Case Report

Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH) and Subsequent Central Diabetes Insipidus: A Rare Presentation of Pituitary Apoplexy

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1. Introduction

Pituitary apoplexy (PA) is a rare clinical emergency induced by sudden haemorrhage or infarction into the pituitary gland, which predominantly occurs into an existing pituitary adenoma [1]. Abrupt onset of severe headache is the main symptom, but neurological symptoms, nausea, visual impairment, ocular palsy, and endocrine disturbances frequently occur [1–3]. Severe hyponatremia due to the syndrome of inappropriate antidiuretic hormone secretion (SIADH) is occasionally reported in PA [4–7] and also occurs in ≈6% of patients undergoing pituitary surgery [8].

In general, SIADH is caused by inappropriate excretion of vasopressin from the pituitary gland, ectopic vasopressin production, or increased ADH sensitivity [9]. The condition was first detected by William Schwartz and Frederic Bartter in 1967, who also established the clinical criteria for SIADH, which includes serum sodium < 135 mmol/l, serum osmolality < 275 mmol/kg, urine sodium > 40 mmol/l, urine osmolality > 100 mmol/kg, absence of clinical signs of volume depletion, absence of known conditions causing hyponatremia, and successful correction of sodium levels with fluid restriction [10]. Various conditions can cause SIADH including granulomatous diseases, malignant tumours, central nervous disease, and drug intake [9]. Rare causes of SIADH such as PA may be overlooked, not least since the two conditions share symptoms and signs including nausea and hyponatremia.

Central diabetes insipidus (CDI) is another rare condition, which is characterized by polyuria (>3 L per day), excessive thirst, polydipsia, and elevated serum sodium levels [11]. It is known that CDI complicates PA with a prevalence of less than 5% and that the condition most often is temporary and resolves within the following weeks [1,3]. To our knowledge,
2. Case Presentation

A previously healthy 41-year-old Caucasian woman was admitted to the Emergency Department at the Regional Hospital of Horsens with a three-day history of severe headache, nausea, and dizziness. The physical examination was unremarkable with no evidence of impaired vision. Regular medication only included oral contraceptives (75 microgram desogestrel). Initial blood screen tests revealed moderate hyponatremia (126 mmol/l) and borderline low levels of iodothyronines ($T_3$ and $T_4$) and thyroid-stimulating hormone (TSH, Table 1). An acute cerebral computed tomography (CT) did not show haemorrhage or infarction, and no mass lesion in the sellar region. Lumbar puncture showed no signs of infection or bleeding. Additional blood tests showed normal anterior pituitary function (Table 1) except moderate hyperprolactinemia. During the first two days of admission, plasma sodium concentrations dropped to a nadir level of 111 mmol/l (Figure 1). On the third day, a magnetic resonance imaging [MRI] of the brain showed recent bleeding into a cystic process (10x10x8 mm) in the sellar region in close proximity to the optic chiasm with displacement of the pituitary gland to the right (Figure 2). Urine and blood examination at day two (Table 1) were consistent with SIADH according to standard criteria [10]. The patient was treated with fluid restriction (day two to day five) and an intravenous bolus of hypertonic saline 3% (day two only), which induced a gradual increase in plasma sodium concentrations (Figure 1). During the following weeks, the patient developed polyuria, polydipsia, and persistent hyponatremia. She was diagnosed with central diabetes insipidus (CDI) and successfully treated with desmopressin (dose 0.1 mg daily).

A MRI follow-up after three and ten months showed no change in the size of the cystic adenoma and automated perimetry showed a normal visual field. Anterior pituitary function remained intact, whereas the patient’s CDI is considered permanent.

3. Discussion

Pituitary apoplexy is a rare but acute condition causing severe headache often associated with visual disturbances including ocular palsy, and altered consciousness. The clinical picture resembles that of subarachnoid haemorrhage (SAH) or meningitis, which often delays the diagnosis [1]. Pituitary imaging confirms the diagnosis by revealing a haemorrhagic or necrotic pituitary tumour [12]. Corticotropic deficiency causing adrenal insufficiency must be evaluated and promptly treated, and acute surgery is indicated if the symptoms worsen [1]. The present case of PA is unique owing to its presentation with isolated posterior pituitary dysfunction that transitioned from SIADH into permanent CDI.

It is well known that neurosurgery and brain trauma may cause hyponatremia, which is often attributable to SIADH [13–15]. Furthermore, it is evident that pituitary surgery may elicit a tri-phasic response with acute hyponatremia, transient hyponatremia around postoperative day 7 (between 3 and 11 days), and subsequent development of CDI [16–19].
Table 1
(a) Standard blood test screen at admission

| Parameter   | Value   | Reference Range | Unit     |
|-------------|---------|-----------------|----------|
| Na⁺         | 126     | (137 - 145)     | mmol/l   |
| K⁺          | 3.5     | (3.5 - 4.6)     | mmol/l   |
| CRP         | 1.8     | (<8)            | mg/l     |
| Leucocytes  | 6.4     | (3.5 - 10)      | 10⁹/l    |
| TSH         | 0.4     | (0.3 - 4.5)     | 10⁻¹ IU/l|
| T₃          | 3.1     | (3.9 - 6.8)     | pmol/l   |
| T₄          | 11.4    | (12 - 21)       | pmol/l   |

(b) Extended blood and urine tests

| Parameter   | Value   | Reference Range | Unit     |
|-------------|---------|-----------------|----------|
| Prolactin   | 1375    | (90 - 580)      | 10⁴ IU/l |
| ACTH        | 36      | (7 - 64)        | ng/l     |
| Cortisol 0 min | 541   | (500)           | nmol/l   |
| Cortisol 30 min | 797    | (70-210)        | µg/l     |
| FSH         | 23      |                 | IU/l     |
| LH          | 6.7     |                 | IU/l     |
| Estrogen    | <15     |                 | pmol/l   |
| IGF-1       | 192     | (280-300)       | mmol/kg  |

Urine

| Parameter   | Value   | Reference Range | Unit     |
|-------------|---------|-----------------|----------|
| U-Osmolality| 744     | (300 - 900)     | mmol/kg  |
| U-Na⁺       | 140     |                 | mmol/l   |

Biochemistry: standard blood test screen and extended blood and urine tests. This table shows selected blood sample concentrations from the standard blood test screening performed on the day of hospital admission and the extended blood test analysis performed on day two of admission. Parenthesis illustrates the normal range. ↓ = below normal range. ↑ = above normal range. CRP= C reactive protein, TSH = thyroid stimulating hormone, T₃= triiodothyronine, T₄ = thyroxine, ACTH= adrenocorticotropic hormone, FSH= follicle-stimulating hormone, LH= luteinizing hormone, and IGF-1= insulin-like growth factor 1.

Our case shows a similar course with SIADH/hyponatremia approximately 5 days following initial symptoms and development of CDI in the ensuing weeks. We therefore speculate that PA may cause sodium disturbances through similar mechanisms as pituitary surgery and brain trauma, which include an acute outburst of ADH from damaged cells in the posterior pituitary gland [14, 15]. This damage may cause subsequent CDI that typically resolves within weeks but occasionally result in permanent CDI [14].

Hyponatremia is the most frequent electrolyte disturbance, especially in hospitalized patients [20], and PA is a rare and often overlooked cause of hyponatremia. Most emergency departments use standard blood test screens at admission, and cerebral CT-scans are also widely used in this setting. Studies have shown that CT only detects 21% of PA, whereas 90% is visualized with MRI [12, 21]. The absence of visual impairment and lack of clear anterior pituitary affection undoubtedly delayed the MRI and hence the final diagnosis in our case.

Pituitary apoplexy remains an important albeit rare differential diagnosis in patients presenting with severe and acutely onset headache, and our case illustrates that PA may masquerade as isolated SIADH and develop into CDI.

Abbreviations
CDI: Central diabetes insipidus
CT: Computed tomography
MRI: Magnetic resonance imaging
PA: Pituitary apoplexy
SAH: Subarachnoid haemorrhage
SIADH: Syndrome of inappropriate antidiuretic hormone secretion.

Disclosure
We confirm that this report is in line with the International Committee of Medical Journal Editors’ (ICMJE) recommendations. No human or animal experiments were conducted.

Conflicts of Interest
The authors declare that there are no conflicts of interest regarding the publication of this article.

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