Brief Communication

Lymphocytic hypophysitis masquerading as pituitary adenoma

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ABSTRACT

Introduction: Pituitary hypophysitis (PH) is characterized by pituitary infiltration of lymphocytes, macrophages, and plasma cells that could lead to loss of pituitary function. Hypophysitis may be autoimmune or secondary to systemic diseases or infections. Based on the histopathological findings PH is classified into lymphocytic, granulomatous, xanthomatous, mixed forms (lymphogranulomatous, xanthogranulomatous), necrotizing and Immunoglobulin- G4 (IgG4) plasmacytic types. **Objective:** To report a case of lymphocytic hypophysitis (LH). **Case Report:** A 15-year-old girl presented with history of headache, amenorrhea, and history of polyuria for past 4 months. Initial evaluation had suppressed follicular stimulating hormone (<0.01 mIU/ml), high prolactin levels (110.85 ng/ml) and diabetes insipidus (DI). Magnetic resonance imaging of sella was suggestive of pituitary macroadenoma with partial compression over optic chiasma. Patient underwent surgical decompression. Yellowish firm tissue was evacuated and xanthochromic fluid was aspirated. Histopathology was suggestive of LH. She resumed her cycles postoperatively after 4 months, prolactin levels normalized, however, she continues to have DI and is on desmopressin spray. This case has been presented here for its rare presentation in an adolescent girl because it is mostly seen in young females and postpartum period and its unique presentation as an expanding pituitary mass with optic chiasma compression. **Conclusion:** Definitive diagnosis of LH is based on histopathological evaluation. Therapeutic approach should be based on the grade of suspicion and clinical manifestations of LH.

Key words: Lymphocytic hypophysitis, autoimmunity, pituitary macroadenoma

Introduction

Pituitary hypophysitis (PH) is characterized by pituitary infiltration of lymphocytes, macrophages, and plasma cells that could lead to loss of pituitary function. Hypophysitis may be autoimmune or secondary to systemic diseases or infections. Based on the histopathological findings, PH can be classified into lymphocytic, granulomatous, xanthomatous, mixed forms (lymphogranulomatous, xanthogranulomatous), necrotizing and IgG4 plasmacytic types.[1] Lymphocytic Infundibuloneurohypophysitis (LINH), subtype of lymphocytic hypophysitis (LH) mostly presents with acute onset diabetes insipidus (DI) and intracranial mass-effect symptoms. The diagnosis can be difficult in many cases as the distinction from pituitary adenomas and other sellar masses is not obvious. Here we report a case of LH masquerading as pituitary adenoma.

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Case Report

A 15-year-old girl presented to endocrinology OPD with history of headache, amenorrhea, and polyuria for past 4 months. On initial evaluation, she had suppressed follicular stimulating hormone (<0.01 mIU/ml), high prolactin levels (110.85 ng/ml) and DI. Magnetic resonance imaging of sella was suggestive of pituitary macroadenoma with partial compression over optic chiasma [Figures 1 and 2]. Patient underwent surgical decompression. Yellowish firm tissue was evacuated and xanthochromic fluid was aspirated. Histopathology was suggestive of LH. Her menstrual cycles resumed postoperatively after 4 months, the prolactin

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levels normalized; however, she continues to have DI and is on desmopressin spray.

This case has been presented here for its rare presentation in an adolescent girl because LH is mostly seen in young females and postpartum period and its unique presentation as an expanding pituitary mass with optic chiasma compression.

Discussion

LH is an uncommon disease and the incidence is one case in nine million individuals per year, and it is found in less than 1% of pituitary surgical cases. Up to the year 2005, about 379 cases of LH have been reported in world literature. LH is characterized by lymphocytic infiltration and can be sub-classified into lymphocytic adenohypophysitis (LAH), LINH, and lymphocytic panhypophysitis. It is common in females and the ratio is 6:1 as compared to males. The average age at diagnosis is 34.5 and 44.7 years for females and males respectively. About 57% of cases of LAH occur during pregnancy or postpartum period. Increased pituitary antigens presentation to the immune system could be the probable cause, due to lactotrophs hyperplasia and increase in pituitary blood flow.[2] LH may be associated with other autoimmune diseases in 20% of cases e.g.: Hashimoto's thyroiditis, diabetes mellitus type 1, hypoparathyroidism, Graves' disease, Addison's disease, and autoimmune polyendocrinopathies; Organ-specific autoimmune: vitiligo, pernicious anemia, alopecia, myasthenia gravis, primary biliary cirrhosis, chronic atrophic gastritis, and nonorgan-specific autoimmune diseases like lupus erythematosus. Variable clinical presentations of LH are seen, which include symptoms related to mass compression of sellar neighborhood regions (optic chiasma, cavernous sinus), hypopituitarism, and hyperprolactinemia. DI as the presenting or the most prominent symptom with intact anterior pituitary function in LH makes the diagnosis of LINH most likely. Mass-effect symptoms involve mostly frontal lobe or present with generalized headache and lethargy. Prolactin is usually normal or may be just slightly elevated. Imura *et al*. studied 17 patients with idiopathic DI of 2-months to 20-years duration. Radiological findings in all, and histopathology in the two patients in whom biopsy was performed, was suggestive LINH. Two patients had mild hyperprolactinemia and nine had impaired secretory responses of growth hormone to insulin-induced hypoglycemia.[3] In LINH, radiological finding of diffuse thickening of the pituitary stalk is very characteristic, with a greater diameter more than 3.5 mm at the level of the median eminence of the hypothalamus.[4] There is a loss of normal smooth tapering of the infundibular stalk with varying degree of asymmetry. Marked gadolinium enhancement of the stalk is quite common, extending even into lower hypothalamus and also loss of the usual neuro-hypophyseal "bright spot."[3]

Definitive diagnosis of LH depends on the microscopic examination of the pituitary tissue in spite of that a presumptive diagnosis can be based on clinical, laboratory and imaging features as explained earlier. Differential diagnosis of LH includes pituitary adenomas and a large number of nonadenomatous lesions of the pituitary. To distinguish them, in functioning adenomas, clinical features of increased hormones are usually noticed at the time of presentation. Nonfunctioning pituitary adenomas, on the other hand, usually have insidious onset, and present either with mass effect symptoms (visual field defects) or with evidence of hormone deficiencies. Hypogonadism rather

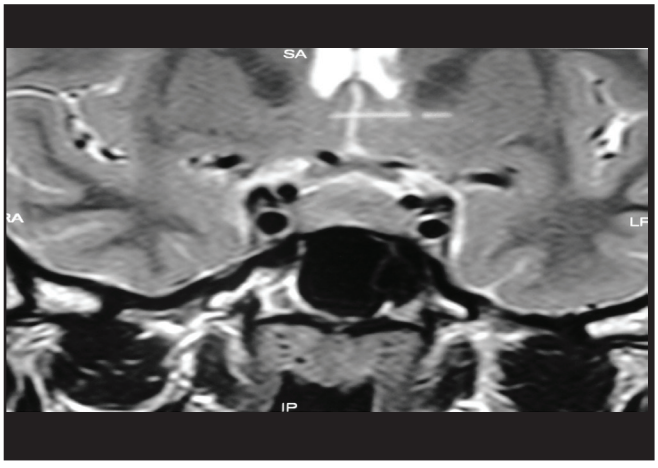

Figure 1: Coronal section magnetic resonance imaging (MRI) of hypothalamo-pituitary region showing pituitary macro-adenoma with partial compression of optic chiasma

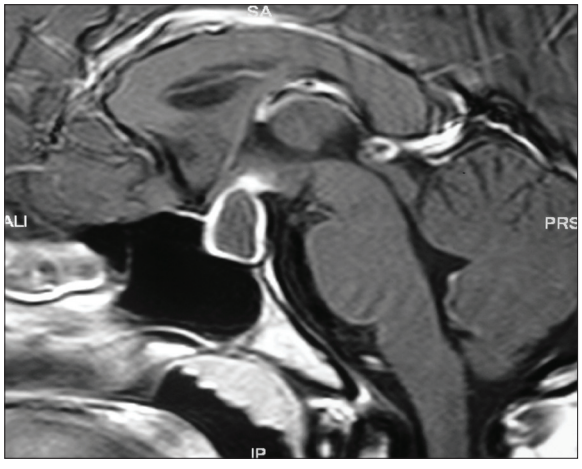

Figure 2: Saggital section MRI of hypothalamo-pituitary region showing pituitary macro-adenoma with partial compression of optic chiasma

than hypocortisolemia or DI, is usually the initial problem in pituitary adenomas.

The differential diagnosis of LINH also includes some rare tumors like germinomas and Langerhans histiocytosis and differentiation can be very difficult.[5] These tumors may present with DI and pituitary stalk thickening. Instead of regression, rapid progression is noticed radio logically in most of the cases. Histopathology is essential if such malignancies are considered. Therefore, therapeutic approach should be based on the grade of suspicious and clinical manifestations of LH. In case of hypopituitarism, though less likely, hormonal replacement is the only approach indicated. In the presence of headache, visual disturbances or other mass effects manifestations, the decision between an immunosuppressive therapeutic trial with glucocorticoids and/or azathioprine and surgery with biopsy depends on clinical judgment. However, if there is no improvement in the symptoms with conservative management, transsphenoidal surgery for diagnosis confirmation and decompression is advised. Preoperative frozen section cytology may prevent unnecessary extensive surgery. The surgical appearance of the lesions varies from soft yellowish to firm, fibrotic, whitish tissue, probably reflecting different stages of the inflammatory process at the time of surgery. Immediate surgery may be necessary when there are signs of optic nerve compression or increased intracranial pressure.[5]

Conclusion

LH is a spectrum of distinct clinical syndromes. It is usually mistaken for tumors, and the patient may be subjected to unnecessary surgical therapy in many cases. The most important step in the management is clinical diagnosis as the definitive diagnosis can only be made by histopathological evaluation. The concurrence of another autoimmune disease and clinical presentation and imaging may help in approaching towards a correct diagnosis.

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