Journal of Clinical Anesthesia (2015) **27**, 164–167

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Journal of Clinical Anesthesia

Case Report

Fatal hyperammonemia after repeat renal transplantation☆

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Received 23 May 2013; revised 17 September 2014; accepted 24 September 2014

Keywords:
Acid-base balance;
Critical care issues;
Transplantation;
Kidney;
Drugs used in anesthesia and critical care medicine;
Fluid management/ replacement therapy

Abstract A 35-year-old man had symptomatic hyperammonemia and normal liver function after repeat kidney transplantation. He presented with gastrointestinal symptoms, which quickly progressed to altered mental status. Therapy was instituted to clear the ammonia, but the ammonia level continued to rise. Eventually, the patient became unresponsive, and an emergent computed tomographic scan showed cerebral herniation. Urine acids and serum organic acids were not diagnostic of any urea cycle disorder. Histology did not reveal a clear etiology for the hyperammonemia.
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1. Introduction

Hyperammonemia in adults is most commonly associated with hepatic dysfunction. Therefore, when a patient presents with an elevated plasma ammonia level in the setting of normal liver function, the differential diagnosis becomes very wide. These patients may require immediate treatment to avoid the neurologic sequelae of cerebral edema, herniation, seizures, coma, and death. A search of the available literature revealed only one other case of hyperammonemia after renal transplant.

2. Case report

A 35-year-old man with a history of congenital solitary kidney and reflux nephropathy had ureteroileal anastomosis and repeat renal transplantation. He presented on post-operative day 9 from deceased donor renal transplantation with nausea, vomiting, and altered mental status.

The patient was born with a left nonfunctioning kidney and right ureteral obstruction. He developed end-stage renal disease secondary to reflux nephropathy eventually requiring cadaveric renal transplant. Allograft failure in the transplant eventually led to a second renal transplant 7 years later.

Relevant patient allergies were to cytogam and vancomycin. His medical history included peptic ulcer disease, gastroesophageal reflux disease, hyperparathyroidism, and hypertension. His pertinent surgical history was notable for parathyroidectomy and bilateral arm arteriovenous fistulas.

On presentation, initial laboratory tests were negative for infection, and his serum creatinine was improved to 7.48 mg/dL compared to 12.36 mg/dL at discharge. He was

☆ Consent: Verbal consent for this publication was obtained from the next of kin. We were not able to reach them for written consent before submission of this case report.

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http://dx.doi.org/10.1016/j.jclinane.2014.09.008
0952-8180/Published by Elsevier Inc.

incidentally found to have an ammonia level of 646 μmol/L (reference range, 11-35 μmol/L), and a repeat level 3 hours later was 939 μmol/L. Of note, his hepatic transaminases and liver synthetic function tests were within normal limits.

Shortly after admission, he was noted to have declining mental status. He was intubated for airway protection and then transferred to the surgical intensive care unit. The genetics service was consulted and recommended placing the patient on extracorporeal membrane oxygenation with dialysis for rapid ammonia clearance. Because of the hemodynamic instability of the patient and the risk of hypotension in the setting of intracranial hypertension, continuous veno-venous dialysis was started. Arginine, sodium phenylbutyrate, and sodium benzoate were also initiated per the genetics consult service. Despite these measures, his ammonia continued to increase, and he eventually became unresponsive by that evening. Emergent computed tomographic scan showed cerebral edema and herniation (Fig. 1). He was found to be brain dead by transcranial Doppler the following morning.

The serum and urine laboratory test results were not consistent with a urea cycle disorder, and no definite etiology for the hyperammonemia was identified on histology. After review of the laboratory and autopsy findings, the pathology team postulated that this immunosuppressed patient with a ureteroileal diversion may have had a urinary tract infection with urease-positive bacteria. It was suspected that the organism could not be cultured due to recent treatment with broad spectrum antibiotics.

3. Discussion

Because significant hyperammonemia is lethal, initial efforts should be focused on decreasing the ammonia concentration to avoid cerebral edema, intracranial hypertension, and irreversible neurologic sequelae [1]. The methods of decreasing ammonia concentration should achieve one of the following goals: excretion of ammonia, decreasing exogenous nitrogen and ammonia production, and providing alternate pathways for ammonia excretion.

Excretion of ammonia is most effectively facilitated by hemodialysis. There are no accepted guidelines on the timing of initiation of hemodialysis. Mathias et al [2] suggests initiation of hemodialysis when ammonia levels are 3-4 times the upper limit of normal and/or levels are rapidly increasing or if the patient is encephalopathic. Clay and Hainline [1] recommend starting dialysis if the ammonia level remains >100 μmol/L and/or the etiology of hyperammonemia is not determined. Enns et al [3] started dialysis for any neonate with hyperammonemic encephalopathy or any patient who did not have a significant drop in ammonia levels within 8 hours of other treatment. Leonard and Morris [4] were more conservative and recommend hemodialysis initiation for any patient with ammonia levels >500 μmol/L. Peritoneal dialysis is not recommended for acute hyperammonemia due to the slower speed of ammonia reduction. Hemodialysis is up to 10 times more effective than peritoneal dialysis in ammonia elimination [2]. Levesque et al [5] demonstrated mean ammonia clearance rates of 261 mL/min and ammonia half-life of 60 minutes with hemodialysis in 1 case report. Some of the risks associated with hemodialysis included rebound increase in ammonia levels, hypokalemia, hypophosphatemia, and hypomagnesemia [2,5]. In addition, careful attention should be paid to the cerebral perfusion pressure and cerebral blood flow in the setting of intracranial hypertension [1].

Exogenous nitrogen load is limited by stopping the protein intake. There should be a concurrent increase in caloric intake in the form of dextrose and lipids. This measure will prevent protein catabolism [1,2,6,7].

In addition to ammonia excretion through dialysis, alternative pathways of nitrogen metabolism are facilitated by administering certain compounds [8]. Sodium benzoate, phenylacetate, and phenybutyrate combine with compounds

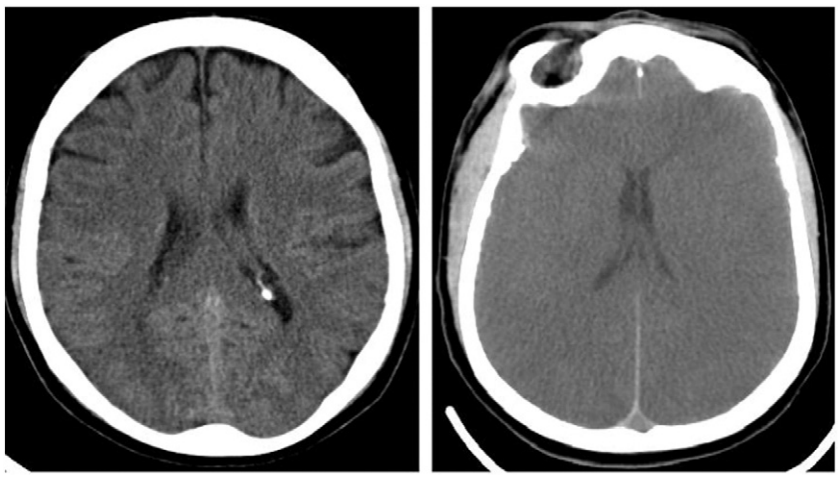

Fig. 1 Preherniation computed tomographic scan (left), cerebral edema, and herniation (right).