A unique case of central hypopituitarism and central diabetes insipidus caused by diffuse large B cell lymphoma

Abstract

We present a case of a 39 year old male presenting with complications of a previously undiagnosed diffuse large B cell lymphoma found to have metastasis to the pituitary infundibular stalk resulting in multifocal pituitary dysfunction. Initially presenting with GI bleed from tumor invasion of gastric vessels, diagnosis of lymphoma was made when gastrectomy became necessary for hemostasis. Hypernatremia on basic laboratory studies led to further investigation and revealed central diabetes insipidus. MRI of the pituitary was performed, showing thickening of the infundibular stalk. Thickening of the pituitary infundibulum is a recognized syndrome, though uncommonly discovered prior to diagnosis of infiltrative process. Central diabetes insipidus due to lymphomatous infundibular stalk infiltration is an uncommon presentation of endocrine deficiency as well as malignancy; this case demonstrates the management of a critically ill patient with central hypopituitarism and central diabetes insipidus due to diffuse B cell Lymphoma.

Introduction

Central diabetes insipidus is a disorder that is characterized by a decrease in the production or secretion of ADH (antidiuretic hormone). Deficiency of ADH results in the inability to sufficiently concentrate urine at the collecting duct of the nephron, and the kidneys produce large volumes of dilute urine regardless of the body’s hydration state.1

Patients with central diabetes insipidus will typically present with polyuria (>50mL/kg/24hr),2 polydipsia, hypernatremia (serum Na level >145 mg/dL),3 elevated serum osmolality (>295 mOsm/L) and decreased urine osmolality (< 300 mOsm/L).4 Untreated DI may lead to hypovolemia, dehydration and electrolyte imbalances which may be particularly life threatening in critical ill patients who may be unable to communicate symptoms due to altered levels of consciousness.4 Non-critically ill patients with intact thirst mechanisms and free water access frequently can manage their fluid losses by increasing oral fluid intake. Diagnosing DI is challenging in patients with altered mental status who may be receiving intravenous fluids during hospitalization.5 The fluid deprivation AVP/DDAVP challenge test is traditionally used to diagnose DI, but often is unable to be safely performed in critical-ill patients.6

Central diabetes insipidus can be caused by various processes that result in decreased ADH production from the hypothalamus, decreased storage of ADH in the posterior pituitary or decreased ADH transport to the posterior pituitary gland due to infundibulum impairment or injury. Most common causes for central diabetes insipidus include trauma, neurosurgery, vascular and autoimmune diseases, malignancy, inflammatory, idiopathic, and other infiltrative processes.7 Physiologically, infiltrative causes can provoke central DI by thickening of the pituitary infundibulum, which is becoming better recognized on MRI. It is also noteworthy that central DI resulting from infundibular thickening is associated with anterior pituitary deficiencies in a majority of cases.8

Case report

We present a case of a 39 year old white male without known prior medical history who presented with hemorrhagic shock from massive GI bleeding that required admission to the Intensive Care Unit. Hemostasis was unable to be achieved with endoscopy or arterial embolization, and the patient ultimately required a partial gastrectomy on hospital day two, to control bleeding. Large volume fluid resuscitation and blood transfusions were required on admission as outlined in Table 1. Because of hemorrhagic shock, the patient received ten liters of lactate ringer infusion, four liters of normal saline infusion, four units of packed red blood cell infusion and one unit of plasma within the first 12 hours of admission. By the end of hospital day two, the patient was hemodynamically stable, but had received thirty two liters of IV fluids, twenty four units of blood products as well as vasopressor support including epinephrine, norepinephrine, phenylephrine, and vasopressin. Upon regaining hemodynamic stability, the patient was able to be discontinued from volume administration and vasopressor support. Because of persistent hypotension besides being on continuous IV vasopressors, the patient was started on Hydrocortisone 100 mg IV every 8 hours.

Table 1 Daily Serum Na and Net In and Outs

<table>
<thead>
<tr>
<th>Hospital course</th>
<th>Serum Na (mmol/L)</th>
<th>Net I&amp;O’s</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission</td>
<td>138</td>
<td></td>
</tr>
<tr>
<td>Hospital Day 1</td>
<td>138</td>
<td>+20.5L</td>
</tr>
<tr>
<td>Hospital Day 2 (Vasopressin Discontinued)</td>
<td>144</td>
<td>+17.6L</td>
</tr>
<tr>
<td>Hospital Day 3</td>
<td>146</td>
<td>-8.2L</td>
</tr>
<tr>
<td>Hospital Day 4 (Desmopressin Initiated)</td>
<td>162</td>
<td>+1.3L</td>
</tr>
<tr>
<td>Hospital Day 5</td>
<td>164</td>
<td>+3.8L</td>
</tr>
<tr>
<td>Hospital Day 6</td>
<td>157</td>
<td>+4.2L</td>
</tr>
</tbody>
</table>

On hospital day three the patient produced 12.8 liters of dilute urine. Labs obtained at that time showed plasma sodium of 164 mmol/L, a serum osmolality of 355 mOsm/L and a urine osmolality of 1.59 mOsm/L.
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The patient had no known previous history of diabetes insipidus nor did he have a family history of endocrine dysfunction and specifically no history of central DI in his family. No recent histories of trauma or neurosurgery, no known intracranial malignancies were documented prior to admission. The patient also had no known history of renal disease and was taking no medications prior to admission.

Although formal work up for diabetes insipidus could not to be performed due to patient’s critical condition, the high serum osmolality, low urine osmolality, hypernatremia, and polyuria were consistent with DI. Initially, it was thought was that the central diabetes insipidus was possibly secondary to pituitary apoplexy in the setting of hemorrhagic shock, but pituitary MRI was performed on hospital day five, which instead revealed infundibular thickening. The pituitary stalk diameter measured 9mm in the AP plane (normal 2.32 mm) (Figure 1) (Figure 2).

Figure 1 Initial pituitary MRI demonstrating infundibular thickening in AP plane.

Figure 2 Follow up MRI hospital day 78 demonstrating interval enlargement of pituitary lesion.

Surgical pathology from gastrectomy stomach specimen (obtained on hospital day two), was also reported on hospital day five. This was notable for diffuse large B cell lymphoma (Figure 3). Infundibular thickening was determined to be likely secondary to diffuse large B cell lymphoma and causative factor of DI (Figure 4).

Figure 3 Lymphoma around gastric mucosa.

Figure 4 CD20 immunohistochemical stain – B-cell marker.

Evaluation of the pituitary function demonstrated a relatively low TSH of 0.11 UIU/mL (normal 0.35-4.94 UIU/mL) and low fT4 of 0.5 ng/dL (normal 0.7-1.5 ng/dL) and low ACTH level <5 (normal 6-50) with a low cortisol level < 3. GH and IGF-1 as well as the gonadal axis were not tested in the critical state of the patient. The patient had a PET scan performed twelve weeks into hospital stay which demonstrated tracer accumulation in the fundus of the stomach and pituitary gland.

It was now thought that the infundibulum thickening was caused by metastatic disease which causes an interruption of the hypothalamus/pituitary axis based on the PET scan (Figure 5). The patient was treated with hormonal replacement including Levothyroxine and Hydrocortisone. Serum sodium normalized and polyuria resolved, following the addition of desmopressin. Oncology was consulted and R-CHOP for the treatment of B-cell lymphoma was initiated. The pituitary function did not recover after initiating of R-CHOP and patient remained dependent on Hydrocortisone, Levothyroxine and Desmopressin.

Discussion

This patient developed multiple pituitary deficiencies, including ADH leading to central diabetes insipidus. Pituitary dysfunction was determined to be caused by pituitary infundibular thickening. Hamilton et al. classified pituitary infundibular lesions by categories of tumor, inflammatory/infectious, and congenital, of which, in their study population, 37% were malignant, 33% were congenital and 30%...
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In a study by the Mayo clinic, of the 49 malignant pituitary stalk lesions identified on MRI, 9 (18%) were caused by lymphomas, 8 (16%) by pituitary adenomas, 6 (12%) caused by germinomas, 6 (12%) caused by metastatic breast cancer, and 5 (10%) by metastatic small cell lung cancer. Of their cohort of patients found to have pituitary infiltration, DI was diagnosed in 28% and 32% had at least 1 anterior pituitary deficiency identified. 71% of those found to have DI also demonstrated anterior pituitary deficiencies. In a majority of malignant cases, a primary cancer diagnosis had already been made prior to the onset of pituitary deficiency.

Posterior pituitary deficiencies have a higher frequency than anterior. This can be possible explained by the blood supply of the pituitary gland. The posterior pituitary is supplied directly by the systemic circulation through hypophyseal arteries. The anterior pituitary is supplied by the portal vessel system to allow delivery of hypothalamic prohormones. The posterior pituitary has a larger area of contact with the adjacent dura. Central DI is therefore the most common symptom associated with metastatic pituitary disease.

This patient’s case was unique in that his cancer was diagnosed concurrently with his hormonal deficiencies. The etiology of his pituitary lesion was confirmed with the radiologic finding of thickened infundibulum.

The patient’s critical illness precluded formal evaluation for central diabetes insipidus with water deprivation testing. Water deprivation with regular monitoring of urine osmolality as well as serum sodium and osmolality followed by DDAVP challenge is the standard diagnostic evaluation of DI. The findings of an elevated serum osmolality, decreased urine osmolality, and hypernatremia in the setting of pituitary infundibular thickening, as well as the patient’s empiric response to desmopressin, is highly suggestive of central DI.

This patient’s clinical case did not merit endocrine evaluation for three days following admission; the delayed manifestation of his pituitary deficiency likely stemmed from his critical state upon admission. Central DI likely was masked initially by large volume fluid resuscitation and vasopressor support including vasopressin for treatment of upper GI bleeding with stress-dose hydrocortisone for hypotension. Adrenal insufficiency was not initially suspected as hypotension was more likely related to hemorrhagic shock. Hypernatremia did not develop until hospital day three likely related to the use of vasopressin as a vasopressor during his initial presentation. The patient later reported polydipsia and polyuria and nocturia for several months prior to his hospitalization indicating that he likely had been ADH deficient prior to his acute hospitalization.

Patients with classic findings suspicious for hypopituitarism and/or central diabetes insipidus should undergo early evaluation and treatment to prevent adverse outcomes related to hormonal deficiencies.

Please see Table 2 for a proposed management algorithm for critically ill patients.

Table 2 Proposed management algorithm for critically ill patients

The pituitary gland. The posterior pituitary is supplied directly by the systemic circulation through hypophyseal arteries. The anterior pituitary is supplied by the portal vessel system to allow delivery of hypothalamic prohormones. The posterior pituitary has a larger area of contact with the adjacent dura. Central DI is therefore the most common symptom associated with metastatic pituitary disease.

Figure 5 PET scan demonstrating intense tracer accumulation in the fundus of the stomach and pituitary gland suggestive of probable active lymphoma.

Citation: Stegink JA, Sehgal V, Konig M. A unique case of central hypopituitarism and central diabetes insipidus caused by diffuse large B cell lymphoma. Endocrinol Metab Int J. 2018;6(4):261–264. DOI: 10.15406/emij.2018.06.00187
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Conclusion
This case illustrates the presentation and management of a critically ill patient with a concurrent endocrine dilemma. Central diabetes insipidus was suspected based on an elevated serum osmolality and low urine osmolality with hypernatremia and associated polyuria. Formal water deprivation testing was not able to be performed, but the presentation led to further discovery of endocrine deficiencies as well as metastatic lymphoma. Central diabetes insipidus related to infundibular infiltration is highly associated with anterior pituitary deficiencies which were also demonstrated in this patient. While malignancy may be the most common cause of infundibular thickening with lymphoma being the most common of these, there are few documented cases in the literature of diffuse large B cell lymphoma causing pituitary infundibular thickening and multiple pituitary deficiencies.

It is important to make an early diagnosis of diabetes insipidus in critical ill patients to prevent severe complications as well as death. Early treatment of the underlying condition may reverse hypopituitarism as well as central diabetes insipidus. Unfortunately, our patient ultimately died (months following initial admission) as his lymphoma was refractory to treatment.

Acknowledgments
None.

Disclosure summary
The authors have nothing to disclose.

References

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