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Pre-existing undiagnosed central diabetes insipidus unmasked after renal transplantation

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Abstract
Central diabetes insipidus (CDI) is characterized clinically by the presence of polyuria with the subsequent development of volume depletion and hypernatremia. In patients with dialysis-dependent end-stage renal disease (ESRD), neither of these findings can be expressed due to the absence of renal function. A 59-year-old woman with anuric ESRD of unknown etiology had been on peritoneal dialysis for 8 years prior to receiving a cadaveric allograft. Postoperatively, she developed persistent polyuria and hypernatremia. A desmopressin test confirmed the diagnosis of CDI. A magnetic resonance imaging (MRI) of the brain revealed an empty sella turcica. Maintenance therapy with intranasal desmopressin resulted in complete resolution of the polyuria. At 6-month follow-up on daily desmopressin, the patient maintains normal serum sodium levels and stable allograft function. This is a unique case of CDI from empty sella syndrome (ESS) that was unmasked only after the restoration of normal renal function following successful renal transplantation.

Keywords: central diabetes insipidus; empty sella syndrome; end-stage kidney disease; renal transplantation

Introduction

Central diabetes insipidus (CDI) results from any condition that impairs the synthesis, transport and release of antidiuretic hormone (ADH). Clinically, ADH deficiency is manifested as an increased thirst mechanism leading to polydipsia and polyuria. The clinical presentation will vary depending on the underlying cause of neurohypophyseal dysfunction, and may include symptoms related to multiple endocrine deficiencies. In the setting of dialysis-dependent end-stage renal disease (ESRD), a new onset of CDI is largely asymptomatic and may, therefore, go unrecognized. We describe a case of CDI in a renal transplant recipient, in whom the restoration of renal function unmasked preexisting CDI, leading to severe polyuria and hypernatremia that were corrected with desmopressin.

Case description

A 59-year-old woman was admitted to undergo deceased donor kidney transplantation. The patient had been diagnosed with ESRD 8 years before and had received peritoneal dialysis since then. Her medical history only included concomitant hypertension, but she never had a native kidney biopsy to confirm the cause of her ESRD. Her native kidney urine output (UOP) declined while she was on peritoneal dialysis to the point where she was completely anuric at the time of transplantation.

Before surgery, the temperature was 36.4°C, her pulse rate was 90 beats per minute, the blood pressure was 137/79 mmHg and the respiratory rate was 16 breaths per minute; the remainder of the examination was normal. The serum sodium level was 136 mmol/L and the levels of the other electrolytes were within the normal limits. The blood urea nitrogen (BUN) and serum creatinine were 32 mg/dL and 2.4 mg/dL, respectively.

Diuresis started within the first hour of surgery and rapidly exceeded 600 mL/h with a total UOP of 10 L 24 h after surgery. Over the following days, her UOP remained high, up to 12 L/day. Her serum sodium and serum osmolality increased up to 161 mmol/L and 327 mOsm/Kg respectively, despite treatment with free water. As the urine osmolality was significantly low, diabetes insipidus was suspected, and intravenous desmopressin 4 µg was given on the sixth hospital day. Three hours later, the urine osmolality rose from 67 to 219 mOsm/Kg, the serum sodium level and serum osmolality dropped from 159 to 146 mmol/L and from 317 to 297 mOsm/Kg respectively, which confirmed the diagnosis of CDI. Maintenance therapy with intranasal desmopressin 10 µg was started with subsequent improvement of the symptoms. Magnetic resonance imaging (MRI) of the brain revealed

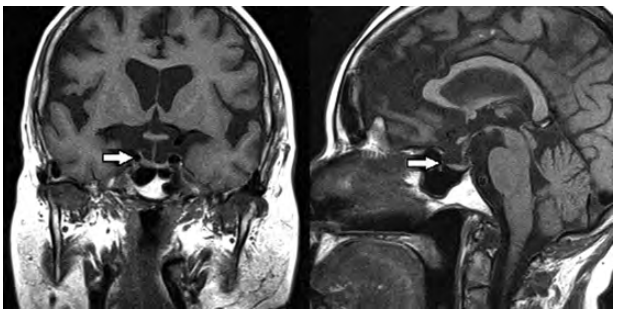

Fig. 1. Coronal and sagittal views of T1-weighted MR image of the brain.

empty sella turcica (Figure 1). The rest of the anterior pituitary hormone levels were within the normal limits.

The patient was discharged with a diagnosis of CDI and empty sella syndrome (ESS). At 6 months follow-up on daily desmopressin, the patient remained clinically stable with normal serum sodium levels and stable renal allograft function.

Discussion

Unrecognized CDI in patients with ESRD which becomes apparent only after successful kidney transplantation is a very rare occurrence, with only five published cases [1–5] (Table 1). This case illustrates the typical pattern of CDI, which includes polyuria, polydipsia, hypernatremia and volume depletion that could not occur in our patient while she was on dialysis because she was anuric. It was only after the placement of a successful renal allograft that these clinical and biochemical manifestations of CDI were able to develop.

Polyuria in the period immediately following the renal transplantation is a transient phenomenon, and it usually represents the first sign of progressive recovery of the kidney function ahead of the decrease in serum creatinine or BUN [6, 7]. In most cases, the UOP is 5–8 L/day and decreases within a few days to normal levels without therapeutic intervention [8]. However, in our patient the UOP remained up to 12 L/day for a week, and hypernatremia and hyperosmolality developed in spite of water deficit replacement with hypotonic fluids which improved only after intravenous desmopressin, confirming the diagnosis of CDI. Polyuria was also the initial symptom in all the previously reported cases, with the UOP ranging from 8 to 20 L/day, and appeared within 24 h after transplantation except in one patient [5], in whom clinical CDI was not evident until 1 week after surgery.

ADH deficiency arose after the occurrence of chronic kidney disease (CKD) in all patients, except in two in whom polyuria improved once they developed CKD and recurred after renal transplantation [1, 2]. People with CKD have an impairment of renal tubular solutes and water excretion, and free water excretion by the failing native kidneys is relatively fixed regardless of the volume status and ADH level. Moreover, regular fluid and solute manipulation with dialysis further mask symptoms of CDI [5]. Either intravenous or intranasal desmopressin has been effective in the initial treatment of a renal transplant recipient with CDI.

Table 1. Characteristics of the published cases of CDI disclosed after renal transplantation

Author/year/country	Gender	Age	Risk factor for CDI	Type of graft	Initial symptom of CDI	Time after transplant when CDI became apparent	U/O	Serum osmolality (mOsm/kg)	Urine osmolality (mOsm/kg)	Serum Na+ (mmol/L)	Initial dose of desmopressin	Dose of desmopressin when discharged
Zeller *et al.*, 1985, USA [1]	F	10	None	Deceased donor	Polyuria	Not mentioned	8.9 L/day	319	Not mentioned	Normal	Not mentioned	10 µg intranasal
Launey-Puybasset *et al.*1990, France [2]	M	42	Genetic	Not mentioned	Polyuria	First day	17 L/day	Not mentioned	Not mentioned	151	Not mentioned	5 µg daily
Henne *et al.* 2001, Germany [3]	F	12	Craniopharyngioma	Living-related donor	Polyuria	First day	1000 mL/h	333	233	155	1 µg/day IV continuous infusion	10 µg intranasal twice daily
Yamaguchi *et al.*, 2008, Japan [4]	M	31	None	Living-related donor	Polyuria	First day	10 L/day	289	280	140	2.5 µg/d intranasal	2.5 µg intranasal daily
Kim and Holdaway 2010, New Zealand [5]	F	60	Hypothalamic ischemia	Deceased donor	Polyuria	First week	9–11 L/day	295	136	137	10 µg twice daily intranasal	10 µg intranasal twice daily
Our patient, 2011, USA.	F	59	ESS	Deceased donor	Polyuria	First day	8–11 L/day	324	67	161	4 µg IV bolus	10 µg intranasal daily

Both primary and secondary forms of CDI have been reported among these post-transplant cases. Craniopharyngioma [3] and ischemic hypothalamic damage secondary to aneurysmal bleed [5] have been described, and the cases where no cause was found were considered idiopathic CDI, including one patient who inherited CDI in an autosomal dominant manner [2]. Our patient had imaging studies that revealed a normal brain, except for an empty sella turcica. An empty sella can be a result of a secondary pituitary injury from any tumor that was either previously removed, treated with radiation or underwent infarction. Alternatively, it can be a primary disorder from a mechanical defect in the sella turcica, leading to cerebrospinal fluid expansion and an enlarged sella [9]. When hormonal deficiencies are present, it carries the designation of ESS [10]. ESS is a rare cause of CDI, and is usually associated with alteration of anterior pituitary function [9, 10]. Since our patient had no history of pituitary or intracranial insult, CDI appears to be a manifestation of primary ESS. To the best of our knowledge, this constitutes the first reported case of isolated CDI as a manifestation of ESS in a recipient of a renal allograft.

In conclusion, this is a unique case demonstrating how the clinical manifestations of CDI can be completely silent and unrecognized in the setting of CKD and also highlights the importance of prompt recognition and treatment with desmopressin, in order to avoid impairment of graft function.

Conflict of interest statement. None declared.

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