Research Paper

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KEYWORDS :

Langerhans Cell Histiocytosis Presenting as Diabetes Insipidus.

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ABSTRACT

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

A 3year old male child presented with polyuria and polydipsia. Investigationsrevealed 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 ?LCH/ Germinoma. Serum andCSF tumour markers for germinoma were negative. Skeletal survey and skinexamination revealed no evidence of LCH. On follow up child had seborrehicdermatitis, ear discharge and palpable cervical lymph node. Repeat MRI brainshowing bulky pituitary stalk. Skin biopsy was suggestive of Langerhans cellHistiocytosis. Chemotherapy was planned according to LCH protocol. Thepresent case highlights the need for serial follow-up and magnetic resonanceimaging 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 asgerminoma and craniopharyngioma, granulomatous lesions like tuberculosis and sarcoidosis and autoimmune disorders like lymphocytic infundibuloneurohypophysitis.**[1]**

LCH is characterised by clonal proliferation & excess accumulation ofpathologic Langerhans cells. Annual incidence of LCH is 0.5 to 5.4 cases permillion persons per year. DI is the earliest and principal manifestation of centralnervous system involvement, and neuroradiology demonstrates a thickenedinfundibular stalk. [1]

Case Report:

A 4-year-old male child presented with polyuria, polydipsia with nocturnalenuresis 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 wasconfirmed by water deprivation test and vasopressin challenge test. Aftervasopressin challenge urine osmolality increased from 51 to 121 mosm/kg.Magnetic resonance imaging (MRI) showed a thickened pituitary stalk ?Germinoma/ LCH (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 humanchorionic gonadotropin (hCG) and CSF hCG levels were in normal range, germinoma was ruled out. Serum cortisol levels and thyroid function tests werenormal. Whole body PET scan was normal. In spite of extensive investigations,no definitive etiology for the central DI and thickened infundibulum could beestablished, and hence the patient was kept under regular follow-up. Repeatedneurological examinations were performed to detect progression of the disease.The DI was treated medically with desmopressin and the clinical response wasimmediate with decrease in urine output and resolution of nocturnal enuresis.After 3 months on follow up child had seborrehic dermatitis, ear discharge and palpable cervical lymph node pointing towards LCH. Hence skin biopsy wasdone, which was suggestive of LCH. Repeat MRI brain was showing bulkypituitary stalk and size was increased from the previous MRI (Figure 2). The child wasplanned for chemotherapy according to LCH protocol.

Figure 1.

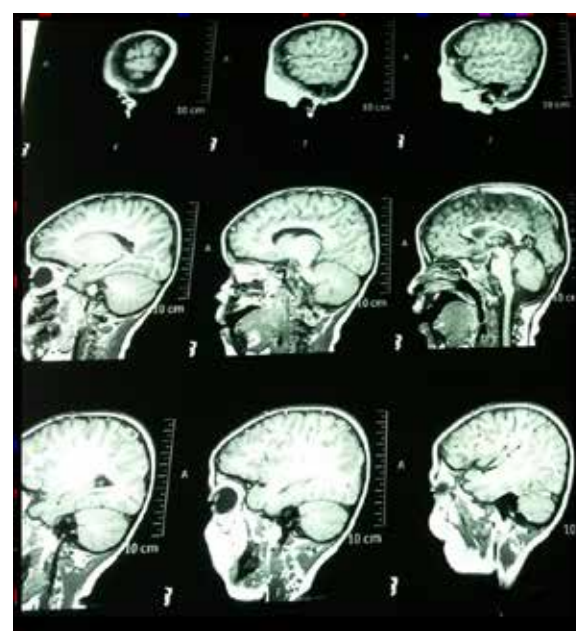
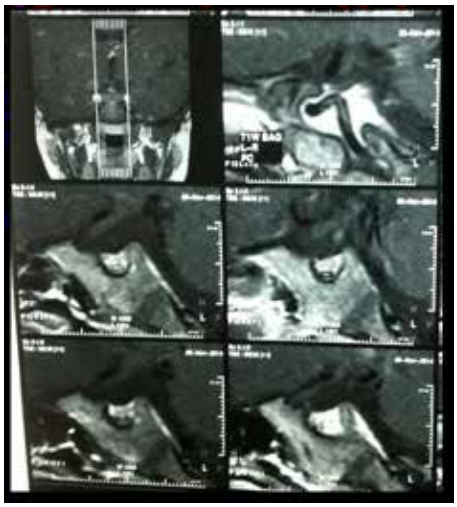


Figure 2.



Discussion

Central DI with thickening of the pituitary stalk on MRI may result fromvarious infiltrative diseases. Although 10% of the cases are idiopathic, othermost common causes include LCH, central nervous system tumours such asgerminoma and craniopharyngioma, granulomatous lesions like tuberculosis,Pituitary gland sarcoidosis and autoimmune disorders like lymphocytic infundibuloneurohypophysitis.[2] To determine the precise etiology on the basis of MRIfindings 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 associatedwith vasopressin-cell autoantibodies and other organ specific autoimmunity andsome of these cases may also show spontaneous resolution of pituitary stalkthickening.

Since the etiological diagnosis of central DI with thickening of the pituitarystalk may not be apparent at the time of detection of DI, serial imaging andclose follow-up of these patients to reach a conclusive diagnosis is necessaryand mandatory to avoid the attendant risks of pituitary stalk biopsy.[2]

LCH is a rare disease caused by activation of monocyte–macrophage system.CNS involvement has been reported in 16% of the cases of LCH.[3] Stalk of thepituitary is the most common site of involvement in the brain. Commonly seenin children of age group between 2 and 5 years. The spectrum of the diseasevaries, ranging from single osteolytic bone lesion (eosinophilic granuloma),multisystem disease (Hand-Schuller Christian disease) with skeletal andextraskeletalreticuloendothelial and pituitary gland involvement seen inchildren 1–5 years of age to rapid fulminant course (Letterer - Siwe Disease)seen most commonly in children less than 2 years of age.[4]

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.[5]

Radiological manifestations of the disease include thickening of pituitary stalkmore than 3 mm, with loss of physiological hyperintense signal in posteriorpituitary on T1W images signifying loss of ADH storage granules.[6] This mayprogress to a mass lesion involving pituitary and hypothalamus. Histologicalexamination is the definitive diagnostic test for LCH. They stain positive forhistochemical stains, S-100 and CD1a.

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

Conclusion:

Isolated LCH of pituitary stalk is rare. Patient with central diabetes insipidushaving pituitary stalk abnormalities needs regular follow up and serial MRI toavoid missing of other systemic manifestations.

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