International Journal of Advances in Medicine
Pallivalappil B et al. Int J Adv Med. 2025 Jan;12(1):124-127
http://www.ijmedicine.com
pISSN 2349-3925 | eISSN 2349-3933

DOI: https://dx.doi.org/10.18203/2349-3933.ijam20243822

Case Report

A rare case of hyponatremia

Bhargavan Pallivalappil[1], Sila Chandran[2]*, Niya Narayanan[3], Anuja Jacob[2]

[1]Department of Medicine, Baby Memorial Hospital, Calicut, Kerala, India
[2]Department of General Medicine, Baby Memorial Hospital, Calicut, Kerala, India
[3]Department of Endocrinology, Baby Memorial Hospital, Calicut, Kerala, India

Received: 15 October 2024
Revised: 25 November 2024
Accepted: 28 November 2024

***Correspondence:**
Dr. Sila Chandran,
E-mail: silachandran273@gmail.com

ABSTRACT

Autoimmune hypophysitis (AH) is a rare inflammatory condition characterized by the immune-mediated destruction of the pituitary gland, leading to pituitary dysfunction. While AH predominantly affects females in their childbearing years, its occurrence in older males, especially at the age of 59, is exceptionally rare. Here, we discuss AH in a middle-aged male who presented with atypical symptoms. A 59-year-old male with no known co-morbidities presented with a 2-week history of headache with retro-orbital pain, accompanied by decreased appetite, fatigue, nausea, vomiting, blurred vision and low-grade fever (for 3 days). The patient also gave a history of hepatitis B infection twenty years ago. On examination, he had icterus, while vital signs and systemic examination were within normal limits. Laboratory investigations revealed elevated C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), unconjugated hyperbilirubinemia, and hyponatremia. Further evaluation of hyponatremia revealed low serum osmolality, increased urine spot sodium, and urine osmolality, suggestive of euvolemic hyponatremia. Hormonal assays indicated low levels of T4, thyroid stimulating hormone (TSH), cortisol, follicle-stimulating hormone (FSH), luteinizing hormone (LH), and testosterone, suggestive of pituitary dysfunction. Magnetic resonance imaging (MRI) of the brain and pituitary gland revealed a bulky pituitary gland with thickening of stalk, suggesting hypophysitis.

Keywords: Autoimmune hypophysitis, Hyponatremia, Head ache, Adenohypophysitis, Lymphocytic panhypophysitis, Lymphocytic infundibuloneurohypophysitis

INTRODUCTION

Autoimmune hypophysitis (AH) is a rare inflammatory condition characterized by immune-mediated destruction of the pituitary gland, leading to pituitary dysfunction.[1] Hypophysitis encompasses various etiologies, including lymphocytic, granulomatous, and xanthomatous subtypes, with lymphocytic hypophysitis being the commonest form.[2]

The exact pathogenesis remains unclear, but it is believed to be an autoimmune reaction targeting pituitary antigens, resulting in glandular inflammation and subsequent hormonal deficiencies.

Clinical manifestations of AH can vary widely, ranging from headache and visual disturbances to symptoms of pituitary hormone deficiencies, such as fatigue, weight loss, and hypogonadism. However, the presentation may be nonspecific, making the diagnosis challenging, especially in older males without predisposing factors or co morbidities.

Given its rarity and diverse clinical presentation, AH often creates diagnostic dilemmas, necessitating a high index of suspicion and a comprehensive diagnostic approach, including hormonal assays, imaging studies (such as magnetic resonance imaging (MRI)), and autoimmune serology. The incidence is reported to be 1 in 7-9 million cases.[1]

In this report, we present a case of AH in a 59-year-old male with no known co-morbidities, underscoring the atypical nature of the condition and emphasizing the importance of considering AH in the differential diagnosis of pituitary disorders, even in uncommon patient scenario.

CASE REPORT

A 59-year-old gentleman presented with a two-week history of holocranial headache with retro-orbital pain, accompanied by decreased appetite, fatigue, nausea, vomiting (2-3 episodes over 1 week), blurred vision and low-grade fever (for 3 days). He had a history of hepatitis B infection twenty years ago. On examination, he had jaundice, while vital signs and systemic examination were unremarkable.

Laboratory investigations revealed elevated C-reactive protein (CRP-89 mg/l [0-5]), erythrocyte sedimentation rate (ESR-51 mm/1st hour [0-20]), unconjugated hyperbilirubinemia (total bilirubin-3.4 mg/dl [0.3-1.2], direct bilirubin-0.86 mg/dl [0-0.2]), and hyponatremia (119 mEq/l [136-145]). Peripheral smear, renal function tests, hepatitis viral markers, abdominal ultrasound, and topical fever workup were all normal. Further evaluation of hyponatremia demonstrated low serum osmolality (239 mOsm/l [290-320]), increased urine spot sodium (42 mEq/l [40-220]) and urine osmolality (337 mOsm/kg [50-1200]). Hormonal assays revealed low levels of thyroid hormones (free T4-0.61 ng/dl [0.56-1.5], TSH-0.40 uIU/ml [0.4-4.5]), cortisol (fasting cortisol-0.5 µg/dl [5-23]), follicle-stimulating hormone (FSH-2.5 mIU/ml [2-12.4]), luteinizing hormone (LH-2.01 mIU/ml [2-8.6]), and testosterone (0.02 ng/ml [2.6-10]) levels suggesting a pituitary dysfunction.

MRI of the brain and pituitary gland demonstrated a bulky pituitary gland without focal or hypoenhancing lesions with enlarged stalk, raising suspicion for autoimmune hypophysitis. Autoimmune workup, including antinuclear antibody (ANA) and immunoglobulin G4 (IgG4) levels, were normal, while antineutrophil cytoplasmic antibodies (ANCA) by indirect immunofluorescence was positive, however MPO and PR-3 by enzyme linked immunosorbent assay (ELISA) were normal.

The patient was initiated on high-dose steroids which was gradually tapered to replacement doses and thyroid hormone supplementation, resulting in symptomatic improvement (no headache or blurred vision) and normalization of sodium (136 mEq/l) and thyroid levels upon follow-up.

This case underscores the diagnostic challenges posed by hypophysitis and the importance of a comprehensive evaluation, including imaging and hormonal assays, to guide appropriate management and to improve clinical outcomes.

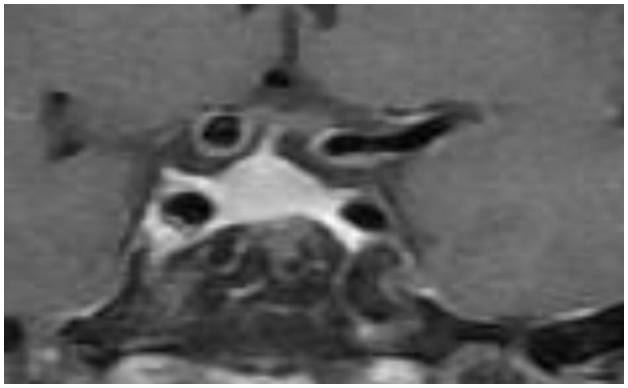

Figure 1: Coronal section T1 weighted post contrast enhancement of MRI brain showing bulky pituitary gland with homogeneous enhancement.

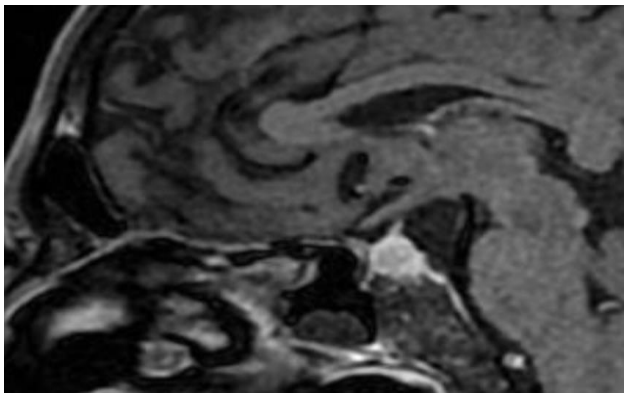

Figure 2: Sagittal section T 1 weighted post contrast image of MRI brain showing enhancement of bulky pituitary and stalk along with mid enhancement of adjacent dura.

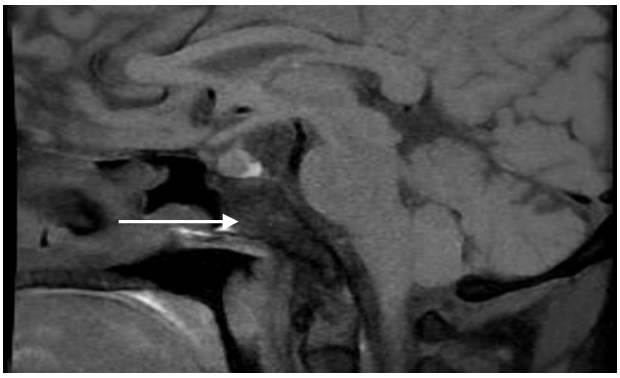

Figure 3: Sagittal section of T1 weighted image of MRI brain showing bright spot representing posterior pituitary.

DISCUSSION

AH presents a complex clinical picture, as illustrated in this case, where the patient exhibits signs of hypopituitarism and symptomatic hyponatremia. The hormonal assays reveal significantly low levels of thyroid hormones, gonadotropins (FSH, LH and testosterone), and

evidence of SIADH. These findings suggest that the anterior pituitary is primarily affected, leading to the symptoms of panhypopituitarism.

MRI findings are pivotal yet often inconclusive in differentiating autoimmune hypophysitis from the more prevalent pituitary adenomas.[3-5] Key MRI features that may suggest AH include symmetrical gland enhancement, absence of erosive changes in the sellar floor, and a homogeneous pituitary mass that enhances post-Gadolinium. In this patient, the MRI revealed a bulky pituitary gland without focal or cystic lesions, aligning with these features. However, it is essential to note that glandular homogeneity is not exclusive to autoimmune hypophysitis; previous studies have shown that some patients can present with cystic appearances.[2]

Endocrine assessment further supports the diagnosis of panhypopituitarism. The patient's symptoms, particularly fatigue linked to hyponatremia, are attributed to inappropriate ADH secretion, highlighting the interconnected nature of anterior and posterior pituitary dysfunction in AH. MRI also shows hyperintensity in the neurohypophysis due to the phospholipid content of neurosecretory granules, complicating the differentiation between the anterior and posterior lobes. This phenomenon, particularly evident in pre-contrast T1-weighted images, underscores the challenge of interpreting imaging results.[6]

Lymphocytic hypophysitis, predominantly affecting females during or shortly after parturition, accounts for a notable subset of AH cases.[7] Although rare in males, its presentation can lead to significant endocrinopathies, often accompanied by circulating pituitary antibodies. Notably, the presence of α-enolase autoantibodies has been associated with this condition, with potential implications for its pathogenesis, particularly in connection with pregnancy.[8,9] The presence of this autoantigen has been reported in other diseases like endometriosis, discoid lupus, and Wegner's granulomatosis.[10]

In clinical practice, it is crucial to exclude other forms of hypophysitis, including granulomatous, xanthomatous, and IgG4-related hypophysitis, as well as other conditions like hemorrhage or infarction. IgG4 remains a strong differential diagnosis, but IgG4 was negative and there were no associated conditions. While histological examination remains the gold standard for diagnosis, the invasive nature of biopsy presents challenges in many cases, as illustrated by this patient.[11] The histological findings of AH typically show infiltration of lymphocytes and plasma cells, which can lead to progressive inflammation and fibrosis, resulting in glandular atrophy.[2] Imaging studies of patients with AH have demonstrated that, over time, a pituitary mass can evolve into an empty sella, reflecting the dynamic nature of this condition.[12]

In this case, the comprehensive assessment indicates that the anterior pituitary is predominantly affected, a classification that can help guide treatment. When both anterior and posterior structures are involved, the terminology shifts to lymphocytic infundib-uloneurohypophysitis or lymphocytic panhypophysitis, underscoring the complexity of AH. In conclusion, AH poses significant diagnostic challenges due to its overlapping features with other conditions. A multidisciplinary approach that includes clinical evaluation, hormonal assessments, neuroimaging, and, when necessary, histological confirmation is essential for accurate diagnosis and effective management. Continued research into the underlying mechanisms and potential biomarkers may enhance our understanding and treatment of this condition in the future.

CONCLUSION

AH is a rare disease. It should be considered with a differential diagnosis of non-secretory pituitary mass with features of LAH, LINH, or LPH. Careful correlation with clinical history and endocrine findings is therefore important for a proper interpretation of MRI findings in AH.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

REFERENCES

1. Yu S, Bethanabatla R, Taha A. A case report of lymphocytic hypophysitis. Surg Neurol Int. 2021;12:263.
2. Caturegli P, Newschaffer C, Olivi A, Pomper MG, Burger PC, Rose NR. Autoimmune Hypophysitis. Endocrine Rev. 2005;26(5):599-614.
3. Faje A. Hypophysitis: Evaluation and management. Clin Diabetes Endocrinol. 2016;2:15.
4. Gutenberg A, Larsen J, Lupi I, Rohde V, Caturegli P. A radiologic score to distinguish autoimmune hypophysitis from nonsecreting pituitary adenoma preoperatively. AJNR Am J Neuroradiol. 2009;30:1766-72.
5. Iuliano SL, Laws ER. The diagnosis and management of lymphocytic hypophysitis. Expert Rev Endocrinol Metab. 2011;6:777-83.
6. Mark LP, Haughton VM. The posterior sella bright spot: a perspective. AJNR Am J Neuroradiol. 1990;11(4):701-2.
7. Yoon JW, Choi DS, Liang HC, Baek HS, Ko IY, Jun HS, et al. Induction of an organ-specific autoimmune disease, lymphocytic hypophysitis, in hamsters by recombinant rubella virus glycoprotein and prevention of disease by neonatal thymectomy. J Virol. 1992;66(2):1210-4.
8. Crock PA. Cytosolic Autoantigens in Lymphocytic Hypophysitis. J Clin Endocrinol Metabolism. 1998;83(2):609-18.
9. O'Dwyer DT, Clifton V, Hall A, Smith R, Robinson PJ, Crock PA. Pituitary autoantibodies in

lymphocytic hypophysitis target both gamma- and alpha-Enolase - a link with pregnancy? Arch Physiol Biochem. 2002;110(1-2):94-8.
10. O'Dwyer DT, Smith AI, Matthew ML, Andronicos NM, Ranson M, Robinson PJ, et al. Identification of the 49-kDa Autoantigen Associated with Lymphocytic Hypophysitis as α-Enolase. J Clin Endocrinol Metabolism. 2002;87(2):752-7.
11. Langlois F, Varlamov EV, Fleseriu M. Hypophysitis, the Growing Spectrum of a Rare Pituitary Disease. J Clin Endocrinol Metabolism. 2021;107(1):10-28.
12. Honegger J, Buchfelder M, Schlaffer S, Droste M, Werner S, Strasburger C, et al. Treatment of Primary Hypophysitis in Germany. J Clin Endocrinol Metabolism. 2015;100(9):3460-9.

Cite this article as: Pallivalappil B, Chandran S, Narayanan N, Jacob A. A rare case of hyponatremia. Int J Adv Med 2025;12:124-7.