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Lymphocytic Hypophysitis in a Pregnant Woman: A Case Report

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ABSTRACT **Published Online: January 27, 2024**

Introduction: Lymphocytic hypophysitis was first reported in 1962, it is a rare immune-mediated inflammatory disorder that causes pituitary dysfunction.

Case report: We report the case of 29-year-old woman at 37 weeks gestation, diagnosed with lymphocytic hypophysitis. The patient received appropriate hormonal replacement treatments. The evolution was favorable.

Conclusions: Lymphocytic hypophysitis is a rare auto-immune disease, occurring mainly in women during the peripartum phase. Clinical presentation is variable, it should be considered in female pregnant patients or in the early postpartum period, with pituitary hypertrophy and/or hormonal deficiencies with diabetes insipidus. To date, the management of this disease is challenging. Prospective controlled studies are necessary but difficult to conduct due to the rarity of lymphocytic hypophysitis.

KEYWORDS: Lymphocytic - Hypophysitis - Pregnancy - Management.

INTRODUCTION

Lymphocytic hypophysitis was first reported in 1962 and is the most common variant of autoimmune hypophysitis [1]. It is a rare immune-mediated inflammatory disorder that causes pituitary dysfunction [2], characterized by diffuse monoclonal lymphocyte infiltration of the gland, which can leave minimal sequelae or progress to fibrosis, leading to temporary or permanent hormonal dysfunction [1,3].

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This entity is highly linked to pregnancy (peri- and postpartum period), and affects women more frequently than men, with a 3:1 ratio. The vast majority of cases occur in women of reproductive age, with incidence peaking in the fourth decade of life. It is rare in children and the elderly [1,3,4]. The incidence is estimated of one case per nine million people, but probably, there are not diagnosticated subclinical forms [3].
Here we describe the case of a pregnant patient with a large pituitary gland due to lymphocytic hypophysitis.

CASE REPORT

A 29-year-old woman at 37 weeks gestation, G2P2, with a medical history of Beta thalassemia diagnosed at the age of 18 years old. She presented diffuse and persistent headache evolving two weeks prior to her admission to our department, associated to blurred vision, intermittent vomiting, polyuria

(5l/24h) with nocturia and polydipsia (6l/24h). At admission the patient reported a remission of the visual impairment and vomiting three days before. Clinical examination was normal with a blood pressure at 110/67 mmhg.

Goldmann visual field testing was performed which was normal in our patient, visual acuity was normal as well. Magnetic resonance imaging of the hypothalamo-pituitary region (Figure 1 and 2), showed diffuse homogenous enlargement of the pituitary gland, poorly individualized pituitary stalk, and the loss of normal posterior pituitary bright spot. intravenous contrast was avoided because of pregnancy

Initial blood tests were normal; glucose 99 mg/dL (74 - 110), sodium 138 mmol/L (135 - 145), potassium 3.7 mmol/L (3.5 - 4.5), hemoglobin 8.9 g/L (12 - 14.5), leucocytes 9,890/L (4100 - 9900). Hormonal testing was compatible with cortisol and thyroid hormone deficiencies : thyrotropin 0.22 mU/L (0.5 - 5), free thyroxine 0.45 ng/dL (0.70 - 1.48), cortisol 4.4 µg/dL (5 - 22).

Treatment with intravenous steroids hydrocortisone 100 mg IV every 8 hours, L-thyroxin 75ug/day and oral desmopressin 60ug per day was initiated. Headache was managed with paracetamol with good response. After four days the patient improved significantly, she was discharged home with a prescription of oral hydrocortisone 20mg per day, L-thyroxin 75ug per day and Desmopressin 120ug per day. The patient gave birth without complication by C-section at 39 weeks and continued her treatment, we noted agalactia as expected.

The evolution was favorable, the patient was followed up monthly, after 5 weeks the patient reported spontaneous galactorrhea and started breastfeeding her baby, hormonal treatments were decreased gradually until discontinuation. four months later a control pituitary MRI was performed, revealing a total normalization of the size of the pituitary gland and normal posterior pituitary bright spot

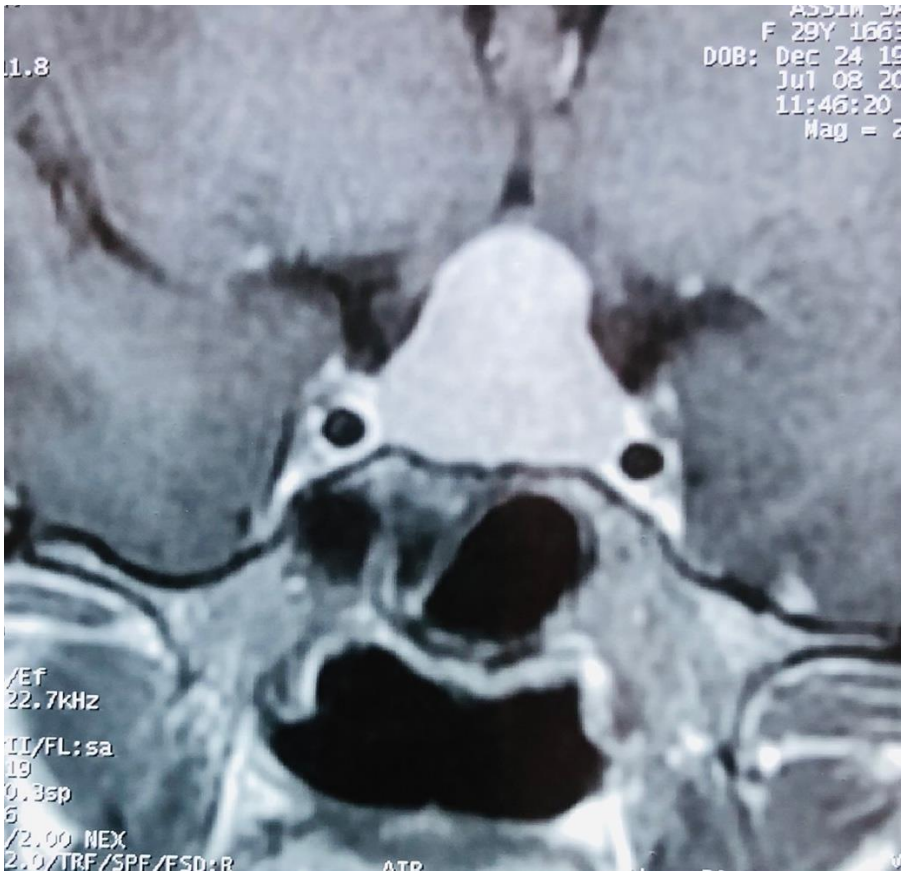

Figure 1: Coronal section of pituitary-MRI showing a diffuse and homogenous enlargement of the pituitary gland.

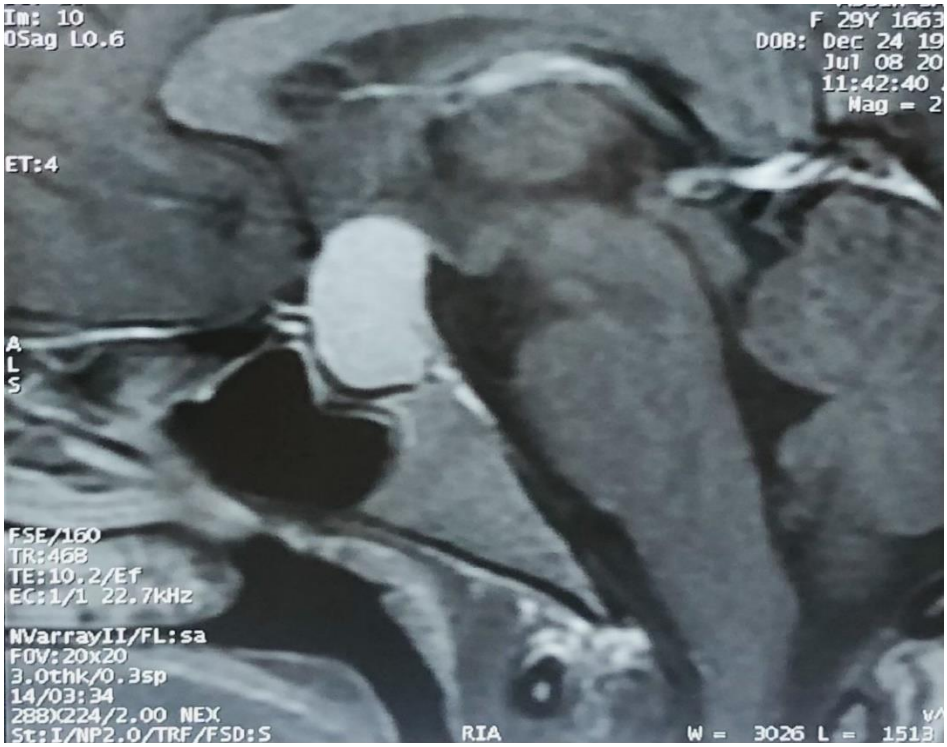

Figure 2: sagittal section of pituitary-MRI showing a diffuse and homogenous enlargement of the pituitary gland and absence of normal posterior pituitary bright spot.

DISCUSSION

Inflammatory disease affecting the pituitary gland is known as hypophysitis. There are many histological subtypes, the most frequent being lymphocytic hypophysitis, and the pathogenesis is varied and diversified [5].

Lymphocytic hypophysitis was first described by Goudie and Pinkerton in 1962 [6]. Although this is the earliest description, it is probable that some of Sheehan's original patient series from the early 1900s included patients with the diagnosis [5].

This disease is more common in women than in men (Rati 3:1) and about 55% of cases occur during pregnancy or postpartum, especially in the last month of pregnancy as it was for our patient, or in the first two months postpartum [3].

The primary histological features include normal pituitary gland tissue with infiltration by lymphocytes, plasma cells, epithelioid histiocytes, macrophages, eosinophils, and inflammation/fibrosis [1]. The pathogenesis of lymphocytic hypophysitis may be due, as the other autoimmune diseases, to the formation of autoantigens, the pathogenic autoantigens targeted by the disease are yet to be identified and a serologic test is not yet available [5].

Clinical presentation of lymphocytic hypophysitis can be variable, headache may be the first and the commonest symptom, which is not the case in pituitary adenoma. It may or may not be accompanied with visual symptoms, symptoms related to anterior hypopituitarism can be noted; including fatigue/cold intolerance from hypothyroidism, lethargy from hypocortisolism, and loss of libido, amenorrhea from low follicle stimulating and luteinizing hormones. And also signs due to abnormality in the functioning of the posterior pituitary can be present, either from direct invasion or compression of the pituitary stalk, leading to deficient antidiuretic hormone causing diabetes insipidus. The presence of diabetes insipidus is strong evidence of hypophisitis because it's not typically found in case of pituitary adenomas [7,8,9].

Magnetic resonance imaging (MRI) shows in 85–95% of hypophysitis cases a generally symmetrically enlarged pituitary gland, and suprasellar extension is common, and administration of gadolinium homogeneously enhances the gland, unlike in adenomas case where gadolinium enhances the gland more focally. In advanced stages, these MRI features may be absent due to shrinkage of the mass with resolution of the inflammatory process, and fibrotic changes and an empty sella may be observed [10].

The diagnosis of lymphocytic hypophysitis can be difficult, the gold standard for diagnosis is histopathological assessment of

a surgically obtained biopsy specimen, however it requires an invasive procedure and it can be avoided in case of typical clinical characteristics [1,6,11]. A presumptive clinical diagnosis can be made in patients who meet the subsequent criteria: a history of gestational or post-partum hypopituitarism; a contrast-enhancing sellar mass with imaging features of lymphocytic hypophysitis ; a pituitary hormone deficiency pattern with early loss of adrenocorticotrophic hormone (ACTH) and thyroid-stimulating hormone (TSH), in contrast to what is usually found in macroadenomas (sequential loss of growth hormone, luteinizing hormone/follicle-stimulating hormone, ACTH and TSH); relatively rapid onset of hypopituitarism, unlike the typical slow development of an adenoma; and a degree of pituitary insufficiency disproportionate to the size of the mass [10].

In around 20% of cases, lymphocytic hypophysitis is associated with other autoimmune diseases. These may include : Hashimoto thyroiditis, diabetes mellitus type 1, hypoparathyroidism, Graves disease, Addison disease, vitiligo, pernicious anemia, alopecia, myasthenia gravis, primary biliary cirrhosis…[5].

The evolution of lymphocytic hypophysitis is both variable and unpredictable. Typically, it progresses gradually, leading to destruction of the pituicytes, with the parenchyma being replaced by fibrosis and pituitary atrophy, causing hypopituitarism. In some cases, the progression is aggressive and neurological deficits advance rapidly [10]. However, spontaneous partial or total recovery of pituitary function, and resolution of pituitary masses in the absence of any intervention, have been well reported [6,10].

Because of this variability, appropriate management remains controversial [6,10]. Controlled trials are not feasible due to the rarity of the disorder [10].

Management includes appropriate replacement therapy of hormone deficiency including; cortisol, thyroid hormones, ADH… [10,12,13].

Corticosteroid therapy has been suggested as a possible treatment for inflammation, and in some cases has been linked to a restoration of pituitary function and a reduction of mass volume [10]. High-dose glucocorticoids remains the cornerstone of medical therapy and first-line treatment of lymphocytic hypophysitis [12,13]. In contrast, some patients with lymphocytic hypophysitis have not responded to glucocorticoid therapy. There are also reported few cases of symptomatic improvement with the administration of corticosteroids, followed by relapse on discontinuation of treatment [10,13]. Nevertheless, it is not known whether the clinical improvement is directly due to corticosteroid therapy, or simply reflects the natural course of the disease. Considering the uncertainty surrounding the efficacy of corticosteroid therapy and its known long-term adverse effects, its use is limited and does not appear to be justified for most patients [10,13].

There are few data on the treatment of refractory lymphocytic hypophysitis, some authors suggest the use of steroid-sparing immunosuppressive drugs such as rituximab and mycophenolate mofetil, this therapeutic combination represents a feasible alternative for the treatment of refractory disease with promising results in some cases [12,13].

Surgery of the pituitary mass is indicated for conservative therapy non-responders patients with progressive radiologic or neurologic degradation or severe and progressive visual disturbances [6,10,11,12]. The optimal surgical approach implies only partial resection to decompress the surrounding structures via a transsphenoidal procedure [10].

Long-term follow-up is mandatory to monitor hormonal deficits, hypopituitarism can be temporary in some patients. if progression to fibrosis did not cause irreversible hypopituitarism, an attempt to withdraw hormone replacement after resolution of the inflammatory phase can be made. Serial visual field examinations with MRI may be necessary especially in patients managed medically [10].

CONCLUSION

Lymphocytic hypophysitis is a rare disease, occurring mainly in women during the peripartum phase. This entity should be considered in patients with pituitary hypertrophy and/or hormonal deficiencies with diabetes insipidus. To date, there is no consensus on the management of this disease, and prospective controlled studies are necessary but difficult to conduct due to the rarity of lymphocytic hypophysitis.

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