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BRIEF REPORT

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Dialysis disequilibrium syndrome: an unusual cause of respiratory failure in the medical intensive care unit

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Abstract We describe a case of the dialysis disequilibrium syndrome (DDS) that was marked by the rapid onset of cerebral edema and the subsequent development of acute respiratory failure. The patient was treated successfully with a combination of mechanical hyperventilation and mannitol. The clinical presentation, pathogenesis, prevention and treatment of the entity are discussed.

Key words Dialysis disequilibrium syndrome (DDS) · Respiratory failure · Cerebral edema · Mechanical ventilation

Introduction

Dialysis is a frequently used treatment modality in the intensive care unit (ICU). The dialysis disequilibrium syndrome (DDS) was first described in 1962 [1] and is a rare, acute complication of dialysis that occurs in the setting of end-stage renal disease. We report a case of DDS that was complicated by acute respiratory failure that resulted in mechanical ventilation. To our knowledge, this is the first reported case of successful recovery from DDS complicated by marked cerebral edema and respiratory failure.

Case report

A 22-year-old Asian female with an unremarkable past medical history presented to the emergency room with a 2-week history of lethargy, decreased appetite, constipation and headache. Physical examination at presentation was remarkable for a weight of 37 kg, an elevated blood pressure at 151/90 mmHg and non-sustained clonus in the lower extremities. Laboratory data revealed sodium of 142(135–145) mEq/l, potassium 4.9(3.5–5.0) mEq/l, chloride 113(92–109) mmol/l, bicarbonate 8(24–31) mmol/l, BUN (blood urea nitrogen) 194(8–25) mg/dl, creatinine 18.3(0.5–1.2) mg/dl, albumin 3.2(3.5–5.0) g/dl, calcium 5.1(8.0–10.4) mg/dl, phosphorus 11.2(2.6–4.6) mg/dl, creatinine phosphokinase 592(20–170) IU/l, hemoglobin 3.3(12–16) g/dl and hematocrit 10(37–47)%. The

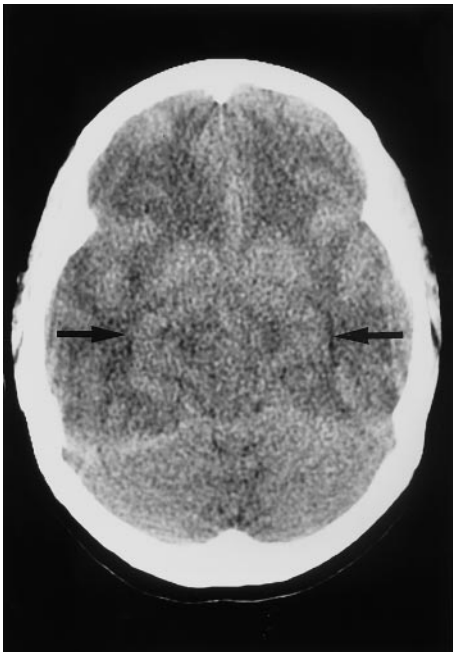

Fig. 1 Head CT showing marked cerebral edema with almost complete obliteration of lateral ventricles (*arrowed*)

measured and calculated serum osmolalities were 353(274–296) mOsm/kg and 358 mOsm/kg, respectively. The urinalysis revealed proteinuria and microscopic hematuria and sediment granular casts. A kidney ultrasound was performed and revealed two small atrophic kidneys. She received two ampoules of 10% calcium gluconate and was initiated on hemodialysis via a temporary femoral venous catheter, using a small-surface area dialyzer of 1 m^2 (C-101, Terumo, Tokyo, Japan). The blood flow was maintained at 150 ml/min for 1.5 h, the ultrafiltration rate kept at a minimum and the dialysate bath adjusted at a high sodium and calcium concentration both to avoid hyponatremia and correct hypocalcemia. Following the first dialysis session, the BUN level fell from 199 to 110 mg/dl, resulting in a urea reduction ratio (URR) of 44%, and she experienced a brief period of somnolence that resolved spontaneously. On hospital day 2, she underwent a second hemodialysis session (15 h following the first session), achieving a URR of 40%.

One and a half hours post-dialysis, she developed hypertension (224/128 mmHg), headache, ventricular ectopia, myoclonic jerks of both arms and hyperreflexia. The myoclonic jerks resolved with lorazepam (2 mg), morphine sulfate (1 mg) and two ampoules of 10% calcium chloride. She subsequently developed Kussmaul breathing, her SaO_2 fell to 70%, both pupils became fixed and dilated and she was intubated and mechanically ventilated. At the time of intubation, her serum glucose was 178(67–109) mg/dl, calcium 8.3, sodium 144 and serum osmolality 334 mOsm/kg. An emergency head computed tomographic (CT) scan was obtained and revealed marked cerebral edema with almost complete obliteration of the lateral ventricles (Fig. 1). She was treated with intravenous mannitol (25 g) and hyperventilation to reduce intracranial pressure. Within 3 h her mental status had returned to normal and her neurologic signs had completely resolved. All subsequent dialysis treatments were adjusted to lower the BUN levels by approximately 30%. She was extubated 3 days later and was eventually discharged from the hospital on maintenance hemodialysis. In 1998 she underwent a successful kidney transplant in China.

Discussion

To our knowledge, this is the first reported case of a patient surviving respiratory arrest as a complication of cerebral edema due to the DDS. This syndrome, which is marked by cerebral edema, is considered to be due to the dialysis procedure per se [1, 2]. The DDS is typically observed in patients with end-stage renal disease (ESRD) who are being initiated on hemodialysis and is much less commonly seen in patients on chronic maintenance dialysis [1].

The clinical manifestations depend on the severity of the syndrome. Mild cases are characterized by restlessness, headache, nausea, vomiting, blurred vision, muscle twitching, disorientation, tremor and hypertension, while major symptomatology is marked by obtundation, seizures, coma and cardiac arrhythmias [1]. The more severe symptoms are much less common today compared with in the past [1]. The DDS usually occurs towards the end of dialysis but may be delayed for up to 24 h. The manifestations tend to be self-limited and full recovery is the usual outcome. When marked cerebral edema develops (as observed in the case we report), neurologic deficits may occur [1, 3] with resulting brain herniation and death [4]. Although cerebral edema is a consistent finding on CT scanning, the DDS remains a clinical diagnosis of exclusion since laboratory tests, including electroencephalography, are non-specific. The development of the above symptoms during dialysis is strongly suggestive of DDS. Nevertheless, there are a number of other disorders that must be excluded including subdural hematoma, metabolic disturbances (e.g. hyponatremia and hypoglycemia), and drug-induced encephalopathy, none of which were present in our patient at the time of onset of her symptoms.

Despite a decline in incidence, the DDS is still observed sporadically in patients with ESRD who are initiated on hemodialysis with large-surface area and high-flux dialyzers and short dialysis sessions. Risk factors for DDS include young age, severe azotemia and the use of a low dialysate sodium concentration. Other risk factors that may be seen in the critically ill patient in the ICU include recent cerebral vascular accidents, head trauma, subdural hematoma or conditions associated with cerebral edema including hyponatremia, hepatic encephalopathy and malignant hypertension [1, 4, 5]. It is postulated that pre-existing neurologic disorders increase the risk of cerebral edema during the initiation of dialysis. Full recovery following both respiratory arrest and florid neurologic findings in the setting of DDS (as observed in our patient) has not been previously reported.

The pathogenesis of the cerebral edema in DDS is not well understood, but there are two main theories, which we will review briefly. The first theory, known as the "reverse urea effect" [3], proposes that, as dialysis progresses, the clearance of urea from brain tissue lags behind that of plasma, resulting in the movement of free water from plasma to brain producing cerebral edema [1, 2, 6]. However, this concept has recently been disputed [2]. Indeed, an experimental animal model of DDS shows that urea levels in cerebral tissue rapidly equilibrate with those of plasma [2]. In addition, intradialytic paradoxical cerebro-spinal fluid acidosis is observed and is aborted by slower dialysis sessions [2]. The second theory proposes that the increase in brain water is due to the formation of new osmotically active solutes, so called "idiogenic osmoles", that create an osmotic gradient resulting in cerebral edema [6]. However, the composition of these idiogenic osmoles and the mechanism responsible for their formation is not clear and this hypothesis remains unproven [7].

A number of strategies are available to prevent DDS and are employed in patients undergoing dialysis for the first time, who are at the greatest risk of developing the syndrome. These preventative measures include the use of volumetric controlled dialysis machines, bicarbonate-based dialysate, high dialysate sodium concentration, earlier recognition of uremic states and earlier initiation of renal replacement therapy. The goal is to achieve a gradual rather than abrupt reduction in BUN concentration. This slow urea removal can be achieved by performing shorter and more frequent dialysis treatments, using small-surface area dialyzers and reduced blood flow rates. Patients who also have marked fluid overload can be treated with sequential hemofiltration (which removes less urea per unit of time) followed by conventional hemodialysis [1]. The prophylactic use of mannitol or anticonvulsants during dialysis is not recommended despite anecdotal reports of their efficacy. However, in certain circumstances where aggressive solute clearance may be warranted phenytoin should be administered prophylactically 12 h before dialysis [8]. Alternative dialysis techniques that have a lower urea clearance, including peritoneal dialysis and continuous hemofiltration should be considered as they are not usually complicated by the development of DDS. Finally, the addition of osmotically active solutes (such as mannitol, glycerol, albumin, urea or fructose) to the dialysate may help reduce the incidence of DDS [1], but is technically cumbersome and not commonly used in the clinical setting.

Once the diagnosis of DDS has been made, treatment consists of either reducing the rate of dialysis or discontinuing it temporarily. In both humans and experimental animals, this strategy of "slow" dialysis has been shown to be effective in preventing the DDS [9]. Severe forms of DDS with seizure activity can be reversed more rapidly by increasing the plasma osmolality with either 5 ml of 23 % saline or 12.5 g of hypertonic mannitol.

In summary, the DDS is an unusual cause of cerebral edema and acute respiratory failure in the ICU setting. Critical care physicians should be aware of this syndrome, as prompt recognition and appropriate management can lead to full recovery.

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