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Case Report

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Unconfounded triphasic ADH response following intracranial hemorrhage: evolution from diabetes insipidus to SIADH

Abstract

Background: Triphasic dysregulation of antidiuretic hormone (ADH), characterized by an initial diabetes insipidus (DI) phase followed by syndrome of inappropriate antidiuretic hormone secretion (SIADH) and subsequent normalization, is classically described in pituitary and neurosurgical settings but is rarely documented in spontaneous intracranial haemorrhage.

Case: A 58-year-old female with chronic kidney disease and recent coronary artery bypass grafting on anticoagulation presented with intracranial haemorrhage complicated by obstructive hydrocephalus requiring external ventricular drainage. She initially developed hypernatremia (165 mmol/L) with elevated serum osmolality (363 mOsm/kg), reduced urine osmolality (178 mOsm/kg) consistent with central diabetes insipidus. This was followed by a transition phase and subsequent hyponatremia (121 mmol/L) with elevated urine sodium and osmolality, fulfilling diagnostic criteria for SIADH. Notably, only a single dose of desmopressin was administered during the clinical course. The clinical course was complicated by thrombotic manifestations with antiphospholipid antibody positivity, for which intravenous immunoglobulin (IVIG) was administered. Biochemical findings and response to fluid restriction supported true SIADH rather than IVIG-related pseudohyponatremia.

Conclusion: This case demonstrates a complete triphasic ADH response in spontaneous intracranial haemorrhage without therapeutic confounding. It highlights the importance of dynamic sodium monitoring, careful phase recognition, and avoidance of misinterpretation due to treatment-related artefacts.

Keywords: intracranial hemorrhage, siadh, diabetes insipidus, hypernatremia, hyponatremia, antiphospholipid syndrome, neurocritical care

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Introduction

Sodium disturbances are frequently encountered in patients with acute neurological injury and are associated with increased morbidity and mortality. These abnormalities typically arise from dysregulation of antidiuretic hormone (ADH), manifesting as diabetes insipidus (DI), syndrome of inappropriate antidiuretic hormone secretion (SIADH), or cerebral salt wasting.

The triphasic ADH response, characterized by an initial polyuric phase due to ADH deficiency, followed by inappropriate ADH secretion and eventual recovery, is well described in neurosurgical and pituitary disorders but is infrequently reported in spontaneous intracranial hemorrhage. However, documentation of a complete triphasic response in spontaneous intracranial haemorrhage without therapeutic confounding remains rare.

Case description

A 58-year-old female with hypertension, type 2 diabetes mellitus, chronic kidney disease (stage 3a), and recent coronary artery bypass grafting presented with intracranial hemorrhage while on anticoagulation. Initial CT imaging revealed posterior fossa hemorrhage with obstructive hydrocephalus. On admission, GCS was E4V4M6. Serum sodium was 165 mmol/L with serum osmolality of 363 mOsm/kg, urine osmolality 178 mOsm/kg. There was no significant hyperglycemia. Due to worsening sensorium, an external ventricular drain (EVD) was placed with post-procedure imaging demonstrating decompression. The combination of marked hypernatremia, elevated serum osmolality, increased urine output and inappropriately low urine concentration and urine osmolality in the absence of hyperglycemia or osmotic diuresis supported a diagnosis of central diabetes insipidus. Fluid management and single dose of desmopressin was administered during the early DI phase. There was no prolonged exposure to desmopressin, mannitol, or glucocorticoids during this period that could have significantly confounded the evolution of sodium disturbances.

Over subsequent days, serum sodium gradually declined, representing a transition phase. This was followed by hyponatremia with a nadir of 121 mmol/L, serum osmolality 262 mOsm/kg. Urine sodium was 109 mmol/L and urine osmolality was 352 mOsm/kg, consistent with SIADH. The patient was managed with fluid restriction and tolvaptan.

During hospitalization, the patient developed digital ischemia with features of dry gangrene. Evaluation revealed antiphospholipid antibody positivity and a left ventricular thrombus. These findings were consistent with antiphospholipid syndrome and added complexity to overall management but were not directly implicated in the observed ADH dysregulation. Intravenous immunoglobulin was administered (1st dose- 12.3.26 and last dose 17.3.26). The patient remains hospitalized with poor neurological recovery but stable hemodynamics. (Figure 1&2)

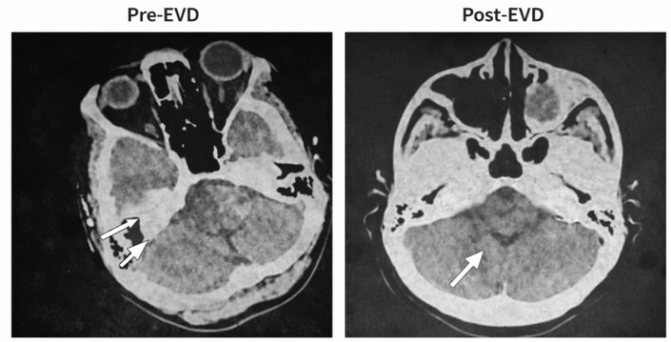
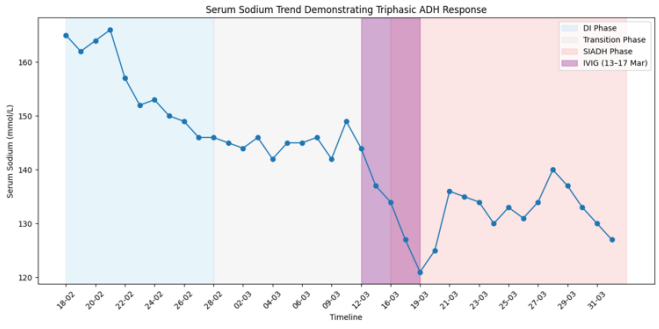


Figure 1 – CT Brain- Axial CT brain showing posterior fossa edema with fourth ventricular effacement (A) and decompression after EVD placement (B).



COMPARISON OF TRANSIENT CENTRAL DI PHASE AND SIADH PHASE

PARAMETER	TRANSIENT CENTRAL DI PHASE (Diabetes Insipidus Phase)	SIADH PHASE (Syndrome of Inappropriate ADH Secretion)
Serum sodium (mEq/L)	165	121
Serum osmolality (mOsm/kg)	363	262
Urine output (mL/day)	1560–1663	850–1000
Urine osmolality (mOsm/kg)	178	352
Urine specific gravity	1.004	1.012
Urine sodium (mEq/L)	Not done	109

Central DI Phase (Transient)
- Hypernatremia
- Hyperosmolality
- High urine output
- Dilute urine (low osmolality, low specific gravity)

SIADH Phase
- Hyponatremia
- Low osmolality
- Normal to mildly increased urine output
- Concentrated urine (high osmolality, higher specific gravity)
- High urine sodium

Figure 2 – Sodium Trend- Serial serum sodium trend demonstrating hypernatremia, transition phase, and SIADH phase

Discussion

This case demonstrates a complete and unconfounded triphasic dysregulation of antidiuretic hormone following spontaneous intracranial haemorrhage. While this phenomenon is well described in pituitary and postoperative neurosurgical settings, its occurrence in spontaneous intracranial pathology without exogenous ADH manipulation is rarely documented. The triphasic pattern — comprising an initial polyuric DI phase, an antidiuretic SIADH phase, and subsequent normalization — was first systematically described in the context of pituitary surgery by Verbalis and colleagues, and has since been recognized as a hallmark of hypothalamo-neurohypophyseal axis injury.[1,2] More recent series and case reports have confirmed its occurrence in diverse neurocritical settings, though documentation in spontaneous intracranial haemorrhage without therapeutic confounding remains exceedingly rare.[3,4] A key strength of this case is the minimal therapeutic confounding, as only a single dose of desmopressin was administered and there was no prolonged ADH-directed therapy or osmotic agent exposure, which are frequently present in previously reported cases and may obscure the natural evolution of ADH physiology.[1,3] This allowed clear delineation of the transition from diabetes insipidus to SIADH based on biochemical parameters and clinical response.

Hypernatremia phase (Central Diabetes Insipidus Physiology) - The initial presentation with severe hypernatremia (serum sodium 165 mmol/L) and elevated serum osmolality (363 mOsm/kg) is consistent with central diabetes insipidus (DI). This likely reflects impaired ADH secretion due to disruption of the hypothalamic–neurohypophyseal axis following acute brain injury. Similar disturbances have been reported in neurocritical care, particularly in association with elevated intracranial pressure and posterior fossa involvement.[5-7] Experimental and clinical studies have demonstrated that hypothalamic injury, raised intracranial pressure, and neurosurgical manipulation can precipitate transient or partial central DI through disruption of vasopressin synthesis and release pathways.[8,9] In the triphasic model, this first phase corresponds to acute axonal injury of the posterior pituitary stalk, with cessation of vasopressin release into the systemic circulation; clinical DI ensues within hours to days of the inciting insult.[1,2,10]

Transition phase - The gradual reduction in serum sodium represents an intermediate transitional phase, likely corresponding to partial recovery of ADH secretion or intermittent release of stored hormone from degenerating posterior pituitary neurons. Although described in hypothalamic injury, this phase is often under-recognized in clinical practice.[7,11] Similar transitional physiology has been described in triphasic responses after pituitary injury and reflects degeneration-induced release of stored vasopressin followed by temporary recovery.[9,12] Robertson and colleagues proposed that this second phase results from uncontrolled leakage of preformed vasopressin from degenerating axon terminals, a mechanism that has been corroborated by subsequent histopathological and clinical studies.[1,13] The duration of this antidiuretic phase is variable and may be brief, underscoring the need for vigilant monitoring to avoid iatrogenic hyponatremia during this window.[2,3]

SIADH Phase - The subsequent development of hyponatremia, accompanied by elevated urine sodium and osmolality, fulfills established diagnostic criteria for the syndrome of inappropriate antidiuretic hormone secretion (SIADH).[14-16] This phase is attributed to dysregulated and excessive ADH release from injured neurohypophyseal structures. In the context of the triphasic response, this third phase may represent either permanent hypothalamic destruction with ongoing vasopressin dysregulation or, less commonly, a transient SIADH-like state before eventual recovery.[1,4] Hensen and colleagues described analogous progression in patients with large hypothalamic lesions, and noted that the severity and reversibility of the SIADH phase correlates with the degree of posterior hypothalamic involvement.[10] Recognition is essential, as management strategies differ fundamentally from the preceding DI phase.

IVIG-Associated Pseudohyponatremia - Intravenous immunoglobulin (IVIG) therapy introduces an important diagnostic confounder. IVIG may result in pseudohyponatremia due to increased plasma protein concentration causing analytical artifact with indirect ion-selective electrode methods, and may also contribute to translocational hyponatremia. However, in this case, elevated urine osmolality, high urine sodium, and clinical response to fluid restriction strongly support true SIADH rather than pseudohyponatremia,

emphasizing the need for careful biochemical interpretation.[17,18]

SIADH versus Cerebral Salt Wasting (CSW) - Differentiating SIADH from cerebral salt wasting remains a clinical challenge. The absence of hypovolemia, lack of natriuresis with volume depletion, and improvement with fluid restriction in this patient favor SIADH over CSW, consistent with existing literature.[7,19,20]

Neurocritical Mechanism - Posterior fossa hemorrhage with associated hydrocephalus likely disrupted hypothalamic osmoreceptors and posterior pituitary ADH regulation. External ventricular drainage (EVD) may further influence intracranial pressure dynamics and contribute to evolving neuroendocrine responses.[11,21] Posterior circulation involvement and hydrocephalus-associated distortion of periventricular structures may further contribute to hypothalamic dysfunction and unstable ADH secretion.[7,21,12] The triphasic ADH response in this context likely reflects a continuum of injury from the hypothalamic nuclei to the posterior pituitary, a pathophysiological framework established by Robertson and confirmed in subsequent imaging and biochemical studies.[1,13] While previously documented predominantly in the peri-transsphenoidal surgical context, growing evidence supports that any insult sufficiently disrupting the hypothalamo-neurohypophyseal tract — including haemorrhage, trauma, and inflammatory lesions — may produce the full triphasic sequence.[3,4,10]

Antiphospholipid Syndrome and Thrombosis - The coexistence of digital ischemia, left ventricular thrombus, and antiphospholipid antibody positivity is consistent with antiphospholipid syndrome (APS), a well-recognized cause of arterial thrombosis.[22,23] Intravenous immunoglobulin (IVIG) therapy represents an important diagnostic confounder, as it may cause pseudohyponatremia due to increased plasma protein concentration or translocational effects. However, in this case, elevated urine osmolality, high urine sodium, and appropriate response to fluid restriction strongly support true SIADH rather than analytical or dilutional artefact.

Conclusion

This case demonstrates a complete triphasic ADH response in spontaneous intracranial haemorrhage without therapeutic confounding. It highlights the importance of recognizing dynamic ADH dysregulation in neurocritical care along with dynamic sodium monitoring, careful phase recognition, and avoidance of misinterpretation due to treatment-related artefacts.

This case is notable for: (i) complete documentation of the triphasic ADH response, (ii) clear biochemical distinction between DI and SIADH phases, (iii) minimal desmopressin exposure without sustained confounding, (iv) diagnostic challenge posed by IVIG therapy, and (v) coexisting APS-related thrombotic complications. Failure to distinguish between phases may result in inappropriate management, including fluid mismanagement or unnecessary pharmacologic intervention. Careful longitudinal biochemical assessment remains essential for accurate diagnosis and optimal outcomes. Recognition of this dynamic process is essential to guide appropriate fluid management and prevent iatrogenic complications.

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Conflicts of interest

All Authors declare that there is no conflicts of interest.

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