Lymphocytic hypophysitis with normal pituitary function mimicking a pituitary adenoma: a case report and review of literature

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Abstract. Lymphocytic hypophysitis (LYH) is a rare autoimmune inflammatory disorder of the pituitary gland usually affecting young women, often in pregnancy or postpartum period. It is rare in non-pregnant females and in men. Patients present with symptoms of an expanding pituitary mass and/or varying degrees of pituitary dysfunction. We hereby report a case of lymphocytic hypophysitis in a 28-year-old non-pregnant female who presented with clinical and radiological features of a pituitary tumor with normal pituitary hormones which on histopathological examination revealed features of lymphocytic hypophysitis. The case is presented here for its rarity and its unique presentation as an expanding pituitary mass with normal pituitary function. Peculiar clinical, radiological and histopathological features of this uncommon entity are discussed.

Introduction

Lymphocytic hypophysitis is a rare autoimmune endocrine disorder of pituitary [1] usually affecting young women often in relation to pregnancy or the immediate postpartum period [2]. Though rare, it has been described in non-pregnant women [3] and men [4]. It was previously believed to affect only anterior pituitary function (i.e. adenohypophysitis) but now it is considered that it may involve posterior pituitary also (infundibulo-hypophysitis), resulting in central diabetes insipidus [5] Lymphocytic hypophysitis frequently mimics a pituitary adenoma with clinical features attributable to an expanding mass or symptoms attributable to hypopituitarism. Radiologically also lymphocytic hypophysitis may mimic a pituitary adenoma [6, 7]. The salient histological feature is a polymorphic lymphoplasmacytic infiltration of pituitary gland associated with destruction of anterior pituitary cells [8].

We hereby report a case of lymphocytic hypophysitis in a 28-year-old non-pregnant female who presented with clinical and radiological features of a pituitary adenoma without any feature of hypopituitarism.

Case description

A 28 year old, unmarried female reported to neurosurgical outpatient department with one month history of diminution of vision and dull headache. There was no history of seizures, or limb weakness. Her past medical history was not significant. Her general physical and systemic examinations were normal. She was conscious and alert. Her higher mental functions were normal. Her vision was 6/12 in both eyes and perimetry revealed bitemporal hemianopia. Funduscopy revealed bilateral disc pallor. Other cranial nerves and rest of the neurological examination was also normal. Routine laboratory investigations were normal, including full blood count, renal function and glucose. Serum electrolytes, serum osmolality, urine osmolality, 24 hour urinary volume and serum levels of hormones viz. T3, T4, TSH, Prolactin, GH, Cortisol, FSH and LH, were within normal limits. MRI scan brain showed an intrasellar mass lesion with a suprasellar extension. There was no cavernous sinus invasion. Clinical and radiological impression of a pituitary adenoma was made. Complete resection of the lesion was performed via a transnasal, trans-septal approach. The tumor peroperatively was partly suckable and partly firm. Intraoperative crush smears revealed tissue bits which could be crushed with difficulty, however, fibrous tissue with a few lymphocytes were noted by the pathologist.
The histopathological examination of the surgical specimen showed fragments of adenohypophyseal tissue with a dense lymphoplasmacytic infiltrate. At places, lymphoid follicles were seen. There were areas of extensive fibrosis and calcification (Figure 2, Inset). There were no granulomas or multinucleated giant cells. There was no histological evidence of a neoplasm. The diagnosis of lymphocytic hypophysitis was made on Hematoxylin-eosin staining (Figure 2). Immunostaining for T and B cell markers i.e., CD-3, CD-20 and CD-68 was done which showed CD-20 (Figure 3a) positivity which was intense in follicles with many lymphocytes in the follicles showing positivity. CD-3 (Figure 3b) positive cells were also seen in the follicles. CD-68 positive cells were interspersed in the follicles and also present in the interstitium with CD-3 and CD-20 positive cells. Chromogranin immunostaining (Figure 3c) was done to confirm that the pathology involved pituitary gland (Figure 3e).

Post operatively, her visual field defect improved and her visual acuity was 6/6 in right eye and 6/9 in left eye. Post operative hormone levels done revealed evidence of hypopituitarism and hence hormone replacement was started. The screen for antinuclear and other antibodies was negative.

**Discussion**

Lymphocytic hypophysitis (LYH) is an uncommon autoimmune disease in which the pituitary gland is infiltrated by lymphocytes,
plasma cells and macrophages and its function is usually impaired [17].

Panhypopituitarism due to lymphoplasmacytic pituitary infiltration was described by Rapp and Pashkis in 1953 [9] but they could not classify this disorder as autoimmune because the concept of endocrine autoimmunity was introduced some years later for Hashimoto's thyroiditis [10]. After the classification of Hashimoto's thyroiditis as an autoimmune endocrine disease, an autoimmune pathogenesis for LYH was suggested by Goudie and Pinkerton [11].

Initially, the diagnosis of lymphocytic hypophysitis was made on autopsy and only a few cases were reported. With advances in imaging many cases have been reported in the last two decades primarily affecting the anterior pituitary [12, 13, 14].

Women are affected more frequently than men with a ratio of about 8:1 [15]. The mean age at diagnosis is 34 years for women and 44.7 years for men, although prepubertal or elderly cases have also been reported [16, 29]. LYH frequently affects women in pregnancy (last six months) and after delivery (first six months) [2]. Our case of lymphocytic hypophysitis in a 28-year-old non-pregnant female presenting as a pituitary adenoma is very rare.

Headache occurs at the onset of the disease and is usually the first symptom [17]. This usually precedes or is coupled with visual field impairment and, more rarely, diplopia due to the invasion of cavernous sinus by an enlarged pituitary mass [14]. Our patient also presented with diminution of vision and field defects. Patients usually present with hormone alterations whether isolated or multiple [12, 14]. A hypopituitarism involving almost all hormones usually occurs when the inflammatory process induces pituitary destruction [14]. Our patient had a normal hormone profile which is very unusual [17]. Imaging is an important diagnostic tool
for the lymphocytic hypophyisis and it is important to differentiate it from tumors in the sellar-parasellar region. X-ray sellar region usually reveals a flat sellar floor in LYH, but a unilaterally depressed one in pituitary adenomas. In patients of LYH, MRI shows an enlarged pituitary with a symmetrical suprasellar extension which displaces the optic chiasm, whereas patients with adenoma show asymmetrical pituitary enlargement with deviation of the stalk; the stalk is thickened but not usually deviated in LYH [13]. The pituitary enhancement after injection of gadolinium is homogeneously intense in LYH and shows enhancement along dura (called dural tail) or arachnoid. Patients with adenomas, on the other hand show delayed and poor enhancement usually without a “dural tail” after gadolinium [17]. Despite these differences on imaging, radiological findings of LYH and adenomas tend to overlap, as was seen in our case where imaging was suggestive of a pituitary adenoma that proved to be LYH on histology. PARA inflammatory space occupying lesions of the pituitary are rare [18] and consequently there are a number of single case reports of the condition but few reports of series [19]. These represent only 0.38% of surgical series of pituitary lesions [18]. Inflammatory hypophyisis may be classified as lymphocytic hypophyisis or granulomatous hypophyisis, both conditions represent the ends of the spectrum of disease [19]. An autoimmune pathogenesis is suggested for lymphocytic hypophyisis [20]. A 30% incidence of coexistence of lymphocytic hypophyisis with other autoimmune disorders is found in the literature [11, 20]. An autoimmune pathogenesis is also suggested by immunohistochemical characterization and ultrastructural evidence showing that cytotoxic lymphocytes intimately contact anterior pituitary cells in lymphocytic hypophyisis. The autoimmune hypophyisis is further supported by the finding that lymphocytic hypophyisis can be experimentally induced in rats by injection of isologous and homologous pituitary tissue [18, 21]. However in our patient there was no evidence of any other auto-immune disease and her anti-nuclear antibodies and other anti-bodies were negative.

Lymphocytic hypophyisis is synonymous with lymphocytic adenohypophyisis, which involves the infiltration of the adenohypophysis by lymphocytes, plasma cells and macrophages. This is common as compared with the lymphocytic-infundibulo-neurohypophyisis which is an inflammatory process involving the posterior lobe of the pituitary and the infundibulum [2, 3, 22]. The lymphoplasmacytic aggregates may be arranged in lymphoid follicles with a germinal center [14] as was seen in our case which is very rare. Lymphoplasmacytic aggregates may surround atrophic acini of pituitary cells [23] whereas the remaining pituitary tissue shows areas of reactive fibrosis [5, 24].

The dense lymphoplasmacytic infiltrate seen in our patient was infiltrating the pituitary gland. Many lymphoid follicles with germinal centers were seen and some areas had undergone fibrosis which gave a firm consistency to the lesion peroperatively. Calcification was seen in our case which has not been reported earlier.

The histopathological changes correlate with the natural history of the disease. At the onset, pituitary gland is enlarged, edematous with lymphocytic infiltration, putting pressure on adjacent structures leading to headache and visual symptoms. At this stage, subclinical hypopituitarism can be present but a spontaneous remission can occur if the pituitary tissue is not destroyed. Subsequently the pituitary parenchyma is destroyed and is replaced by fibrous tissue. At this stage, symptoms of partial or total hypopituitarism appear [20, 23]. In a series of 14 cases of inflammatory hypophyisis the length of symptoms from presentation varied from acute onset to 9 years [19]. Though the natural course of infundibulohypophyisis is poorly understood Amagai [25] described a patient of infundibulohypophyisis who presented with enlargement of pituitary stalk and pituitary gland with excessive thirst but was not given any treatment at that time. Two years later the patient presented with features of panhypopituitarism with features of lymphocytic hypophyisis and granuloma formation on histology [25]. Our case had a preserved pituitary function reflecting either an early stage of disease or a partial involvement of the gland, but fibrosis and calcification seen in our case reflect that the disease process has been there for a long time. Lymphocytic hypophyisis has been described with ruptured Rathkes cleft cysts [26, 27] cranioopharyngi-
Lymphocytic hypophysitis is rare in non-pregnant females, hereby a case mimicking a pituitary adenoma with normal pituitary function is presented. Follicle formation and calcification is unusual which makes it rarest of the rare entities.

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References


