Transient Diabetes Insipidus After Discontinuation of Vasopressin in Neurological Intensive Care Unit Patients: Case Series and Literature Review

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BACKGROUND: **Arginine vasopressin (AVP) is a common second-line or third-line vasopressor used in critically ill neurosurgical patients. Neurosurgical indications include hyperdynamic therapy for vasospasm, maintenance of cerebral perfusion pressure in patients with intracranial hypertension, and prevention of hypotension in patients with sepsis.**

CASE DESCRIPTION: **A series of 6 neurosurgical patients receiving AVP infusions developed severe but transient diabetes insipidus (tDI) after cessation of AVP. To our knowledge, no previous reports of this phenomenon in neurosurgical patients have been published. We reviewed the clinical histories, intensive care unit treatment, medication administration records, and laboratory values of these patients, and we found recurrent elevated serum sodium and urine output and decreased urine specific gravity after discontinuation of AVP. Resolution of tDI occurred upon resumption of AVP or administration of desmopressin. Elevated serum sodium levels were often severe, resulting in worsened clinical outcomes. When AVP was resumed, tDI typically recurred if AVP was again tapered and discontinued. Routine administration of desmopressin was useful in controlling sodium levels until the tDI resolved.**

CONCLUSIONS: **Recognition of this phenomenon has caused us to change our clinical management of neurosurgical patients receiving AVP. We hypothesize that tDI is caused by downregulation of the V2 receptor mass in the renal distal convoluted tubule and collecting duct cells. When AVP is discontinued, patients develop nephrogenic tDI secondary to decreased V2 receptor binding, which explains why desmopressin is effective in correcting tDI. Future research includes a large prospective study to determine risk factors for tDI, its incidence, and its pathophysiology.**

INTRODUCTION

Arginine vasopressin (AVP) is commonly used in critically ill neurosurgical patients who require multiple agents for blood pressure support. Neurosurgical indications include hyperdynamic therapy for treatment of vasospasm, maintenance of cerebral perfusion pressure in patients with intracranial hypertension, and prevention of hypotension in patients with sepsis. Although several cardiovascular complications are known to be associated with AVP, including decreased cardiac output and end-organ ischemia secondary to peripheral vasoconstriction, few studies have reported on the fluid and electrolyte complications associated with AVP.[1] At our institution, it has been the experience of the neurocritical care and neurosurgical staff that patients receiving AVP infusions are at risk of developing severe but transient diabetes insipidus (tDI) within hours after discontinuation of AVP infusion.

A literature search on this subject retrieved only 2 previously published case reports of this phenomenon. One report in 2004 detailed a 53-year-old male patient with a history of syndrome of inappropriate antidiuretic hormone (SIADH) who was in septic shock,[2] and one report in 2005 detailed a 34-year-old male patient

Key words
- Diabetes insipidus
- Hypernatremia
- Neurosurgical intensive care
- Vasopressin infusion

Abbreviations and Acronyms
AVP: Arginine vasopressin
CSW: Cerebral salt wasting
CT: Computed tomography
DI: Diabetes insipidus
GCS: Glasgow Coma Scale
OR: Operating room
SAH: Subarachnoid hemorrhage
SIADH: Syndrome of inappropriate antidiuretic hormone
tDI: Transient diabetes insipidus
V2R: V2 receptor

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Table 1. Characteristics of 6 Patients with Transient Diabetes Insipidus After Discontinuation of Vasopressin

Patient	Age (years)	Sex	Pathology	AVP Indication	Comorbidity
1	48	M	Aneurysmal SAH; ACoA clipped	Vasospasm	Asthma; required barbiturates
2	43	F	Aneurysmal SAH; L MCA bifurcation clipped	Vasospasm	None reported; required barbiturates
3	23	F	IPH/IVH; clipping for L PCA aneurysm rupture	Pressure support of CPP	None; required barbiturates
4	57	M	GBM, HCP, AKI, sepsis	Sepsis	Hypertension; diabetes mellitus
5	48	M	EDH, IPH, traumatic SAH, craniotomy for EDH	Vasospasm	Ankylosing spondylitis
6	58	M	SAH, R PCoA coiled	Vasospasm; myocardial infarction requiring IABP	None known

AVP, arginine vasopressin; M, male; SAH, subarachnoid hemorrhage; ACoA, anterior communicating artery; F, female; L, left; MCA, middle cerebral artery; IPH, intraparenchymal hemorrhage; IVH, intraventricular hemorrhage; PCA, posterior cerebral artery; CPP, cerebral perfusion pressure; GBM, glioblastoma; HCP, hydrocephalus; AKI, acute kidney injury; EDH, epidural hematoma; R, right; PCoA, posterior communicating artery; IABP, intra-aortic balloon pump.

with obesity and pneumonia and who was experiencing respiratory failure.[3] In both cases, the patients were treated effectively with scheduled and then as-needed doses of exogenous desmopressin. The following report is, to our knowledge, the first case series (n = 6) of this phenomenon and the first report of this phenomenon in neurosurgical patients. The cases are presented in chronological order, and additional case highlights are included to illustrate how our management of patients on AVP has changed since we recognized this phenomenon. A literature review and hypothesis about the underlying pathophysiology follows the case descriptions.

METHOD

After approval from the Institutional Review Board of St. Joseph's Hospital and Medical Center, we retrospectively reviewed the charts of 6 neurosurgery patients who were treated with AVP infusion and who subsequently developed tDI. All patients were treated at the authors' home institution between 2008 and 2012. We extracted patient demographics, clinical courses, laboratory data trends, and medical records. We present these cases in chronological order to illustrate the changes in patient management that occurred over time as we became more familiar with this phenomenon. We also provide a summary of our current management strategy for patients receiving AVP and concurrent sodium replacement.

The six patients (4 men and 2 women) had a variety of overlapping disease processes, including aneurysmal subarachnoid hemorrhage (SAH) from multiple different vascular territories, traumatic SAH, aneurysmal intraparenchymal and intraventricular hemorrhage, glioblastoma, epidural hematoma and traumatic brain injury, and sepsis. Indications for the use of AVP included the maintenance of supranormal blood pressure for the treatment of vasospasm, the augmentation of mean arterial pressure for the support of cerebral perfusion pressure in the setting of intracranial hypertension, and the avoidance of hypotension in sepsis. Three of the 6 patients received barbiturates as treatment for intracranial hypertension. Three of the 6 patients were being treated for SIADH and/or cerebral salt wasting (CSW) before their development of diabetes insipidus (DI), and 2 of the 3 patients were receiving demeclocycline. The patients had no other comorbidities in common. None of the patients had imaging findings suggestive of an injury to the hypothalamus. Table 1 summarizes the characteristics of the 6 patients.

At our institution, DI is diagnosed in the neurosurgical intensive care unit when 3 criteria are met: a serum sodium level greater than 147 mEq/L, a urine output greater than 200 mL/hr, and a urine specific gravity less than 1.005. The urine specific gravity is frequently used at our institution instead of urine osmolality when a quick, bedside assessment of overall urine solute concentration is needed. Despite the limitations of urine specific gravity, specifically the overestimation of specific gravity in patients who have received intravenous contrast agents, this overestimation is not believed to be clinically significant because DI is diagnosed with a low urine specific gravity.

CASE SERIES

Clinical details for patients 1, 3, and 5 are provided below. Table 1 and Figures 1–6 provide summary clinical details and laboratory values for all 6 patients.

Patient 1

A 48-year-old man presented to the emergency department with a Glasgow Coma Scale (GCS) score of 14, and computed tomography (CT) angiography showing a Fisher grade II SAH and an anterior communicating artery aneurysm. On the day of admission, an external ventricular drain was placed, and the patient was taken to the operating room (OR) for an emergent right orbitozygomatic craniotomy and aneurysm clipping procedure. The patient's postoperative course was complicated by severe symptomatic vasospasm that required endovascular treatment in addition to blood pressure augmentation and sodium replacement. On hospital day 11, an AVP infusion was started as a third-line vasopressor, in addition to norepinephrine and phenylephrine (Figure 1). The patient was being treated concurrently for SIADH with 3% hypertonic saline and demeclocycline. On hospital day 14, the AVP infusion was stopped. Over the next 12 hours, the patient developed significant diuresis (urinating as much as 1000 mL/hour) and