Langerhans Cell Histiocytosis: A Rare Cause of Central Diabetes Insipidus

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Abstract

Objective: To report adult patients with Langerhans cell histiocytosis who presented with a recent onset of polyuria, secondary amenorrhea and galactorrhea.

Methods: We report the clinical presentations, laboratory test results, imaging findings, histological findings and clinical courses of two cases of adult Langerhans cell histiocytosis.

Results: Our evaluation revealed the presence of central diabetes insipidus. Magnetic resonance imaging of the pituitary showed a thickening of the pituitary stalk. The skeleton survey, chest radiography and biochemistry revealed an osteolytic lesion at the posterior pituitary, pituitary stalk, or hypothalamus. We report two young women with an acute onset of CDI, in whom magnetic resonance imaging (MRI) revealed a thickening of the pituitary stalk [2]. Langerhans cell histiocytosis (LCH) had been diagnosed as the cause of CDI in these two patients.

Conclusions: We reported two cases of adult Langerhans cell histiocytosis. These patients presented with central diabetes insipidus and galactorrhea. Both MRI findings revealed a unifocal infiltration of the infundibulum.

Case 1

A 22-year-old woman presented with polydipsia, polyuria and secondary amenorrhea. Physical examination revealed only galactorrhea. Other physical examinations were within normal limits. Her 24 h urine output was 7 liters. Her laboratory results revealed water diuresis with a urine specific gravity of 1.001 and hypotonic urine, which resulted in the resolution of polyuria. She did not receive any specific treatment for LCH. A biopsy at the right frontal bone was performed and revealed LCH (Figure 2). The patient received intranasal desmopressin treatment, which resulted in the resolution of polyuria. She did not receive any specific treatment for CDI. After follow-up period for 2 years, her galactorrhea improved and her prolactin level normalized without any change in other anterior pituitary hormone level. The follow-up imaging as assessed by a film skull and an MRI of the pituitary also demonstrated a decrease in the size of the pituitary stalk and osteolytic lesion at frontal bone (Figure 1 I-L).

Case 2

A 26-year-old woman presented with polyuria, nocturia, and secondary amenorrhea as well as weight loss of 5 kg in one month. Physical examination revealed galactorrhea. Other results were within normal range. Laboratory analyses showed water diuresis with the presence of central diabetes insipidus. Magnetic resonance imaging of the pituitary revealed a thickening of the pituitary stalk (4.4 mm in diameter), an absence of the posterior bright spot on T1-weighted imaging and a normal signal intensity of the pituitary gland (Figure 1 A-D). Because LCH is one of the causes of pituitary stalk thickening, a bone survey was performed. The bone survey revealed a single osteolytic lesion at frontal bone of skull (Figure 1 E-F). Computed tomography (CT) was performed and showed extra-axial soft tissue forming (measuring about 1.1 x 2.0 cm), which was associated with osteolytic bony destruction at right frontal region (Figure 1 G-H).

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hypernatremia. A water deprivation and vasopressin test confirmed the diagnosis of CDI. Other pituitary hormones were within normal limits.

An MRI of the pituitary demonstrated a round and thick infundibular mass, 5 mm in diameter (Figure 3). The pituitary gland showed homogenous enhancement relative to the normal size, position and signal of the posterior bright spot. Because LCH and germ cell tumors were possible causes of the thickening of the pituitary stalk, a bone survey and serum tumor marker were performed but showed no abnormality.

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Table 1: Water deprivation testing.

Figure 2: Pathology of skull bone biopsy revealed langerhans cell histiocytosis. A) The squash technique revealed Langerhans cells in which histiocyte-like-cells contained round to oval nuclei with finely granular nuclear chromatin. Most of them show indistinct nucleoli. Grooved and cleaved nuclei are common. A few small lymphocytes are present in the background. (H&E Squash technique, x400). B) Langerhans cell histiocytosis. Langerhans cells are present in a background of mixed inflammatory cells composed of eosinophils, lymphocytes, plasma cells, and neutrophils (H&E, x400). C) Langerhans cell histiocytosis. Higher magnification reveals characteristic folded/convoluted nuclei of the Langerhans cells. (H&E, x600) D) Immunoperoxidase staining for CD1a (x400), E) S100 protein and CD68 and F) highlight Langerhans cell (CD1a, x400).

Figure 3: Pituitary stalk thickening at diagnosis and decreased size of the pituitary stalk after a 6-year follow up. Magnetic resonance imaging of pituitary at the diagnosis revealed an enlarged pituitary stalk of 7 x 6 x 5 mm (arrow) without a demonstrated posterior bright spot. A and B) T1W sagittal view without and with Gadolinium, respectively; C and D) T1W coronal view without and with Gadolinium, respectively. Magnetic resonance imaging of pituitary 6 years after diagnosis demonstrated a reduction in the size of the pituitary nodule at pituitary stalk from 7 x 6 x 5 mm to 2 mm. (arrow) and loss of posterior bright spot. E and F) T1W sagittal view without and with Gadolinium, respectively. G and H) T1W coronal view without and with Gadolinium, respectively.

The patient had been diagnosed with CDI and treated with intranasal desmopressin. The 10-month follow-up MRI of the pituitary revealed a progressive thickening of the pituitary stalk of 7 x 6 x 5 mm. Thus, a pituitary stalk biopsy through right front temporal craniotomy was performed and revealed LCH (Figure not shown). She received intranasal desmopressin treatment without specific treatment for LCH. Yearly follow-up MRIs of the pituitary gland and hormone levels revealed a significant decrease in pituitary stalk thickening (Figure 3 E-H); however, there was no change in her pituitary functions.

Discussion

We report two young patients who presented with central diabetes...
insipidus and galactorrhea. Central diabetes insipidus is rare in general population with an estimated prevalence of 1:25,000 [3]. Any disease process involving the hypothalamus or pituitary stalk can lead to CDI. The etiologies of CDI include idiopathic category (42%), neoplasms (28%), infection or inflammation (13%), trauma (5%) and others (12%) [4]. The MRI of the pituitary revealed a thickening of the pituitary stalk in these patients together with the clinical manifestations prompt the differential diagnosis of germinoma, craniopharyngioma, sarcoidosis, tuberculosis, lymphocytic infundibulo-hypophysitis and Langerhans cell histiocytosis [1,4]. Histology confirmed the diagnosis of Langerhans cell histiocytosis in our patients. Langerhans cell histiocytosis has been reported to be the cause of CDI only in 6-15% of cases [5,6].

LCH is a rare disease that is characterized by the aberrant proliferation of specific dendritic cells. Langerhans cells belong to the monocyte-macrophage system [7]. The normal epidermal Langerhans cell is an antigen-presenting cell that is characterized by the intracytoplasmic Birbeck granule and by the expression of CD1a glycoprotein [8]. These cells can infiltrate and destroy many tissues, especially bone, lung, and skin tissues, and the hypothalamic-pituitary axis. They are also found in the liver, spleen and lymph nodes, but with less frequency. This disease usually considered to be a disease of childhood, however, the diagnosis is frequently made in adulthood [9]. Moreover, many cases of childhood onset progress into adult life [10]. To date, many cases of the adult onset LCH have been reported. The pathophysiology of LCH is still unknown. The course of the disease is fairly unpredictable and varies from spontaneous resolution or progress to a debilitating form, which compromises the vital functions with occasionally fatal consequences [11].

LCH is more often encountered in children, with a peak age range of 1-3 years. The incidence is 3-5 cases per million per year [12]. Adult LCH is uncommon with an estimated prevalence of 1-2 cases per million. LCH in adults can develop at any age, but the mean age at diagnosis is 33 years [13]. Recent studies [9,14,15] have reported that as many as 30-39% of diagnosed cases in adults depend on the age of the included population. LCH in adults has different clinical features than LCH in children. Skin, lung and bone involvement and CDI are common manifestations with adult LCH whereas the involvement of the liver, spleen, lymph nodes and bone marrow is much less frequent [16].

The hypothalamic-pituitary system is involved in 5-50% of child cases of LCH and 14% of adult patients with LCH. Central diabetes insipidus is the most common manifestation of endocrine dysfunction [9] and usually develops within a year after the diagnosis of LCH. Central diabetes insipidus developed in 17-25% of children with LCH and 14-29.6% of adult onset LCH [9,17]. In fact, CDI can also be the first presenting symptom of LCH [2,18], as was the case with our patients. Several pathogenesis of CDI have been postulated including an autoimmune process that involves antibodies reacting against vasopressin, LCH-infiltration and scarring in the hypothalamic pituitary area [6,19,20]. CDI is usually permanent, and the patients against vasopressin, LCH-infiltration and scarring in the hypothalamic axis. They are also found in the liver, spleen and lymph nodes, but with less frequency. This disease usually considered to be a disease of childhood, however, the diagnosis is frequently made in adulthood [9]. Moreover, many cases of childhood onset progress into adult life [10]. To date, many cases of the adult onset LCH have been reported. The pathophysiology of LCH is still unknown. The course of the disease is fairly unpredictable and varies from spontaneous resolution or progress to a debilitating form, which compromises the vital functions with occasionally fatal consequences [11].

Conclusion
We report two cases of adult Langerhans cell histiocytosis who presented with central diabetes insipidus and galactorrhea. MRI findings for both patients revealed a unifocal infiltration of the infundibulum. The pathology examination led to the diagnosis of LCH. Replacement therapy with intranasal administration of desmopressin helped resolve symptoms. The stalk lesion decreased in size without specific treatment. Long-term follow up with proper supplementation to correct hormonal deficiencies may be the proper management in patients with isolated sellar or bone involvement that frequently experience a slower progression of the disease.

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References


