

Central diabetes insipidus and burn trauma

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Abstract

Diabetes insipidus (DI) is characterized by polyuria and polydipsia. In most cases, the condition results from either an inadequate release or resistance to the activity of antidiuretic hormone in the renal collecting tubules. The underlying pathophysiology may be related to the destruction or degeneration of neurons from inflammatory, autoimmune diseases, vascular diseases, Langerhans cell histiocytosis, sarcoidosis, or trauma. However, a large majority of diabetes insipidus cases (50%) are considered idiopathic. An exceedingly rare cause of idiopathic central DI occurs in burn injuries, which has only been reported in eight cases. We present an extremely rare case of idiopathic DI in a 15-year-old male with 76% total body surface area (TBSA) burns with the development of idiopathic central DI. An extensive literature review was accomplished to compare this case with the small number of previously reported case reports of idiopathic DI in burn patients.

Keywords

Diabetes insipidus, central diabetes insipidus, nephrogenic diabetes insipidus, burn injury, desmopressin

Lay Summary

Diabetes insipidus (DI) is a rare complication of burn injuries that results from the destruction of neurons involved in the secretion of antidiuretic hormone from the pituitary gland. Only eight cases of DI have been reported in the literature in association to burn injuries. The patient in this case report received immediate fluid resuscitation, burn treatment, and intensive observation after the initial burn injury. The rapid response was likely the main reason for the absence of neurological damage as reported in the CT image. Therefore, the treatment of burn injuries remains an important step for reducing neurological damage and hormonal dysregulation leading to diabetes insipidus.

Introduction

Diabetes insipidus (DI) is an endocrine disorder characterized by excessive urination and polydipsia due to either an inadequate release of antidiuretic hormone or resistance to antidiuretic

hormone in the renal collecting tubules.¹ The primary causes of central DI include autoimmune disorders, vascular abnormalities, or trauma; however, more than 50% of DI are idiopathic.¹ In contrast, nephrogenic DI is due to renal insensitivity towards ADH activity and may occur from

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either congenital factors or acquired factors, such as electrolyte abnormalities, obstruction, or drug-induced.¹ An exceedingly rare cause of idiopathic central DI occurs in burn injuries. Although the mechanism of action remains unknown, it is believed that a combination of reduced blood flow and carbon monoxide from smoke fumes might affect neurons involved in releasing anti-diuretic hormone (ADH). We present a case of a 15-year-old male with 76% total body surface area (TBSA) burns with the development of idiopathic central DI. Furthermore, this case is compared to a small number of previously reported case reports of idiopathic DI in burn patients (eight cases) through a review of the literature.

Case report

A 15-year-old Caucasian male was transported to the TJH Regional Burn Center at UMC, Lubbock, TX after sustaining major burns 76% total body surface area (TBSA) from lighting trash on fire doused with gasoline. The patient's past medical history includes asthma and epilepsy, and home medications include Claritin-D taken twice daily and Xopenex HFA 45 mcg/inh. All other pertinent histories are noncontributory. On arrival, physical examination of the patient revealed hypothermia with a tympanic temperature of 93.6°F (34.2°C), a normotensive blood pressure of 134/82 mmHg, and a labile heart rate ranging from 106 to 146 beats/min. The patient was tachypneic with a respiratory rate of 25 respirations per minute. Skin assessment demonstrated partial to full thickness burns on 76% of the TBSA covering the head, neck, bilateral upper extremities, anterior chest, bilateral lower extremities, and back.

The patient was intubated at the scene by emergency medical services (EMS) due to presence of carbonaceous sputum. Prior to arrival, the level 1 trauma team activation was initiated. Upon presentation three hours post-injury, standard burn resuscitation was administered. Additionally, the patient underwent bronchoscopy due to a secondary concern for smoke inhalation injury. Bronchoscopy findings were significant for moderate amounts of carbonaceous deposits throughout the upper and lower bronchus, worse on the right side, with grade II inhalation injury assigned. Fluid resuscitation was calculated based on the modified Parkland formula (2 cc x 76 TBSA x 80 kg) requiring a total of 12 L of fluid within the first 24 h of which 2.4 L of crystalloid was administered prior to arrival. Due to the circumferential burns present on the upper

extremities and concern of the development of compartment syndrome, bilateral forearm escharotomies were performed. The patient required large amounts of lactated ringers to maintain minimally acceptable urine output (UO) (0.5cc/kg/hr), which led to the addition of 1.1 L of 5% albumin and 3.5 units of fresh frozen plasma (FFP).

The patient received 2.5 L of fluid prior to arrival, and fluids were started at a rate of 350 mL/hour upon arrival. Per protocol, this rate was titrated up to a rate of 600 mL/hour in order to meet the goal urine output of at least 0.5 mL/kg/hour and mean arterial pressure (MAP) of at least 60 mmHg. Due to the high rate of fluid administration needed to meet this urine output goal, HAT (hydrocortisone, ascorbic acid, thiamine) was started for 48 h. Additionally, both fresh frozen plasma (FFP) and 5% albumin solution were started at a rate of 100 mL/hour for a total of 4 units of FFP and 75 gms of albumin in total over the course of 24 h.

The patient's total fluid resuscitation goal was met within 24 h of admission. Maintenance fluid of D5 ½ normal saline with 20 milliequivalents of potassium chloride at a rate of 125mL/hour was then started. Urine output was well above the goal at approximately 1 mL/kg/hr. By hospital day 2, maintenance fluids were discontinued, and urine output continued to be adequate.

Treatment for the burn shock was reduced by the second post injury day (PID) and he was successfully extubated. The patient underwent a total of eight operations while admitted, beginning with escharotomies to bilateral forearms PID 0 followed by excision & grafting (E&G) to bilateral hands PID 4. No immediate postoperative complications occurred (i.e., bleeding). However, the patient developed septic shock secondary to *Acinetobacter* bacteremia with decreased mentation on PID 7 prompting re-intubation. The patient's vitals were significant for a temperature of 106.7° F (41.5°C), heart rate of 173 beats per minute, respiratory rate of 25 respirations per minute, mean arterial pressure (MAP) of 59 and laboratory findings were significant for PO₂ of 50 mmHg, lactate of 1.98 mmol/L, and procalcitonin of 9.8 ng/ml. Blood and sputum cultures were positive for carbapenem-resistant *Acinetobacter baumannii*. Antimicrobial treatment was initiated with 3 g Unasyn three times daily, 1 mg/kg Eravacycline two times daily, and 15,000 to 25,000 units/kg/day Polymyxin for 14 days. By PID 9, the patient was hemodynamically stable and underwent E&G left lower extremity. He was extubated PID 10 and underwent E&G of the left upper

extremity followed by E&G of the chest and abdomen PID 13.

The patient's status deteriorated again on PID 14 after becoming hypotensive with BP of 70/30 and MAP as low as 38 mmHg necessitating resuscitation. Tissue cultures remained positive for *A. baumannii* and *Pseudomonas Aeruginosa*, and ciprofloxacin and meropenem were initiated. Patient developed colonic pseudo-obstruction for which a cecostomy tube was placed on PID 16. On PID 18, the patient desaturated due to mucus plugging and bronchospasm, which necessitated re-intubation and a chest tube was placed due to a left hemothorax seen on chest x-ray. The patient clinically improved over the next 24 h and was extubated with chest tube removal. The patient underwent subsequent operations including Epicel harvest from right upper extremity and right lower extremity PID 23, Epicel to right upper extremity and right lower extremity PID 24, E&G left upper extremity and left lower extremity PID 51, and E&G right lower extremity, right upper extremity, and right flank on PID 58 (Figure 1).

Over the following two weeks (PID 29 to PID 43), his serum sodium was elevated and urine output gradually increased. Mean serum electrolytes were abnormal for much of this time, requiring standard replacement per day of potassium, magnesium, and phosphate as needed. Electrolyte levels were further altered due to new onset polyuria of 4.1cc/kg/hr over 24 h on PID 26, increased from an average of 2.9cc/kg/hr for the previous week. This new onset diuresis was originally

attributed to the high nitrogen load from tube feeding and urine alkalization from citrate and acetate-containing medications, namely Gabapentin (acetate-containing) for neuropathic pain and Epogen (citrate-containing) to stimulate red blood cell production. However, due to the persistent hypernatremia and polyuria, the patient's care team suspected DI and considered administering desmopressin (DDAVP) orally. Serum and urine osmolality showed borderline results for confirmation of this diagnosis of 304 mOsm/kg and 460 mOsm/kg, respectively (Figure 2). Pediatric endocrinology was consulted secondary to increased urine output of 5L (3.1cc/kg/hr) in 24 h, serum sodium level of 149 mmol/L, serum osmolality of 308 mOsm/kg, and urine osmolality of 430 mOsm/kg, which further raised suspicion for DI. A single dose of 2 mcg DDAVP was administered on PID 31, yet urine output continued to increase to 5.5L (3.4cc/kg/hr) collected in the next 24 h and serum sodium level, serum osmolality, and urine osmolality remained nearly unchanged.

Another dose of 2 mcg DDAVP was administered, followed by DDAVP three times daily as recommended by the endocrine team. Urine electrolytes, osmolality, and specific gravity were measured every 3 h to monitor response. The patient had massive diuresis on PID 41, 10 days after the first dose of DDAVP therapy, with UO increasing from 2.9cc/kg/hr (4.6 L/24h) to 4.3cc/kg/hr (6.9 L/24h). Therefore, the dose was increased

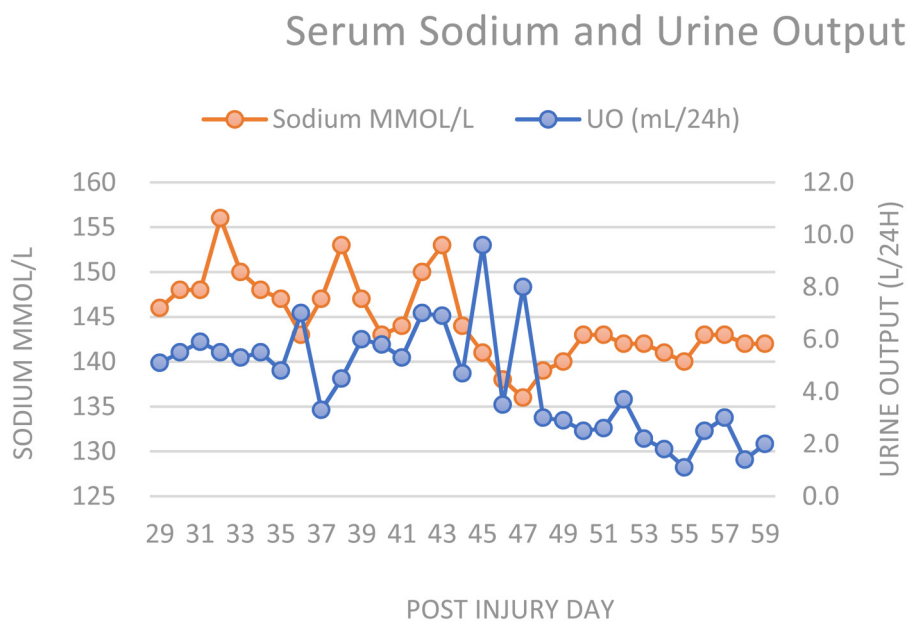


Figure 1. Serum sodium and urinary output during hospitalization.

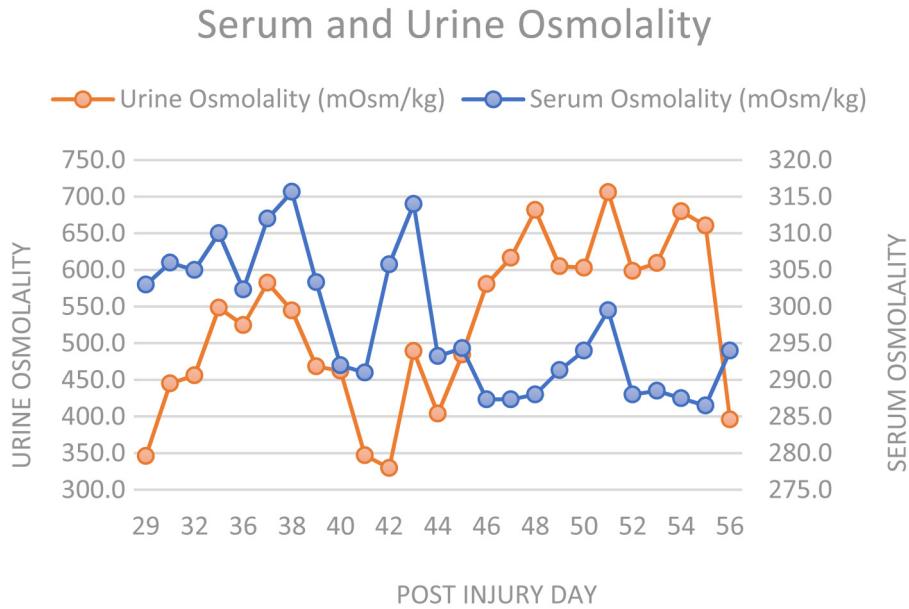


Figure 2. Serum and urinary osmolality during hospitalization.

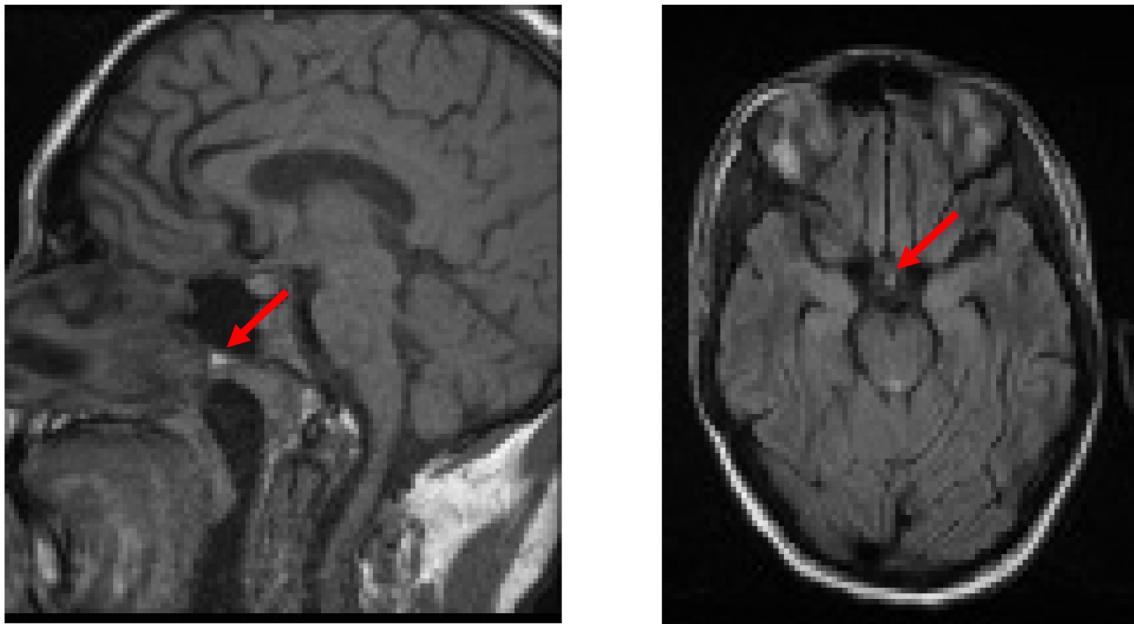


Figure 3. A sagittal and transverse cross section of brain showing pituitary gland.

from 3 mcg to 4 mcg three times daily. The MRI of the brain showed the pituitary gland normal in size, configuration, and enhancement. No other intracranial enhancement was of note besides a tiny bright spot on the pituitary gland, as shown in Figure 3. However, this was determined to be a benign change in the MRI. Urine output (UO) increased from 2.9cc/kg/hr (4.7L/24hr) on PID 44 to 5.0cc/kg/hr (9.5L/24hr) on PID 45, therefore the DDAVP dose was increased to 5 mcg

four times daily with incremental improvement in polyuria over the next several days. The dose was decreased to 4 mcg four times daily on PID 57 with continued resolution of his polyuria. After his second dose of DDAVP on PID 59 the endocrine team recommended to hold the remaining DDAVP doses for that day and reassess for further need. There was no significant increase in the urine osmolality and serum electrolytes and osmolality remained in the normal range; therefore,

Table 1. Characteristics of burn patients with diabetes insipidus.

Author	Year	Number of Patients	Age (Years)	Gender	Burn Injury Source	Total Body Surface Area (%)	Treatment
Vani et al. ¹²	2021	1	32	Male	N/A	50%	0.2 mcg/kg/hr (i.v.)
Dash et al. ¹³	2017	1	35	Female	Facial burns from domestic quarrel	40%	None
Muyldermans et al. ⁸	2016	1	34	Male	Burns with sevoflurane	52%	2 µg Desmopressin twice daily (i.v.)
Gende et al. ⁹	2011	1	23	Female	Kerosene burn	65%	Carbamazepine at 200 mg three times a day (oral)
Inoue et al. ⁷	2008	3	31,21, and 20	2 Males, 1 Female	Smoke inhalation burn from charcoal	None	One patient died from shock before treatment was initiated for diabetes insipidus
Ozdemir et al. ⁵	2002	1	29	Female	Electric shock injury	None	2-4 µg Desmopressin twice daily (subcutaneous)
Urquhart et al. ⁶	1994	2	Young	Male	High-voltage electrical burn	None	None; vasopressin (i.v.)
Haleblian et al. ⁴	1985	1	58	Female	Apartment fire	30%	Vasopressin 0.2 units/hr (i.v.)

the endocrine team recommended to cease DDAVP therapy on PID 60 and continue monitoring the UO. The patient continued to clinically improve and was discharged to a rehabilitation facility on PID 61.

Methods

A comprehensive literature review was performed at the end of April 2022 within the PubMed database using the keyword search phrases “burn” and “diabetes insipidus” with no date restriction. Initially, 17 articles were included after the initial search; however, eight studies were excluded. The other nine studies were not included because they did not examine burn injuries and the development of diabetes insipidus. Of the nine studies, one case report was not included due to language

restrictions. Our findings, including a review of the results, are summarized in Table 1.

Discussion

Despite being well-understood, the diagnostic challenge for DI requires confirming both the presence of polyuria and the underlying cause in order to provide the correct treatment regimen.² A misdiagnosis of the underlying cause can lead to an inappropriate level of desmopressin that can lead to hyponatremia and death.² This is especially true in the case of rarer causes of DI, such as burn wounds. Diabetes insipidus is most often caused by the destruction or degeneration of neurons in the supraoptic and paraventricular nuclei or from insensitivity to antidiuretic hormone at the kidney level. Genetic mutations in arginine vasopressin 2

receptor and the aquaporin 2 protein can also lead to familial autosomal recessive and dominant forms of nephrogenic diabetes insipidus.³ Most causes of diabetes insipidus (20%–50%) are considered idiopathic.³ As shown in Table 1, burn-associated diabetes insipidus is a rare complication. We found only eight known case reports describing DI associated with burn injury.^{4–9} The previous case reports of burn-related diabetes insipidus occur in younger patients with total body surface areas greater than 30%. Both male and female patients were equally likely to develop burn-related diabetes insipidus. Anesthetic agents received by our patient during his various procedures consisted of Fentanyl, Lidocaine 2%, Propofol, Ketamine, Rocuronium, Midazolam, and Dexmedetomidine. It is possible that the type of burn injury and its severity may be important risk factors for burn-related diabetes insipidus. Compared to many cases of diabetes insipidus, the patient reported in this case report did not show any abnormalities affecting the pituitary stalk or the hypothalamic-pituitary axis.¹⁰ The most common medications for burn-related diabetes insipidus included desmopressin (0.05 mg orally twice a day or 1–2 mcg IV twice a day), vasopressin (0.5 units/hour IV), and carbamazepine (200 mg orally 2 to 3 times a day) depending on the severity of diabetes insipidus and access to desmopressin.⁹

Current pathological studies post-mortem fluid samples suggest cutaneous fluid loss through sweating and burns leads to hypernatremia and cerebral dehydration resulting in central nervous system depression (impaired mental function, confusion, coma, and death) and damage.¹¹ The patient in this case report received immediate fluid resuscitation, burn treatment, and intensive observation after the initial burn injury. The rapid response was likely the main reason for the absence of neurological damage as reported in the CT image. Therefore, the treatment of burn injuries remains an important step for reducing neurological damage and hormonal dysregulation leading to diabetes insipidus. However, further research is required to elucidate the mechanism and risk factors for this rare complication


Declaration of conflicting interests

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