RESEARCH PAPER

Rare Cause of Severe Hyponatremia presenting with Seizure

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ABSTRACT

We report a 33-year-old female, a known case of hypothyroidism, who presented to the emergency department with a history of one episode of seizure a day prior. On presentation, patient was drowsy and confused with a GCS of E2V2M5, with global hypotonia, but preserved reflexes. On further questioning, relatives gave history of episodes of hypotension once every few months, and further a history of postpartum hemorrhage (PPH) following her second delivery 12 years ago, following which patient developed absence of lactation and subsequent amenorrhea. Laboratory investigations confirmed severe hyponatraemia (serum Na^+ 107 mEq/L), profoundly low thyroid hormones (Free T3 <1.07, Free T4 <0.4) with an inappropriately normal TSH (1.37 mIU/L), and low prolactin (2.69 ng/mL), pointing towards central hypothyroidism. MRI Pituitary revealed a partially empty sella with flattening of the pituitary gland, consistent with Sheehan's Syndrome. Management with hydrocortisone, thyroxine and sex hormone replacement led to significant clinical improvement.

Keywords: Sheehan's Syndrome, Hypopituitarism, Hyponatraemia, Seizure, Hypocortisolism, Central Hypothyroidism, Empty Sella, Postpartum Haemorrhage

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INTRODUCTION

Sheehan's Syndrome was first described by Harold Leeming Sheehan in 1937. [1] It is a well-recognized, but overlooked cause of hypopituitarism resulting from pituitary necrosis following severe PPH. The enlarged, hyper-vascular pituitary gland of pregnancy becomes particularly vulnerable to ischaemia during this period of hemorhhagic shock.

Sheehan's Syndrome often remains a diagnostic challenge due to its insidious onset and highly variable presentation. Clinical features range from failure of lactation and amenorrhoea in the immediate postpartum period, to hypothyroidism and hyponatremia. The hypothyroidism may manifest years to decades later, often leading to misdiagnosis or significant diagnostic delay.

Seizures as the presenting manifestation of Sheehan's Syndrome, secondary to severe hyponatraemia driven by concurrent hypocortisolism and central hypothyroidism, represent an uncommon and diagnostically challenging presentation. This case report aims to highlight the importance of recognizing Sheehan's Syndrome in women with a remote history of PPH presenting with neurological manifestations.

CASE REPORT

A 33-year-old female presented to the emergency department with one episode of tonic posturing of bilateral

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upper and lower limbs that had occurred a day prior, which lasted for 20–30 minutes. The episode was associated with up-rolling of eyeballs, clenching of teeth, and a tongue bite. On arrival, the patient was in a drowsy state with a GCS of E2V2M5 with intermittent minimal response. There was no history of fever, headache, trauma, or prior seizure episodes in the past.

Recent History

Three days prior to the current presentation, the patient had been admitted to an outside hospital for complaints of giddiness and was found to have low blood pressure. She was managed with intravenous fluids and salt capsules, but had waxing and waning levels of consciousness during the stay. On the second day of that admission, she developed the seizure episode and was referred to the tertiary centre for further evaluation and management.

Obstetric and Gynaecological History

The patient has two children, both delivered via normal vaginal delivery. The first pregnancy was uneventful; however, she developed postpartum haemorrhage (PPH) in her second delivery. After this event, the patient noted complete absence of lactation and subsequently developed amenorrhoea, which has persisted for the last 12 years. A few months after the PPH, she was diagnosed with hypothyroidism and was started on thyroxine tablet (25 mcg once daily). The patient also gives a history of multiple hospital admissions in last 12 years in view of hypotension.

On Examination

The patient was drowsy, responding to some verbal commands, but in a state of confusion. Vital signs: blood pressure 90/60 mmHg, pulse rate 92/min, SpO_2 98% on room air. On general examination, facial puffiness was present, along with mild non-pitting pedal oedema. There was pallor, but no icterus, cyanosis, clubbing, or lymphadenopathy. Cardiovascular examination: First and second heart sounds normal. Respiratory examination: bilateral vesicular breath sounds. Per-abdominal examination: soft, non-tender, no organomegaly. CNS examination: GCS E2V2M5, drowsy and confused. Detailed motor examination could not be performed as patient was unable to follow commands; however, global hypotonia was noted in all four limbs with normal reflexes and down-going plantars.

Provisional Diagnosis

Seizure secondary to hyponatraemia under evaluation, in a known case of hypothyroidism, secondary to probable Sheehan's Syndrome.

Investigations

Significant laboratory and radiological investigations are summarized in Table 1 and Table 2, respectively.

Table 1 – Laboratory Investigations

Parameter	Value	Reference Range
Haemoglobin	10.0 g/dL	11.6–15.0 g/dL
TLC	5,900 / µL	4,000–10,000 / µL
Platelets	1,81,000 / µL	1.5–4.1 lakhs / µL
MCV	81.5 fL	80–100 fL
Serum Na^+ / K^+ / Cl^-	**107 / 3.33 / 75.6 mEq/L**	136–145 / 3.5–5.1 / 98–107 mEq/L
Urinary Na^+ / K^+ / Cl^-	67.6 / 41.2 / 80.7 mEq/L	—
Serum Osmolality	**219 mOsm/kg**	275–300 mOsm/kg
Urine Osmolality	**209.7 mOsm/kg**	300–900 mOsm/kg
FeNa	**5.3%**	1-2 %
Urea / Creatinine	18 / 0.97 mg/dL	17–49 / 0.6–1.2 mg/dL
Total / Direct Bilirubin	1.0 / 0.3 mg/dL	<1.2 / <0.5 mg/dL
SGOT / SGPT / ALP	**170** / 33 / 83 U/L	8–43 / 7–45 / 35–104 U/L
Total Proteins / S. Albumin	6.9 / 4.0 g/dL	6.4–8.3 / 3.5–5.2 g/dL
Urine Routine Microscopy	Normal; Proteins: Absent	—
NT-Pro BNP	229.8 pg/mL	<125 pg/mL
Ca / Mg / PO_4	9 / 2.25 / 2.4 mg/dL	8.6–10.2 / 1.6–2.6 / 2.4–5.1 mg/dL
Vitamin D	20.7 ng/mL	20–50 ng/mL
Serum Cortisol (12pm)	0.7 µg/dL	3.7 – 19.4 µg/dL
T3 / T4 / TSH	**0.30 / 0.91** / 1.37	0.64–1.52 ng/dL / 4.87–11.72 µg/dL / 0.35–4.94 mIU/L
Free T3 / Free T4	**<1.07 / <0.4**	1.71–3.71 pg/mL / 0.70–1.48 ng/dL
Serum Renin / Aldosterone	**2.3** µIU/ml / 2.43 ng/dL	2.8-39.9 µIU/ml / 1.17 – 23.6 ng/dL
LH / FSH	2.39 / 5.83 mIU/mL	—
AMH	1.13 ng/mL	—
Prolactin	**2.69 ng/mL**	2–29 ng/mL
ANA Blot / ANA IF	Negative	Negative

Table 2 – Radiological Investigations

Modality	Findings
ECG	Low voltage complexes with T-wave inversions in V1–V4 [Figure 1]
Chest X-ray	No abnormality detected; no evidence of pleural effusion or cardiomegaly
MRI Pituitary	**Sella turcica is partially filled with CSF signal, with resultant flattening of the pituitary gland — features consistent with partially empty sella** [Figure 2 & 3]
USG Abdomen + Pelvis	Small-sized uterus 54 × 27 × 37 mm (CC × AP × TR); bilateral ovaries — Right 5 cc, Left 4 cc; mild free fluid in pouch of Douglas
USG Neck	Small spongiform nodule in the left lobe of thyroid — TI-RADS 2; few subcentimetric lymph nodes bilaterally

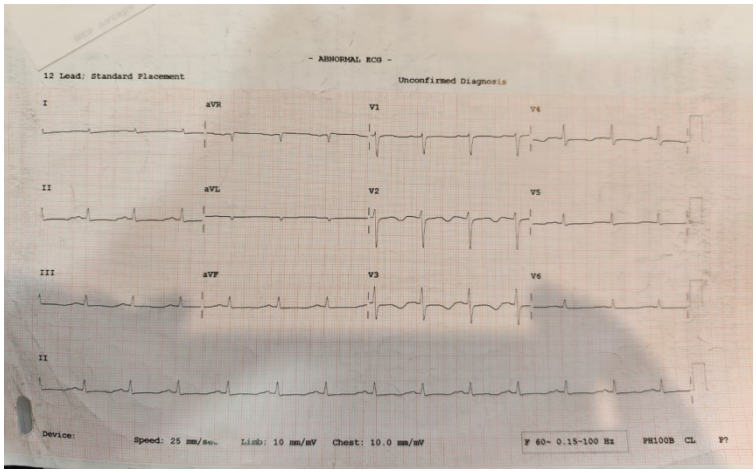


Figure 1 – ECG showing low voltage complexes and T-wave inversions in V1–V4

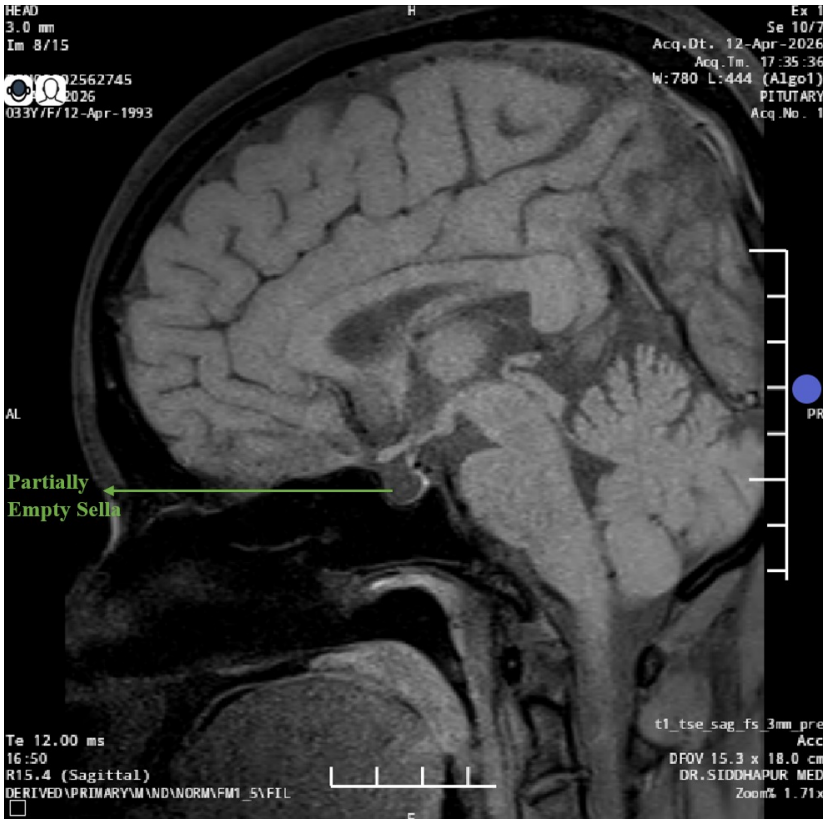


Figure 2 – MRI Pituitary (Sagittal Axis) showing partially empty sella

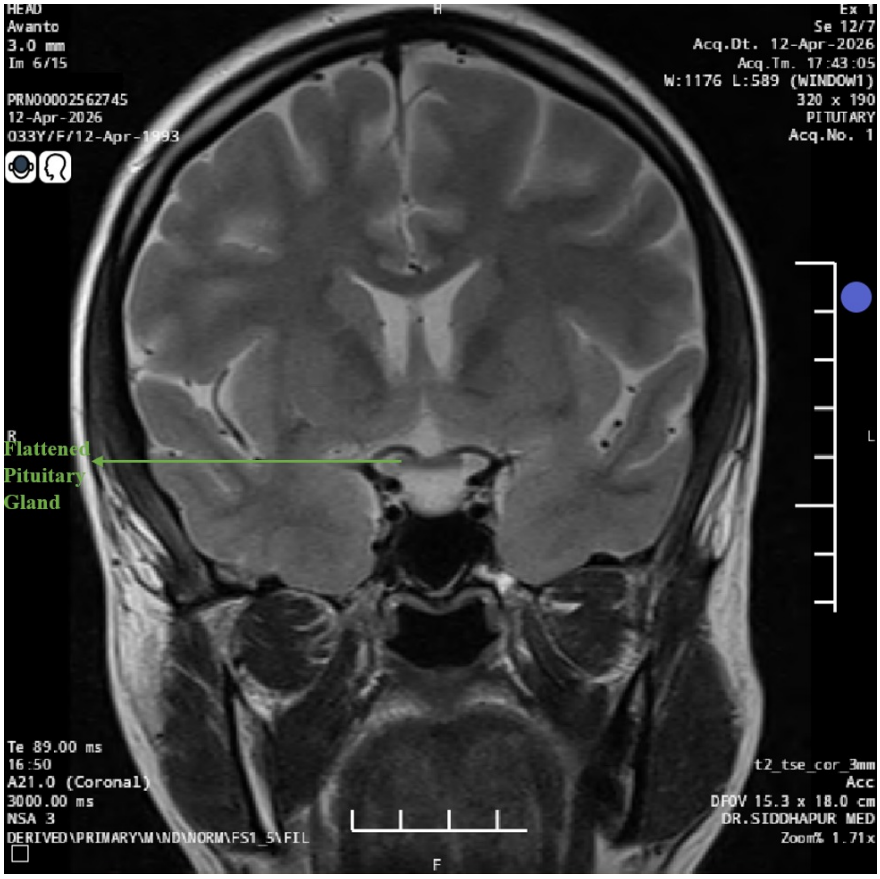
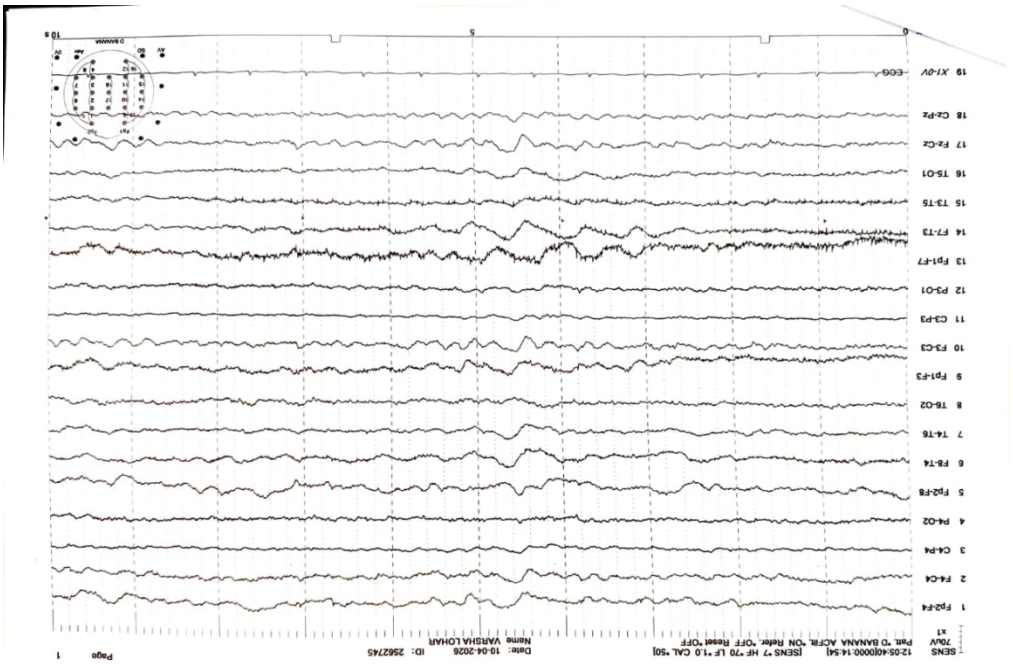


Figure 3 – MRI Pituitary (Coronal Axis) showing flattening of the pituitary gland

EEG Findings



[Figure 4] EEG revealed generalized delta-to-theta range slowing, suggestive of encephalopathy. No epileptiform activity was noted.

Final Diagnosis

Based on the clinical history of PPH following the second delivery, subsequent absence of lactation and amenorrhoea, longstanding hypothyroidism on sub-therapeutic replacement, recurrent admissions for hypotension, and the current presentation with seizures

secondary to profound hyponatraemia — along with laboratory evidence of central hypothyroidism (low FT3, low FT4 with inappropriately normal TSH), low prolactin (2.69 ng/mL), low-norcammal gonadotrophins with an atrophic uterus and small ovaries on USG, and MRI findings of a partially empty sella, Sheehan's Syndrome was diagnosed.

Final diagnosis was:

Seizure secondary to Hyponatraemia, secondary to Hypocortisolism and Hypothyroidism, secondary to Panhypopituitarism due to Sheehan's Syndrome.

Treatment Given in Hospital
Management was initiated in a stepwise, multi-disciplinary manner involving endocrinology and neurology:

Endocrinology (Initial Consultation):
- Tab. Thyroxine 100 mcg — once daily
- Inj. Hydrocortisone 100 mg — QID (stress dosing)

Neurology Consultation:
- Correction of metabolic/electrolyte parameters
- EEG performed
- Inj. Levetiracetam 500 mg IV — 1-0-1 (continued)

Endocrinology (Subsequent Review — Provisional Diagnosis of Panhypopituitarism):
- Withhold Inj. Hydrocortisone; transition to physiological replacement
- Tab. Hydrocortisone 10 mg — 1-1-0
- Tab. Estradiol Valerate 2 mg — 0-0-1 (Day 1 – 21 of each menstrual cycle)
- Tab. Medroxyprogesterone 10 mg — 1-0-1 (Day 12 – 21 of each menstrual cycle)

Full In-Hospital Regimen:
- Tab. Tolvaptan 15 mg — 1-0-0 × 2 days
- Salt capsules — 1-1-1 × 2 days

Followed by
- Inj. Hydrocortisone 50 mg QID → TID → Tab. Hydrocortisone 10 mg 1-1-0
- Tab. Estradiol Valerate 2 mg — 0-0-1
- Tab. Medroxyprogesterone 10 mg — 1-0-1
- Inj. Levetiracetam 500 mg IV — 1-0-1
- Tab. Calcium 500 mg — 0-1-1

DISCUSSION
Sheehan's Syndrome remains one of the most common causes of hypopituitarism in developing countries, where obstetric haemorrhage and inadequate peripartum care continue to pose significant clinical challenges. The condition arises from ischaemic necrosis of the anterior pituitary due to hypotension and vascular spasm during massive PPH. The clinical spectrum ranges from isolated hormone deficiency to panhypopituitarism, depending on the degree of pituitary involvement. [2] [3]

In our patient, failure of lactation immediately post-delivery and subsequent amenorrhoea were the first indicators of pituitary insufficiency, suggestive of affection of prolactin and gonadotrophin axes respectively. Despite these early warning signs, the patient was not evaluated further since 12 years despite history of hypothyroidism and recurrent hypotensive episodes, underscoring the profound diagnostic delays fairly evident in such cases. [4]

The presenting manifestation — seizure episode secondary to severe hyponatraemia (Na^+ 107 mEq/L) — was possibly driven by hypocortisolism and hypothyroidism. In hypocortisolism, the loss of cortisol-mediated suppression of ADH leads to a syndrome of inappropriate antidiuresis (SIADH-like picture), causing dilutional hyponatraemia. [5] Severe hypothyroidism independently contributes to hyponatraemia through reduced GFR and increased ADH activity. [6] The hypo-osmolar hyponatraemia, with urine osmolality inappropriately elevated relative to serum osmolality, and elevated FeNa of 5.3% — was consistent with the euvolaemic hyponatraemia picture. [7]

The laboratory findings were diagnostic of central (secondary) hypothyroidism: profoundly low FT3 (<1.07 pg/mL) and FT4 (<0.4 ng/dL) with a normal-range TSH (1.37 mIU/L). In primary hypothyroidism, TSH would be markedly elevated; the "normal" TSH in the setting of low thyroid hormones is the hallmark of hypothalamo-pituitary axis insufficiency and must not be misinterpreted as euthyroidism. This distinction is critical, as sub-therapeutic thyroxine replacement without cortisol replacement can precipitate an adrenal crisis. The prior under-treatment of hypothyroidism without pituitary axis investigation had likely contributed to recurrent symptomatic hypotension and the current hyponatraemic crisis.

The MRI finding of a partially empty sella with flattening of the pituitary gland confirmed Sheehan's Syndrome as the underlying aetiology. Low prolactin (2.69 ng/mL), low-normal LH/FSH, and an atrophic uterus with small-volume bilateral ovaries on USG further corroborated the diagnosis of panhypopituitarism. [3] The ECG finding of low voltage complexes with T-wave inversions in V1–V4 is consistent with hypothyroidism-related metabolic cardiomyopathy, a well-recognized but often overlooked manifestation of severe thyroid hormone deficiency. [8]

Management of Sheehan's Syndrome-related adrenal crisis requires glucocorticoid replacement as the priority, before initiating thyroid hormone replacement. Administering thyroxine without adequate cortisol replacement can precipitate adrenal crisis by accelerating the cortisol metabolism. [9] Intravenous hydrocortisone was intiated at 50 mg QID, with stepwise de-escalation to physiological oral replacement. Tolvaptan, a selective vasopressin V2-receptor antagonist, was used in the early stage for acute management of severe hyponatraemia effectively over two days. Sex hormone replacement with estradiol valerate and

medroxyprogesterone addressed the gonadotrophin deficiency component. [10]

CLINICAL IMPLICATIONS

- Sheehan's Syndrome should be suspected in any female with a history of PPH presenting with hyponatraemia, hypotension, or unexplained neurological manifestations — even years after the inciting event.
- Seizures in women with known hypothyroidism and a history of PPH should trigger a systematic diagnostic workup for pituitary insufficiency, including basal cortisol, pituitary hormone panel, and MRI pituitary.
- A normal TSH in the presence of low thyroid hormones should be further evaluated for the pituitary axis issues rather than labelling it as euthyroidism.
- In panhypopituitarism, glucocorticoid replacement must always precede thyroid hormone replacement to prevent adrenal crisis.

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