Central Diabetes Insipidus in A Young Man with Intracranial Germ Cell Tumors: A case report

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Case Report

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Abstract

Background

Central diabetes insipidus (CDI) in patients with intracranial germ cell tumors (GCTs) could develop due to suprasellar involvement or postoperative complication after transsphenoidal surgery (TSS). However, it is important to early recognize the pre-existing CDI caused by GCTS with normal sodium (Na\(^+\)) level before surgery.

Case presentation

A 25-year-old male presented with progressive fatigue, weakness, polydipsia and loss of libido in the past one year. Laboratory finding was unremarkable without hypernatremia. Hormonal testing indicating anterior pituitary insufficiency. Brain magnetic resonance imaging showed two mass lesions in the sellar/suprasellar and pineal regions with obstructive hydrocephalus. The patient developed polyuria with hypernatremia after 6-hour fasting and TSS with incisional biopsy. Diagnosis of intracranial GCTs with CDI was confirmed by pathology and desmopressin test. Without surgical damage to posterior pituitary or tumor resection which might led to postoperative CDI, pre-existing CDI before surgery could be unrecognized by normal serum Na\(^+\) and unrestricted water intake.

Conclusions  Clinicians should notice the typical manifestations of intracranial GCTs, especially in CDI, to avoid potential complications. Fluid restriction before surgery is a risk factor to develop hypernatremia caused by CDI that was masked by polydipsia before surgery.

Background

Intracranial germ cell tumors (GCTs) are a subset of extragonadal GCTs that typically arise in midline locations, such as the pineal and suprasellar regions (1). Intracranial GCTs commonly occurred in the second decades of life with median age at diagnosis of 10 to 14 years.(1, 2) Males are more commonly affected than females with a male-to-female incidence ratio approximately from 3:1 to 4:1.(3) The symptoms of intracranial GCTs depend on location of the tumors. Tumors in the pineal region typically led to compression and obstruction of cerebral aqueduct which caused obstructive hydrocephalus and increased intracranial pressure.(4) Another clinical presentation associated to pineal GCTs is neuro-ophthalmologic abnormalities, especially paralysis of upward gaze and convergence, is reported in 50% of the patients.(5) Tumors in the suprasellar region usually present with decreased visual acuity or bitemporal hemianopsia due to compression of optic chiasm.(6) Once suprasellar tumors invade into adenohypophysis, patients present with hypothalamic/pituitary dysfunctions, including central diabetes insipidus (CDI), delayed puberty, adrenal insufficiency, or central hypothyroidism.(6) CDI is the most common presentation which is reported in more than 80% of cases with suprasellar germ cell tumors (7).

CDI is characterised by deficiency of antidiuretic hormone (ADH) secretion which is a rare disease in children and young adults. The aetiologies of CDI could be inherited, acquired or idiopathic. It was
reported that idiopathic CDI account for up to 50% of the cases. Patients with CDI typically present with polyuria, polydipsia, and diluted urine. The other known causes of CDI include intracranial tumors (such as germinoma and craniopharyngioma) or infiltrative disease (such as Langerhans’ cell histiocytosis), inflammatory, autoimmune, trauma resulting from an accident or neurosurgery. In patients who undergo transsphenoidal surgery (TSS) for pituitary and suprasellar tumors, CDI is a recognized postoperative endocrine complication. It is usually caused by disturbance of the hypothalamus, pituitary stalk, or the posterior pituitary gland intraoperatively. In contrast, other causes of CDI in patient undergoing TSS for pituitary and suprasellar tumors are of less appreciated, leading to inappropriate management. In this report, we describe a young male with intracranial GCTs developed CDI with acute hypernatremia after transsphenoidal surgical biopsy. Without surgical damage to posterior pituitary or tumor resection which are thought to be the causes of postoperative CDI, pre-existing CDI before surgery could be unrecognized by normal serum Na\(^+\) and unrestricted water intake. Once a patient was NPO with fluid restriction for surgery, life threatening hypernatremia related to CDI might occurred in the perioperative period. Our case highlights that clinicians should notice the typical manifestations of intracranial GCTs, especially in CDI, to avoid potential complications.

**Case presentation**

A 25-year-old male presented to our hospital with general weakness and 20-kg body weight gain recently. He has progressive fatigue, weakness, polydipsia and loss of libido for one year. Six months before admission, he was diagnosed as adrenal insufficiency, and oral prednisolone 10 mg daily was prescribed since then. However, the symptoms got worse. On presentation, his blood pressure was 121/80 mm Hg and heart rate was 81 beats per minute. Pertinent physical examination revealed central obesity with wide purple striae on abdominal wall and both inner thighs. Neurological examinations were normal and no other associated symptoms such as nausea, vomiting, dizziness, sensory complaints, or visual deficit were present. Laboratory finding was unremarkable except for leucocytosis (while blood cell 13.78 x 10\(^9\)/L). Other biochemistry data, including sodium (Na\(^+\)) (137, reference range 136-145 mmol/l), potassium (K\(^+\)) (4.1, reference range 3.5–5.1 mmol/l), creatinine, blood urea nitrogen, and liver profiles, were all within normal limits. Hormonal testing revealed low cortisol level at 0.49 µg/dL (reference range 4.82–19.5 µg/dL) and inappropriately normal adrenocorticotropic hormone level at 6.6 pg/mL (reference range 0.1–46.0 pg/mL), low LH level at less than 0.1 mIU/mL (reference range 1.7–8.6 mIU/mL), relative low TSH at 4.85 uIU/mL (reference range 0.25–5.0 uIU/mL) and low free T4 level at 0.8 ng/dL (reference range 0.89–1.78 ng/dL), indicating anterior pituitary insufficiency confirmed by the triple bolus test which showed dysfunction of hypothalamic–pituitary–adrenal axis (HPA) and hypothalamic-pituitary-gonadal (HPG) axis shown in Table 1. Further insulin tolerance test (ITT) supported the diagnosis of secondary adrenal insufficiency (Table 1). Contrast-enhanced magnetic resonance imaging (MRI) of brain showed two mass lesions with heterogenous enhancement in the sellar/suprasellar and pineal regions, measuring 1.81 cm x 1.72 cm x 1.63 cm and 2.16 x 1.85 x 2.15 cm, respectively (Fig. 1A, B and C). The pineal mass was responsible for obstructive hydrocephalus. The patient received TSS with incisional biopsy of seller/suprasellar tumor. However, polyuria with diluted urine (urine osmolality 125 mOsm/kg
H2O) developed with hyperosmolar hyponatremia (Na+ 165 mmol/L) at day one after 6-hour fasting and TSS (Fig. 2). There was no cerebrospinal fluid (CSF) leak or any complication post operation. As shown in Fig. 2, urine specific gravity increased from 1.006 to 1.012 and urine osmolality increased from 125 to 325 mOsm/kg H2O two hours after administration of desmopressin supported the diagnosis of central diabetes insipidus. With immediate desmopressin treatment, serum sodium declined to normal level on the third day after surgery. The histologic pathology finding of sellar/suprasellar tumor was compatible with germinoma. The patient underwent ventriculoperitoneal shunt placement for obstructive hydrocephalus and the first cycle of chemotherapy. The patient was discharged uneventfully.

Table 1
Result of endocrine testing with triple bolus test and insulin tolerance test

<table>
<thead>
<tr>
<th>Hormone</th>
<th>Baseline</th>
<th>30’</th>
<th>60’</th>
<th>90’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol (µg/dL)</td>
<td>0.28</td>
<td>15.13</td>
<td>13.12</td>
<td>12.37</td>
</tr>
<tr>
<td>LH (mIU/mL)</td>
<td>&lt; 0.1</td>
<td>&lt; 0.1</td>
<td>&lt; 0.1</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>FSH (mIU/mL)</td>
<td>0.17</td>
<td>0.15</td>
<td>0.36</td>
<td>0.51</td>
</tr>
<tr>
<td>TSH (µIU/ml)</td>
<td>4.85</td>
<td>2.82</td>
<td>11.04</td>
<td>20.78</td>
</tr>
<tr>
<td>Prolactin (ng/mL)</td>
<td>11.3</td>
<td>10.3</td>
<td>20.2</td>
<td>17.2</td>
</tr>
</tbody>
</table>

Insulin tolerance test

<table>
<thead>
<tr>
<th>Serum glucose (mg/dL)</th>
<th>30’</th>
<th>60’</th>
<th>90’</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cortisol (µg/dL)</td>
<td>0.47</td>
<td>0.49</td>
<td>0.41</td>
</tr>
</tbody>
</table>

Discussion and Conclusions

Here, we described a 25-year-old young male with pineal and suprasellar GCT developed hypernatremia and polyuria after transsphenoidal biopsy of suprasellar lesion. Before admission, he has normal Na+ level with unrecognized CDI masked by his polydipsia. After NPO with fluid restriction for surgery, polyuria and hypernatremia developed. Diagnosis of intracranial GCTs with CDI was confirmed by DDAVP test. This case highlights that clinicians should be aware of unrecognized manifestations associated with intracranial GCTs before surgery, especially in CDI, to avoid potential complications.

CDI, characterized by polyuria, hyponatremia, and diluted urine, is a result of deficiency or impaired secretion of vasopressin. Most patients with acquired CDI are caused by destruction of the neurohypophysis, including destruction of vasopressin neurons by pressure or infiltration of brain lesions, or by surgical damage.(11) However, different diagnosis for post-surgical hyponatremia in patients with
intracranial lesion appears to be challenging. Most patients with intracranial GCTs do not seek medical attention until development of neurologic symptoms such as headache, visual defects, or diplopia. The symptoms of pituitary dysfunctions are relatively chronic and subtle, and usually diagnosed incidentally. (6) This patient did not present with typical symptom such as headache, vomiting, ataxia, and behavioural changes caused obstructive hydrocephalus related to pineal tumor. In addition, manifestation of CDI caused by sellar-suprasellar tumor may not lead to overt hypernatremia in patients with unimpaired thirst and unrestricted access to fluids.(12, 13) According to this non-specific presentation including progressive fatigue, weakness, and loss of libido, this patient received inappropriate management for adrenal insuiciency. Therefore, patients with CDI in the age of adult to middle age tend to be not noticed by physicians without hypernatremia. Once fluid replacement is insufficient for surgery, the diagnosis of CDI will be delayed until acute hypernatremia develops.

Traumatic CDI is another complication after TSS for suprasellar and sellar tumors. Postoperative CDI is thought to be caused by surgical damage and resection to the hypothalamus, pituitary stalk, or posterior pituitary gland during surgery.(10, 14) The rate of CDI after TSS ranged from 8–62%, with incidence varying by tumor pathology, especially TSS for resection of pituitary adenoma (PA), Rathke cleft cyst (RCC), or craniopharyngioma.(9, 10, 14) The other validated risk factors include intraoperative CSF leak, males, and younger age.(9, 10, 15) Our patient underwent TSS with incisional biopsy of suprasellar tumor. Without gross tumor resection or intraoperative CSF leak, surgical damage to posterior pituitary or the infundibulum which led to traumatic CDI is not likely.

Management for CDI caused by intracranial GCTs includes oral or intravenous desmopressin, but early recognizing hidden case with prophylactic use of desmopressin before surgery is most important. When patients with intracranial GCTs are restricted to fluid intake, closely monitoring clinical symptoms, signs, and laboratory data, especially electrolytes were mandatory. One retrospective study reported its practice for CDI including measuring serum Na\(^+\) and urine-specific gravity every 6 hour or after every void and with diligent monitoring of fluid intake and output (9). Prompt management with desmopressin and hydration to prevent from dehydration and acute hypernatremia during NPO with fluid restriction before surgery for intracranial GCTs with CDI.

Our case highlights the fact that clinicians should notice the typical manifestations of intracranial GCTs, especially in CDI. Once the patient was NPO with fluid restriction for TSS, life threatening hypernatremia related to CDI might occurred in the perioperative period. To our knowledge, this is the first known report of CDI with acute hypernatremia after TSS which was caused by unrecognized pre-existing CDI and subsequent iatrogenic water restriction, instead of other common mechanisms. There are several limitations to our report. We did not confirm the diagnosis of CDI of our patient before the surgery. The diagnosis of intracranial GCTs associated CDI was inferred from the patient’s polydipsia and polyuria and no significant damage to posterior pituitary during operation.

**Abbreviations**
CDI: Central diabetes insipidus

GCTs: Germ cell tumors

TSS: Transsphenoidal surgery

ADH: Antidiuretic hormone

ITT: Insulin tolerance test

HPA: Hypothalamic–pituitary–adrenal axis

HPG: Hypothalamic-pituitary-gonadal

MRI: Magnetic resonance imaging

CSF: Cerebrospinal fluid

PA: Pituitary adenoma

RCC: Rathke cleft cysts

**Declarations**

**Ethics approval and consent to participate:** This study was reviewed and approved by the Institutional Review Board of Tri-Service General Hospital, approval number B202315001. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

**Consent for publication:** Written informed consent was obtained from the patient for publication of this case.

**Availability of data and materials:** The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

**Competing interests:** The authors declare that they have no competing interests.

**Funding:** There is no funding support for this study.

**Authors' contributions:** CCS participated in the diagnosis and treatment of the patient, provided follow-up, and acquired clinical data. CWS, CCC and CCS drafted and reviewed the manuscript. CWS, CCC and CCS conducted investigations, reviewed the literature, and assisted in polishing the manuscript for final publication. All the authors read and approved the final manuscript.

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References


Figures

Figure 1

Sagittal T1-weighted (A), and sagittal post-gadolinium T1-weighted (B) images showing enhancing sellar/suprasellar and pineal masses (white arrow) with an obstructive hydrocephalus. Coronal (C) T2-weighted-image revealing a suprasellar/sellar mass with slightly hyperintense (white arrow).

Figure 2

Desmopressin 4μg

(Time)

Serum Na⁺ (mmol/L)

Urine osmolality (mOsm/kg H₂O)
Serum Na⁺ and urine osmolality trends and the timing of DDAVP test after transsphenoidal surgery