



Case Report

# A case report of lymphocytic hypophysitis

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## ABSTRACT

**Background:** Lymphocytic hypophysitis (LH) is a rare condition that mostly affects women of the reproductive age. Because it is infrequently encountered, it is not often considered as a differential diagnosis of sellar masses. The diagnosis is made clinically with the aid of magnetic resonance imaging (MRI) and should be considered if the patient has endocrine derangements in addition to a sellar mass.

**Case Description:** A 37-year-old female presents with a complaint of headaches and CT imaging showed a sellar mass. She was also being investigated simultaneously by the endocrine department and was diagnosed with panhypopituitarism. She proceeded to surgery for a presumed pituitary adenoma but histopathology returned as LH.

**Conclusion:** It is important to have a wide differential diagnosis when managing pituitary masses. Clinical correlation with atypical MRI findings is useful to determine the diagnosis of LH.

**Keywords:** Hypophysitis, Neuroendocrine, Neuroradiology

## INTRODUCTION

Lymphocytic hypophysitis (LH) was first reported in 1962 and is the most common variant of autoimmune hypophysitis.<sup>[3]</sup> It is a rare disease of the pituitary gland and is characterized by diffuse lymphocyte infiltration of the gland. If left untreated, LH can lead to pituitary gland fibrosis and atrophy.<sup>[2]</sup> It can be caused by a primary inflammatory process of the gland or inflammation secondary to other causes such as immunotherapy, systemic inflammatory disorders, infections, and rarely pituitary adenomas.<sup>[2,9]</sup>

Autoimmune hypophysitis is often classified according to histopathology with the other histological subtypes being granulomatous, xanthomatous, and plasmacytic.<sup>[2]</sup> It can also be morphologically categorized according to whether inflammation involves the anterior pituitary gland (adenohypophysitis), posterior gland and stalk (infundibuloneurohypophysitis), or the entire gland (panhypophysitis).<sup>[2]</sup>

The estimated annual incidence of hypophysitis is 1 in 7–9 million and there have been over 390 cases reported of LH.<sup>[2]</sup> LH is strongly associated with pregnancy and occurs more frequently in woman than men at a 3:1 ratio.<sup>[1,8]</sup> The majority of cases are found among reproductive-aged woman with the incidence peaking during the 4<sup>th</sup> decade of life. It is uncommon in children and the elderly.<sup>[5]</sup>

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Given the rarity of the condition, we would like to present what may be the first case of LH in New Zealand.

## CASE REPORT

A 37-year-old female was referred to the neurology service with a complaint of headache for the past 4–5 months. The headaches were severe and distributed over the entirety of her head and associated with fatigue and weight gain. The patient's only medical history was primary amenorrhea secondary to an imperforate hymen.

She was trialed on migraine medications and a CT head was done which showed a pituitary mass. A subsequent magnetic resonance imaging (MRI) scan described the pituitary gland as enlarged with diffuse enhancement consistent with a macroadenoma [Figure 1]. The lesion measured 14 × 15 × 12 mm and abutted the optic chiasm but did not cause compression of the optic nerve. Neuroophthalmology testing showed that she also had bitemporal hemianopia.

Simultaneously, the patient was being evaluated by endocrinology for deranged thyroid function tests. Further testing revealed a low cortisol level, LH, FSH, oestradiol, free T4, and TSH. She was diagnosed with hypopituitarism and treated with hydrocortisone and thyroxine.

The patient was referred to neurosurgery for resection of the pituitary lesion. This was done with a transsphenoidal approach and the surgery was uncomplicated. The histology returned as LH. The postoperative course was complicated by the development of diabetes insipidus, CSF leak requiring a return to theater and a readmission for meningitis. The patient is now recovering well on subsequent follow-up appointments.

## DISCUSSION

LH is rare autoimmune disease and is challenging to diagnose. It predominantly affects women of the reproductive age and the most common symptom is persistent headache and endocrine deficiencies.<sup>[2]</sup> It is characterized by lymphocytic infiltration of the pituitary gland leading to fibrosis.<sup>[7]</sup>

Like other autoimmune diseases, the pathogenesis is due to the formation of autoantigens.<sup>[3]</sup> Unfortunately, the pathogenic autoantigens targeted by the disease are yet to be identified and a serologic test is not yet available.<sup>[3]</sup> Diagnosis depends on clinical suspicion and must take into account the symptoms, demographics of the patient, evidence of pituitary dysfunction, and neuroimaging.<sup>[5]</sup> Histopathological assessment remains the gold standard for diagnosis, however, it requires an invasive procedure. The primary features on histological evaluation include normal pituitary gland tissue with infiltration by lymphocytes, plasma cells, epithelioid histiocytes, macrophages, eosinophils, and inflammation/fibrosis.<sup>[5]</sup>

MRI is the imaging modality of choice when investigating pituitary pathology, however, it is difficult to differentiate between LH and pituitary adenomas.<sup>[2,4,6]</sup> There is no single radiologic feature that can distinguish LH from a pituitary adenoma. Gutenberg *et al.* created a radiologic scoring system that can be used to guide decision-making [Table 1].<sup>[4]</sup> Using this scoring system, our neuroradiologist retrospectively scored our patient-1 (gadolinium enhancement medium) which is suggestive of LH rather than a pituitary adenoma [Table 1].

A limitation of Gutenberg *et al.*'s scoring system is that it has not been tested against other types of sellar masses as the study exclusively compared autoimmune hypophysitis to adenomas.<sup>[4]</sup> While pituitary adenomas are the most common sellar mass, its use may be limited when trying to distinguish between other lesions that can mimic autoimmune hypophysitis radiologically such as pituitary germinoma and lymphoma.<sup>[4]</sup> Although the scoring system has not been validated by data from other intuitions, the authors offer it as another tool that can be used to aid diagnosis.

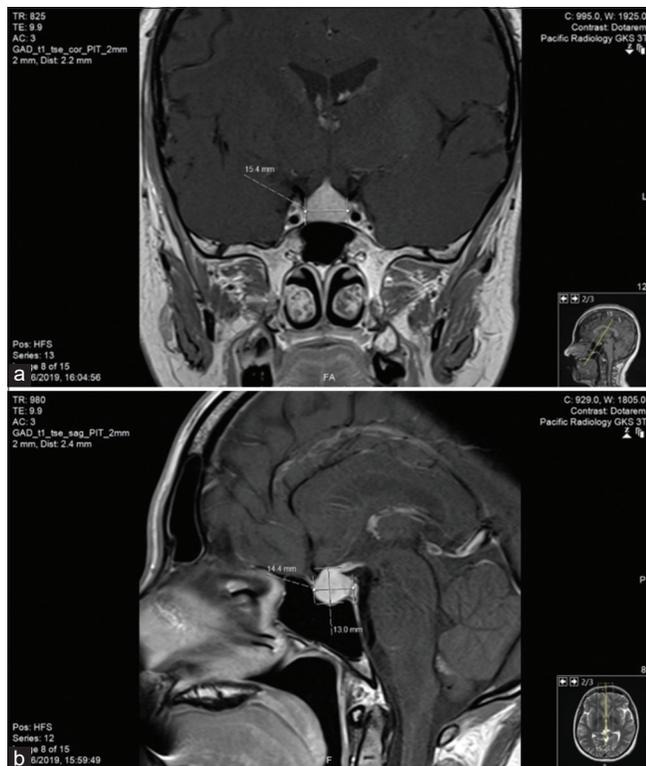
In regard to treatment, it is important to note that no prospective controlled studies exist that have examined the treatment of hypophysitis.<sup>[2]</sup> Current opinion is favoring medical management as the preferred first-line therapy further highlighting the importance of making a correct diagnosis.<sup>[4,7]</sup> Medical therapy is initially based on the use of high-dose corticosteroids followed by a tapering course. The extent and the duration depend on the clinical response.<sup>[2,6]</sup> Appropriate treatment of pituitary hormone deficiencies should also be commenced.<sup>[2]</sup> Immune-modulating drugs such as methotrexate can be considered in patients who have persistent symptoms or relapses after corticosteroid therapy.<sup>[2,6]</sup> Surgical treatment is indicated after failure of medical management in patients with intractable symptoms.<sup>[6]</sup> There are case reports describing the use of Gamma Knife radiosurgery to treat LH, however, there is limited evidence for its use at this stage.<sup>[6]</sup>

**Table 1:** Radiologic scoring system from Gutenberg *et al.*<sup>[4]</sup>

### Scoring system for differentiating autoimmune hypophysitis from nonsecreting pituitary adenoma

Features	Score (if yes)
Age ≤ 30 years	-1
Relation to pregnancy	-4
Pituitary volume (cm <sup>3</sup> ) ≥ 6	+2
Gd enhancement type (medium or high)	-1
Gd enhancement features (heterogeneous)	+1
Asymmetric pituitary gland	+3
Loss of posterior pituitary bright spot	-2
Enlarged stalk size	-5
Mucosal thickening present	+2

A positive score ≥ 1 suggests a diagnosis of adenoma while a score ≤ 0 is indicative of hypophysitis



**Figure 1:** (a and b) MRI imaging of the pituitary lesion in the coronal and sagittal planes.

## CONCLUSION

Our case highlights the difficulty of diagnosing and treating the rare condition of LH. It is important to have a high index of suspicion when presented with patients with intractable headaches, panhypopituitarism, and a sellar mass. Distinguishing LH from a pituitary adenoma is important due to the increasing evidence which suggests that medical management is the preferred first-line option for LH.

## Declaration of patient consent

Patient's consent not required as patients identity is not disclosed or compromised.

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Nil.

## Conflicts of interest

There are no conflicts of interest.

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