

## Autoimmune hypophysitis: A case report

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### ABSTRACT

Autoimmune hypophysitis is an autoimmune inflammation of the pituitary gland. It may result in hypopituitarism depending upon the part of pituitary affected. Here, we report the case of autoimmune hypophysitis in a 30-year-old male who was admitted with complaints of generalised swelling for one month and fever and cough for one week. The patient's Thyroid-stimulating hormone (TSH) was more than 139, anti-thyroid peroxidase antibody (anti-TPO) was more than 1000 and serum sodium was 107 and a tiny streak of tissue along the periphery with an empty sella as seen on MRI. The patient was given tablet Levothyroxine 100 microgram, Telmisartan 40 mg and Hydrocortisone 10mg twice daily. With medications, the patient improved and was discharged.

**Keywords:** Autoimmune hypophysitis, Empty sella, Hypopituitarism.

Autoimmune hypophysitis is a rare disorder that may mimic pituitary adenoma and occurs mostly in women in the peripartum period. Primary hypophysitis is a rare disease. The incidence is estimated to be ~1 in 9 million/year [1] and only a few cases have been reported in men [2]. The symptoms depend on the part of the pituitary affected. Lymphocytic adenohypophysitis (LAH) occurs when the anterior cells are affected by autoimmune inflammation resulting in either hypothyroidism (if TSH producing cells are damaged) or adrenal insufficiency (if ACTH producing cells are affected). Lymphocytic infundibulo neurohypophysitis (LINH) occurs when the posterior pituitary is affected. It is estimated that typically, it takes 12-40 years for autoimmune destruction to present symptoms. Approximately, 80% of patients with pituitary antibodies also have antibodies to thyroid gland or its hormone [3] and 20% of autoimmune thyroid patients have pituitary antibodies [4].

### CASE REPORT

A 30-year-old unmarried male presented with complaints of generalised swelling for one month, with fever and cough for one week. There was a history of lethargy and obstructive sleep apnea (as noticed by family members). There was a past history of recurrent jaundice (for 2-3 times) 10-12 years back. The patient was non-diabetic and the history was not suggestive of any intake of drugs or immunosuppressive agents. There was no history of trauma or any intracranial irradiation.

General examination revealed blood pressure of 170/110 mm Hg and the rest of the vitals were stable. Pedal edema was present with Body Mass Index (BMI) of 32.5. The laboratory investigations were shown in Table 1.

Hyponatremia was corrected by giving 3% sodium chloride solution intravenously along with oral sodium chloride supplementation. For hypothyroidism and hypertension, tablet Levothyroxine 100 microgram and tablet Telmisartan 40mg were given to the patient respectively. The patient was given Tablet Hydrocortisone 10mg twice daily. After therapy, patient improved and was discharged. On follow-up after one and a half month, the patient's blood pressure was 130/90 mm of Hg, thyroid-stimulating hormone was 35 microIU/L and serum sodium was 135 mEq/l. The patient resumes his normal duty.

### DISCUSSION

Autoimmune hypophysitis is a potential cause of secondary empty sella considering that pituitary gland, following the

**Table 1: Laboratory investigations of the patient.**

S. sodium	107mEq/l
Random plasma glucose (RPG)	114 mg/dl
T3	< 0.40mmol/L
T4	<6.00mmol/L
TSH	>139microIU/L
Anti-thyroid peroxidase antibody	>1000IU/L
Creatinine	0.9
Haemoglobin	9.4
Magnetic resonance Imaging Brain	Sella shows CSF collection with tiny streak of tissue along the periphery. Empty sella
Antinuclear antibody	Negative (1:80 dilution)
Haemoglobin typing	Adult Haemoglobin with high A2

initial increase in size, gradually becomes atrophic and fibrotic [5]. Histopathologically, there are five forms of hypophysitis: lymphocytic granulomatous, xanthomatous, IgG4 related and necrotizing. Lymphocytic hypophysitis is the most common form. In the acute phase, it may present as sella or parasellar mass and in the chronic phase, autoimmune hypophysitis may present as an empty sella syndrome. The clinical features of empty sella are headache, hypertension, visual symptoms and hypopituitarism but most of the time it may be asymptomatic.

Biopsy and the histological examination is the only means of accurate diagnosis as no autoantigen has been discovered [6]. However, a biopsy of the pituitary is not easily performed with safety as it sits under the brain. Tests for normal pituitary gland hormone production tend to be expensive and some cases are difficult to administer. In addition, certain hormone levels vary largely throughout the day and in response to metabolic factors making abnormal level difficult to calibrate [7-12]. Furthermore, anti-pituitary antibodies can be expected to be positive in 18% of women during the postpartum period [13].

An autoimmune etiology for lymphocytic hypophysitis was suggested by the presence of pituitary antibodies that may recognize  $\alpha$ -enolase, Growth hormone, the pituitary gland-specific factors 1a and 2 (PGSF1a and PGSF2), regulatory prohormone-processing enzymes commonly produced in the pituitary gland (PC1/3, PC2, CPE and 7B2), secretogranin II, chromosome 14 open reading frame 166 (C14orf166), the corticotroph-specific transcription factor TPIT and chorionic somatomammotrophin (HCS) [14-22]. However, the pathogenic role of these autoantibodies is unclear and they are not specific to hypophysitis. For example, pituitary antibodies were identified by indirect immunofluorescence in ~45% of patients with biopsy-proven hypophysitis, but were also found in the serum of patients with isolated central diabetes insipidus (35%), germinomas (33%), isolated anterior hormone deficiencies (29%), prolactinomas (27%), Rathke's cleft cysts (25%), craniopharyngiomas (17%) nonfunctioning pituitary tumors (13%), GH-secreting pituitary tumors (12%) and healthy subjects (5%) [23,24]. They can also be found in patients with autoimmune endocrine disorders, especially Hashimoto thyroiditis [24].

In the above context, Hashimoto's thyroiditis with incidental finding of empty sella on MRI of the brain may be a differential diagnosis. In the presence of MRI brain suggestive of empty sella with a tiny streak of tissue along the periphery in the sella, the possibility of autoimmune hypophysitis cannot be ruled out as there is no confirmatory test available till date.

Conservative management is recommended for primary hypophysitis unless symptoms are severe and progressive. The only exception to this rule is IgG4-related hypophysitis that – like other manifestations of the disease – should be promptly treated to revert symptoms and prevent fibrosis [25]. The mainstay of treatment is glucocorticoid, which often cause remission of symptoms within a few weeks. A typical starting dose is prednisone 30-40 mg/day (or equivalent), which should be continued for 2-4 weeks, and then tapered gradually over 2-6 months [26].

Hormone deficiencies improved with glucocorticoids only in 15% of patients, while they remained stable or worsened in 70% and 15% of cases, respectively [27]. In glucocorticoid-resistant cases and when high-dose glucocorticoids cause unacceptable side effects, immunosuppressive drugs such as azathioprine, methotrexate, and cyclosporine A have been used successfully [28]. Surgery should be considered only in cases with serious and progressive deficits of the visual field, visual acuity, or nerve paralysis not responsive to medical treatment.

## CONCLUSION

Although autoimmune hypophysitis is a rare disorder, it is being increasingly recognised. In the absence of a surgical emergency, such as impending loss of vision, medical management combined with sequential MRI is preferable. Diagnosis and management will be further improved when a robust immunological diagnostic test becomes available.

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