Central Diabetes Insipidus in a Child due to Histiocytosis X

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Abstract

Central diabetes insipidus (CDI) occur due to deficiency of vasopressin which is synthesized in supraoptic and paraventricular nuclei of hypothalamus and stored in posterior pituitary. There are many causes of CDI among them histiocytosis X or lymphohistiocytosis (LCH) is a rare cause.

Here we are reporting a 2 years old boy with histiocytosis-Xor presented with CDI. The boy presented with polyuria and polydipsia, low urine specific gravity and osmolality with normal blood sugar and osmolality. Positive response to water deprivation test followed by oral DDAVP establish the diagnosis of CDI.

X-Ray skull showed osteolytic punched out lesion and T1 weighted MRI of brain showed thickening of pituitary stalk with absence of bright signal of posterior pituitary. Trephine biopsy showed bone marrow was infiltrated by many eosinophil, some macrophage, lymphocyte and plasma cells.

On the basis of all these diagnosis was made as CDI due to histiocytosis-X. Due to hypothalamic- pituitary axis infiltration CDI may be the earliest manifestation of LCH, even before it is diagnosed. Therefore, for diagnostic workup of CDI, LCH should be considered.

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Case report

A 2 years old boy 3rd issue of his non-consanguineous parents presented with polyuria and polydipsia since his 9 months of age. He used to void 25-30 times per day with nocturia and wake up several times at night to drink water. He usually drinks 3 liter of water per day and voids nearly same volume for the last 6 months.

He had no history of head ache, nausea, vomiting, convulsion, unconsciousness, blurring of vision, any cranio-cerebral trauma or surgery, any contact with TB patient or taking any toxic food or offending drug. His medical history was unremarkable and there was no family member with similar illness. He was born at term at home without any perinatal complication with normal birth weight. His developmental parameters were normal. He was from a middleclass family and used to take family food although his appetite was not good.

He was grossly emaciated, mildly pale with normal vitals. BCG mark was present and skin was dry, rough, devoid of subcutaneous fat and folded over buttock and medial aspect of thigh. There was no dehydration and lymphadenopathy. His WAZ=-4.4, HAZ = - 2.92, WHZ= - 7.25 and BMI was 12.3 which is much below the 3rd centile. His other physical findings showed no abnormality.

Investigation profile revealed that Hb level was less than normal (8.7 g/ dl), urine routine examination showed low specific gravity (1.004), normal pH (7.3) and no hematuria and proteinuria. Urine culture showed no growth of any bacteria. Random blood sugar was 3.8 mmol/L and serum creatinine was 35.2 micro mole/L which were normal for his age. Serum osmolality was normal (272 mosm/L), urine osmolality was low (52 mosm/L) and serum electrolyte was normal (Na- 137 mmol/L, k- 4.3 mmol/L, Cl- 101.6 mmol/L and TCO2- 22 mmol/L).

After water deprivation there was no change of serum osmolality but urine osmolality raised from 52 mosm/L to 263 mosm/L. Finally, after giving 120 micro grams oral DDAVP urine osmolality further raised to 360 mmol/L but

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serum osmolality not raised.

X-Ray of skull showed osteolytic "punched out" lesion over parietal region with normal size of pituitary fossa and ultrasonography of KUB showed normal findings. MRI of brain with T1 image showed thickening of pituitary stalk with absence of brightness of posterior pituitary. Trephine biopsy showed bone marrow was infiltrated by many eosinophil, some macrophage, lymphocyte and plasma cells.Thyroid function status was normal. Immunohistochemistry and mutation analysis could not be done due to financial constraints.

On the basis of history and above findings the patient was diagnosed as a case of central diabetes insipidus due to histeocytosis-x with secondary malnutrition. Along with all supportive treatment oral DDAVP was given and multi drug anticancer chemotherapy with vinblastine and prednisolone was started as per advice of Hemato-oncology department and the symptoms improved. Patient was discharged with regular follow up schedule.

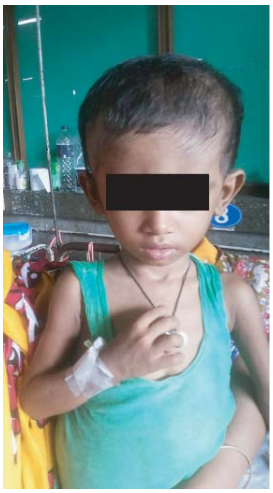

Figure 1: Photography of the patient with central DI

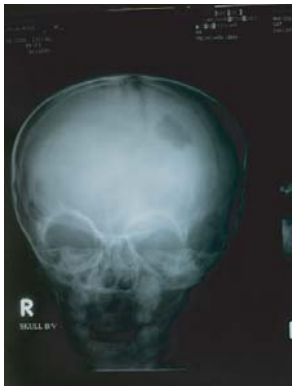

Figure 2: X-ray skull showing osteolytic "punched out" lesion

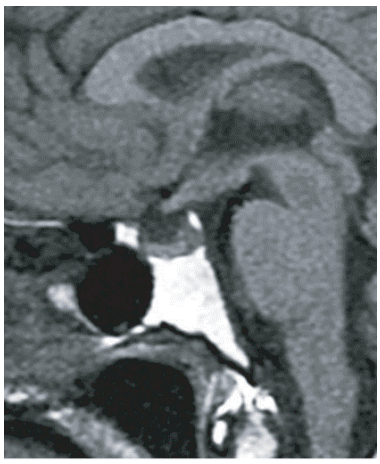

Figure 3 : T1 WI Image of brain shows absence of normal hyper intense posterior pituitary lobe with thickening of pituitary stalk

Discussion

Central DI occur due to degeneration or destruction of supraoptic or paraventricular nucleus of hypothalamus, which are responsible for vasopressin synthesis. Through the hypothalamic-hypophyseal tract vasopressin is transported to posterior pituitary where it is stored. If more than 80% of these cells are damaged CDI occurs due to deficiency of vasopressin.[1] CDI may be idiopathic or due to neurogenic cause involving hypothalamo-pituitary region. Approximately 29% of CDI is idiopathic, 50% due to primary brain tumor in pituitary region and 16% due to histiocytosis-X.[1] Other causes include head trauma, intracranial haemorrhage, hypoxia, thromboembolism, infection (TB meningitis, encephalitis etc.).

LCH is a rare disease and can be occur at any age, with male preponderancein children.[2] The incidence is approximately 5 cases per million children.[3] There is clonal proliferation and accumulation of antigen presenting dendritic cells due to continuous immune stimulation.[4] Dendritic cells express high level of T- cell co-stimulatory molecules and proinflamatory cytokines. This cytokines and chemokines produce "cytokine storm"[5] causes tissue damage. The clinical presentation is highly variable and ranges from life threatening multisystem involvement to self-healing isolated bones or skin lesion. Approximately 65% have single system disease[6] and among them 80% have bone disease.[7]

The clinical presentation of LCH is highly variable depending on the infiltration of organs. The disease course, treatment modality and prognosis of LCH depends on type of organ involvement.[8]

Our patient presented with polyuria which is defined by 24 hours urine output more than 4 ml/kg/hr.[9] High serum osmolality and

low urine osmolality along with low urinary specific gravity suggest the diagnosis of DI. A positive water deprivation test along with DDAVP responsiveness make the diagnosis of CDI.

Radiography is the gold standard for diagnostic procedure of LCH.[10] In this patient X-ray skull showed osteolytic "punched out" lesion with sharp margin. MRI of brain showed lac of hyper-intense signal of the posterior pituitary on T1 weighted image with thickening of pituitary stalk. Trephine biopsy showed bone marrow was infiltrated by many eosinophil, some macrophage, lymphocyte and plasma cells. All these results confirm the diagnosis of LCH.

Treatment options for LCH differ due to its wide disease spectrum. For single skin or bone lesion conservative treatment can be given but for multisystem disease intensive combination chemotherapy is indicated. As the reported patient presented with multisystem disease standard drug regimen with vinblastine and prednisolone for initial 6 weeks of intensive phase followed by maintenance phase of total duration of 12 months was recommended.[8] DDAVP is the drug of choice for LCH induced CDI.[11]

Prognosis of LCH depends on the extent of disease and is guarded for disseminated disease, even sometimes have fatal outcomes.[12]

CDI may be the initial presentation of LCH long before the diagnosis of LCH has been established. Therefore, evaluation of a patient with CDI, LCH should also be kept in mind though it is not common.

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