept under regular follow-up. Repeated neurological examinations were performed to detect progression of the disease. The DI was treated medically with desmopressin and the clinical response was immediate with decrease in urine output and resolution of nocturnal enuresis. After 3 months on follow-up child had seborrheic dermatitis, ear discharge and palpable cervical lymph node pointing towards LCH. Hence skin biopsy was done, which was suggestive of LCH. Repeat MRI brain was showing bulky pituitary stalk and size was increased from the previous MRI (Figure 2). The child was planned for chemotherapy according to LCH protocol.

Figure 1.
Discussion
Central DI with thickening of the pituitary stalk on MRI may result from various infiltrative diseases. Although 10% of the cases are idopathic, other common causes include LCH, central nervous system tumours such as germinoma and craniopharyngioma, granulomatous lesions like tuberculosis, pituitary gland sarcoidosis and autoimmune disorders like lymphocytic infundibuloneurohypophysitis. To determine the precise etiology on the basis of MRI findings is a difficult task. Serial MRI studies are required for diagnosis. Germinomas are rapidly evolving, serial scans elicit their diagnosis. Lymphocytic infundibulo-neurohypophysitis has been seen to be associated with vasopressin-cell autoantibodies and other organ specific autoimmunity and some of these cases may also show spontaneous resolution of pituitary stalk thickening.

Since the etiological diagnosis of central DI with thickening of the pituitary stalk may not be apparent at the time of detection of DI, serial imaging and close follow-up of these patients to reach a conclusive diagnosis is necessary and mandatory to avoid the attendant risks of pituitary stalk biopsy.

LCH is a rare disease caused by activation of monocyte–macrophage system. CNS involvement has been reported in 16% of the cases of LCH. Stalk of the pituitary is the most common site of involvement in the brain. Commonly seen in children of age group between 2 and 5 years. The spectrum of the disease varies, ranging from single osteolytic bone lesion (eosinophilic granuloma), multisystem disease (Hand-Schuller Christian disease) with skeletal and extraskelatal reticuloendothelial and pituitary gland involvement seen in children 1–5 years of age to rapid fulminant course (Letterer-Siwe Disease) seen most commonly in children less than 2 years of age.

The clinical presentation depends on the site involved in central nervous system. DI is the most common presentation and is seen in 25% of the cases.

Radiological manifestations of the disease include thickening of pituitary stalk more than 3 mm, with loss of physiological hypointense signal in posterior pituitary on T1W images signifying loss of ADH storage granules. This may progress to a mass lesion involving pituitary and hypothalamus. Histological examination is the definitive diagnostic test for LCH. They stain positive for histochemical stains, S-100 and CD1a.

The treatment of LCH is challenging and a single modality of treatment has not been established. DI is usually permanent and requires lifelong vasopressin. An active lesion is treated by chemotherapy. Although radiation is not the treatment of choice, it may be used as an alternative. A complete clinical resolution is unusual. For tumorous lesions, surgery, radiation or standard LCH chemotherapy may be employed.

Conclusion: Isolated LCH of pituitary stalk is rare. Patient with central diabetes insipidus having pituitary stalk abnormalities needs regular follow-up and serial MRI to avoid missing of other systemic manifestations.

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REFERENCE