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# **Unveiling Hypophysitis: A Case Report of Rare Cause of Central Diabetes Insipidus in a Pediatric Patient**

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# **STATEMENT OF CONTRIBUTION**

The authors collectively contributed to this project with distinct roles and expertise. Bibek Shrestha played a central role in conceptualization, data curation, formal analysis, methodology, project administration, original writing, review, editing, and visualization.Vivek Karn, Priyesh Shrestha, Macchindra Lamichhane, Pradeep Raj Regmi and Dhiraj Adhikari contributed to supervision, validation, and investigations. Each author's contribution was integral to the project's success, ensuring the accuracy and reliability of the findings presented in this work.

# **DISCLOSURE**

None

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None

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# **CONFLICT OF INTEREST**

None

# **PATIENT CONSENT STATEMENT**

Written informed consent was obtained from the patient’s guardian for publication of this case report and accompanying images, complying with the requirements as mentioned in Wiley’s CCR Consent Form.

**Manuscript**

**Type: Case Report**

# **Unveiling Hypophysitis: A Case Report of Rare Cause of Central Diabetes Insipidus in a Pediatric Patient**

# **Key Clinical Message**

Hypophysitis is a rare inflammatory disorder of the pituitary gland, and its association with central diabetes insipidus is even more uncommon, particularly in pediatric patients. This case highlights the diagnostic challenges posed by hypophysitis-related CDI, emphasizing the need for a high index of suspicion in children presenting with polyuria and polydipsia. Magnetic resonance imaging findings, particularly pituitary stalk thickening and absence of the posterior pituitary bright spot, are crucial for diagnosis. The water deprivation test, along with a robust response to vasopressin, helps differentiate CDI from nephrogenic diabetes insipidus and primary polydipsia. Early recognition and management with desmopressin therapy are essential to prevent complications. Additionally, close follow-up is warranted to monitor for potential progression to panhypopituitarism or other endocrine dysfunctions. This case underscores the importance of considering hypophysitis in pediatric CDI and highlights the role of endocrine and imaging evaluations in guiding management.

# **Introduction**

Hypophysitis is an inflammatory condition affecting the pituitary gland, characterized by various subtypes based on etiology, histology, and anatomy [1]. Primary hypophysitis includes lymphocytic, granulomatous, and xanthomatous forms, with lymphocytic being the most common and potentially autoimmune in nature. Secondary hypophysitis can result from surrounding lesions or systemic diseases. It can present with a range of clinical manifestations, including pituitary hormone deficiencies and mass effects. Among these, the involvement of the posterior pituitary leading to central diabetes insipidus (CDI) is extremely uncommon. Clinical presentation may involve compression symptoms, hypopituitarism, diabetes insipidus, or hyperprolactinemia [2]. CDI is a condition characterized by polyuria and polydipsia due to insufficient secretion of vasopressin. Diagnosis involves clinical observation, water deprivation tests, and advanced imaging techniques like Magnetic resonance imaging (MRI) [3]. Hypophysitis is a rare condition, and its association with CDI is even more uncommon [4]. In pediatric patients, the diagnosis of hypophysitis is particularly challenging due to its nonspecific symptoms and overlapping features with other sellar and suprasellar pathologies. Early recognition and appropriate management are crucial in preventing long-term complications [5].

Here we present a case of 7 years old male, with the diagnosis of hypophysitis leading to CDI which is an uncommon association. It underscores the importance of considering hypophysitis in the differential diagnosis of CDI, emphasizing the role of endocrine evaluation and imaging in early diagnosis and management.

# **Case History/Examination**

A 7-years old, male child, previously healthy, presented with a one-month history of increased thirst and excessive urination. The patient reported polydipsia, with frequent episodes of drinking water even during the night, accompanied by polyuria characterized by increased frequency and volume of urination, occurring approximately 5–10 minutes after fluid intake. Nocturia was also reported during this period. Notably, there were no associated symptoms of polyphagia or increased appetite. The patient denied any history of head trauma, headaches, vomiting, photophobia, dizziness, or visual disturbances. Additionally, there was no reported use of diuretics or other medications. Symptoms such as myalgia, tingling sensations, or other neurological complaints were absent. A systematic review of the cardiovascular, neurological, and genitourinary systems revealed no significant findings. On examinations, the patient was conscious, alert, and oriented to time, place, and person, with intact memory and a non-irritable. There were no signs of pallor, icterus, clubbing, cyanosis, edema, lymphadenopathy, or dehydration. The patient’s vital signs were within normal limits: temperature 97°F, heart rate 120 beats per minute, respiratory rate 18 breaths per minute, blood pressure 120/80 mmHg, and capillary refill time of less than 3 seconds. Neurological examination revealed a Glasgow Coma Scale (GCS) score of 15/15, with bilaterally equal and reactive pupils. The patient demonstrated a normal gait. Motor power, reflexes, and sensory function in both the upper and lower limbs were intact. Examinations of the respiratory, gastrointestinal, and cardiovascular systems revealed no abnormalities, with findings within normal limits.

# **Methods**

Based on history and examination, several differential diagnoses were considered. These include diabetes insipidus (central or nephrogenic), psychogenic polydipsia, diabetes mellitus, renal tubular disorders, hypercalcemia, hypokalemia, chronic kidney disease with impaired urinary concentrating ability and adrenal insufficiency. These potential diagnoses were formulated based on the patient’s symptoms of polydipsia, polyuria, and nocturia, along with the absence of significant systemic findings during the examination. The laboratory investigations revealed a serum sodium level of 140 mmol/L (normal: 135–145 mmol/L) and a serum potassium level of 3.8 mmol/L (normal: 3.5–5.0 mmol/L), both within normal limits. The urine creatinine was 2.0 mg/dL (reference: 20–320 mg/dL for 24-hour urine), with a spot urine creatinine of 44 mg/dL. Urine culture was sterile, and the urine specific gravity was 1.005 (normal: 1.010–1.030), indicating dilute urine. The urine osmolality was 513 mOsm/kg (normal: 300–900 mOsm/kg), while the serum osmolality was 294 mOsm/kg (normal: 275–295 mOsm/kg). Thyroid function tests showed a T3 level of 4.98 pmol/L (normal: 3.1–6.8 pmol/L), T4 level of 11.87 pmol/L (normal: 10–22 pmol/L), and TSH level of 4.059 µIU/mL (normal: 0.5–4.5 µIU/mL), all within normal limits. The cortisol level was 8.7 µg/dL (reference: 10–20 µg/dL in the morning), which was low if measured in the morning. Gonadotropin levels were markedly low, with an LH level of 0.00 mIU/mL (normal: 0.7–7.9 mIU/mL) and an FSH level of 0.17 mIU/mL (normal: 1.5–12.4 mIU/mL). The water deprivation test revealed the patient’s inability to concentrate on urine despite dehydration, with a low urine osmolality of 68 mOsm/kg at baseline. Following vasopressin administration, urine osmolality increased significantly from 155.8 mOsm/kg to 513 mOsm/kg, accompanied by a marked reduction in urine output. This robust response confirms a deficiency in endogenous vasopressin production, consistent with a diagnosis of CDI. The results exclude nephrogenic diabetes insipidus and primary polydipsia, as the kidneys effectively responded to exogenous vasopressin. (Table 1) Contrast-enhanced MRI of the brain revealed a pituitary gland of normal size, measuring 7 × 13 × 4.4 mm. However, the characteristic T1-weighted posterior pituitary bright spot was absent. Additionally, there was symmetrical enhancing thickening of the pituitary infundibulum. (Figure 1, 2, 3) These imaging findings were consistent with hypophysitis, suggesting inflammatory involvement of the hypothalamic-pituitary axis.

# **Conclusion and Results**

Following, clinical history, examination and investigations including radiological investigation confirmed the diagnosis of CDI secondary to hypophysitis. For the management of central diabetes insipidus, the patient was initially started on intravenous vasopressin at a dose of 1 mcg twice daily, which was subsequently transitioned to the subcutaneous route. Throughout the treatment course, vital signs and serum electrolyte levels were closely monitored and remained within normal limits. After two days of subcutaneous desmopressin therapy, the patient was transitioned to oral desmopressin at a dose of 0.05 mg four times daily. The patient remained clinically stable and was subsequently discharged with a follow-up plan to monitor for potential complications of hypophysitis, as well as weekly sodium and potassium assessments. During the weekly follow-up over one month, the patient maintained a stable clinical condition with no recurrence of symptoms or treatment-related complications.

# **Discussion**

Hypophysitis is a rare inflammatory condition of the pituitary gland that can lead to varying degrees of pituitary dysfunction. It is classified into primary and secondary forms, with autoimmune causes being the most common. Patients typically present with headaches, pituitary dysfunction, and gland enlargement [6]. Diabetes insipidus (DI) is a water imbalance disorder characterized by polyuria and polydipsia. There are four main types of DI: central, nephrogenic, gestational, and dipsogenic. Central DI results from insufficient antidiuretic hormone (ADH) production, while nephrogenic DI is caused by kidney resistance to ADH [7,8]. CDI is a condition characterized by polyuria and polydipsia, resulting from impaired synthesis or secretion of arginine vasopressin (AVP) in the hypothalamic-neurohypophysis system [9]. Common causes include germinomas, craniopharyngiomas, Langerhans cell histiocytosis, autoimmune disorders, trauma, and rarely, genetic defects. Diagnosis involves clinical observation, laboratory tests, and MRI, which can reveal pituitary hyperintensity and changes in pituitary stalk shape and size [10]. In this case patient had polydipsia, with frequent episodes of drinking water even during the night, accompanied by polyuria characterized by increased frequency and volume of urination, occurring approximately 5–10 minutes after fluid intake. Nocturia was also reported during this period. Diagnosis involves differentiating CDI from nephrogenic diabetes insipidus and primary polydipsia [11]. The water deprivation test is the gold standard, but it has interpretative challenges [12]. Radiological investigation plays a crucial role in diagnosing CDI. Computed tomography (CT) can reveal modifications in the hypothalamic-pituitary region, including small, round, isodense masses that enhance with contrast. However, MRI has become the preferred method due to its superior resolution and ability to differentiate between anterior and posterior pituitary lobes [13]. Hypophysitis is a rare condition, and its association with CDI is even more uncommon [5]. Radiological investigation is crucial for diagnosis, with key MRI features including diffuse, modest pituitary enlargement, homogeneous enhancement, and possible stalk thickening [14]. Differential diagnosis is important, as various neoplastic and non-neoplastic lesions can mimic hypophysitis [15]. The differential diagnosis of CDI includes nephrogenic diabetes insipidus, psychogenic polydipsia, and endocrinopathies such as adrenal insufficiency and diabetes mellitus. The water deprivation test and response to vasopressin administration play a crucial role in confirming CDI and differentiating it from nephrogenic causes. In this case, the patient’s marked improvement in urine concentration following vasopressin administration confirmed central rather than nephrogenic DI. Also, CE MRI of the brain revealed a pituitary gland of normal size, measuring 7 × 13 × 4.4 mm and the characteristic T1-weighted posterior pituitary bright spot was absent with symmetrical enhancing thickening.

Treatment primarily involves desmopressin (dDAVP) administration and free water replacement. Oral dDAVP has become the preferred long-term treatment option over other formulations. While intranasal administration is common, subcutaneous DDAVP has shown promise in infants and children, maintaining serum sodium levels within a narrower range compared to intranasal deliver [16,17]. Vasopressin administration is associated with hyponatremia, and this effect is due to its antidiuretic activity via renal V2 receptors, leading to free water reabsorption [18]. In our case, subcutaneous desmopressin was started and later, it was changed to oral for long term treatment along with weekly sodium monitoring. This case underscores the importance of recognizing hypophysitis as a rare yet significant cause of CDI in pediatric patients, emphasizing the role of early imaging, endocrine evaluation, and appropriate therapeutic intervention in ensuring favorable outcomes.

# **List of Figures**

1. Figure 1: Contrast enhanced Magnetic Resonance Imaging Sagittal view showing symmetrical enhanced thickening of infundibulum with loss of pituitary bright spot.
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1. Table 1: Water Deprivation Test Result Interpretation

# **Declarations**

1. Ethics approval and consent to participate: The Institutional Review Board of the Institute of Medicine, Nepal, does not mandate ethical approval for the writing or publication of case reports, and patient consent was obtained. Informed written consent was obtained from the patient before writing this case report.
2. Consent for publication: Written informed consent was obtained from the patient’s guardian for publication of this case report and accompanying images, complying with the requirements as mentioned in Wiley’s CCR Consent Form.
3. Availability of data and materials: The datasets used and/or analyzed during the current study are available from the corresponding author upon reasonable request.
4. Competing interests: None
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