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Hypertonic saline-induced urolithiasis presenting as acute renal failure in a child with traumatic brain injury: A case report

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ABSTRACT

We report the case of a 4 year old female with severe traumatic brain injury who developed bilateral obstructing ureteral stones after hypertonic saline treatment. She developed calcium phosphate stones after two weeks of hypertonic saline therapy, and was successfully treated with ureteral stents and ureteroscopy. She has remained stone-free since that time. We postulate that an incomplete type 1 renal tubular acidosis made her intolerant to the acid and sodium load of the saline, and discuss other lithogenic factors of her presentation.

Introduction

The incidence of nephrolithiasis is increasing, with pediatric disease rising 6–10% annually over the last 25 years.[1] Children may not present with classic stone symptoms due to poor communication abilities, and a higher index of suspicion may be required to diagnose them. Accurate 24-h urine collection is difficult, and they are lost to adult nephrologists and urologist as they age. The majority of stone-forming children have an underlying metabolic or infectious etiology, and a family history and bilateral stone burden are commonly seen in those with metabolic derangements.[1,2] Immobility, medications, and other etiologies may precipitate stones or unmask underlying abnormalities, as evidenced by the following case.

Case presentation

A previously healthy 4 year old female presented to our hospital after sustaining a traumatic brain injury in a high-energy motor vehicle collision. A head CT scan revealed intracranial hemorrhage, for which she underwent an emergent craniotomy and external ventricular drain placement. Her workup included a CT abdomen and pelvis, which demonstrated normal kidneys and bladder without stones or hydronephrosis. Her family history was significant for nephrolithiasis in her mother and maternal grandmother.

She received 5 days of 3% hypertonic saline (HTS) as treatment for cerebral edema, with serum sodium in the 150's and a peak of 161mmol/L. She then received 6 days of sodium acetate, during which time her urine pH was 9. HTS was then restarted at 7%, with urinary output of 2–3.5ml/kg/hr over the following days with no urinary pH measurements. She received levetiracetam 20mg/kg BID from hospital days 5–25, and received enteral feeding throughout her hospital stay.

On hospital day 15, she was noted to be anuric and febrile. Her BUN was 58mg/dL with a creatinine rising to 2.47mg/dL from a baseline of 0.27. Labs showed a serum sodium of 150mmol/L, serum corrected calcium of 10.0mg/dL, and a serum phosphate of 5.3mg/dL. Renal ultrasound demonstrated bilateral hydroureteronephrosis and hyperechoic debris with shadow artifact in the collecting systems (Fig. 1). Non-contrast CT revealed bilateral stones throughout both collecting systems ranging from 2 to 5mm in diameter (Fig. 2).

She was taken urgently for cystoscopy and bilateral ureteral stent placement. Her creatinine returned to baseline two days later. Stone analysis revealed calcium phosphate. Urine cultures and analysis showed no evidence of infection and repeat renal ultrasound showed resolution of hydroureteronephrosis (Fig. 3).

Ureteroscopy two months later revealed no stones, and a large coagulum within the renal pelvis. She has remained stone-free without medical therapy with normal renal function.

Discussion

This is the first reported case of nephrolithiasis in the setting of traumatic brain injury and hypertonic saline administration.

A review of renal physiology is crucial in understanding the potential mechanism of stone formation. Filtered sodium passes through the proximal tubule of the nephron and is then reabsorbed by the NKCC2 channel of the thick ascending limb with potassium and chloride. Some

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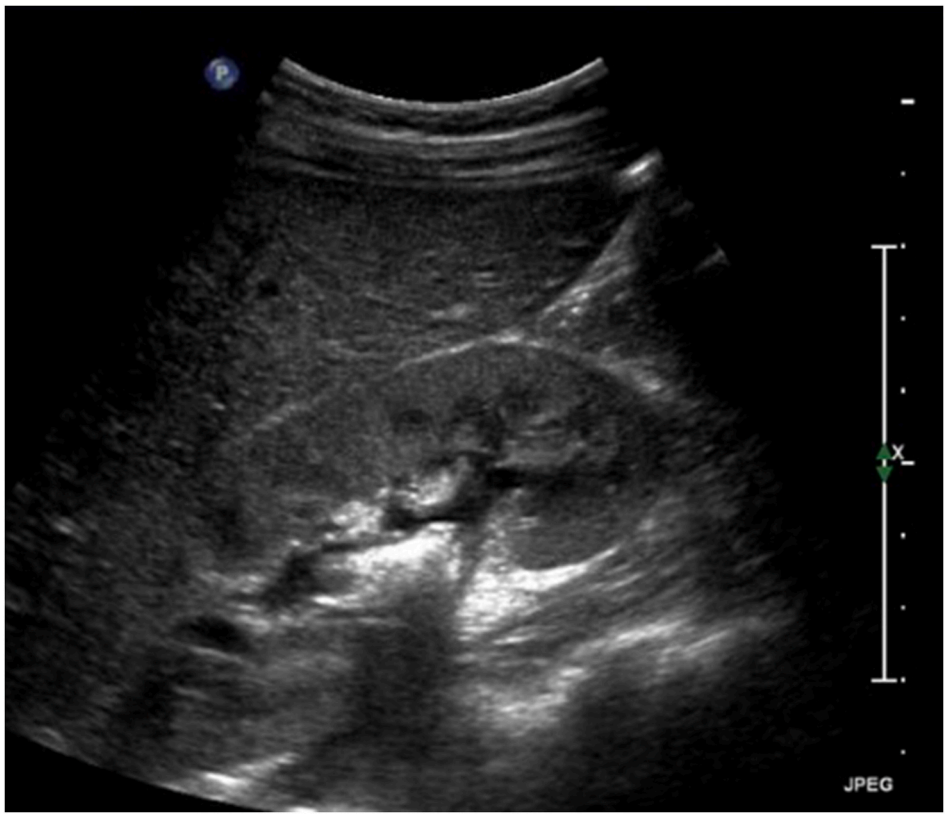

Fig. 1. Preoperative longitudinal ultrasound of right kidney demonstrating shadowing debris in renal pelvis.

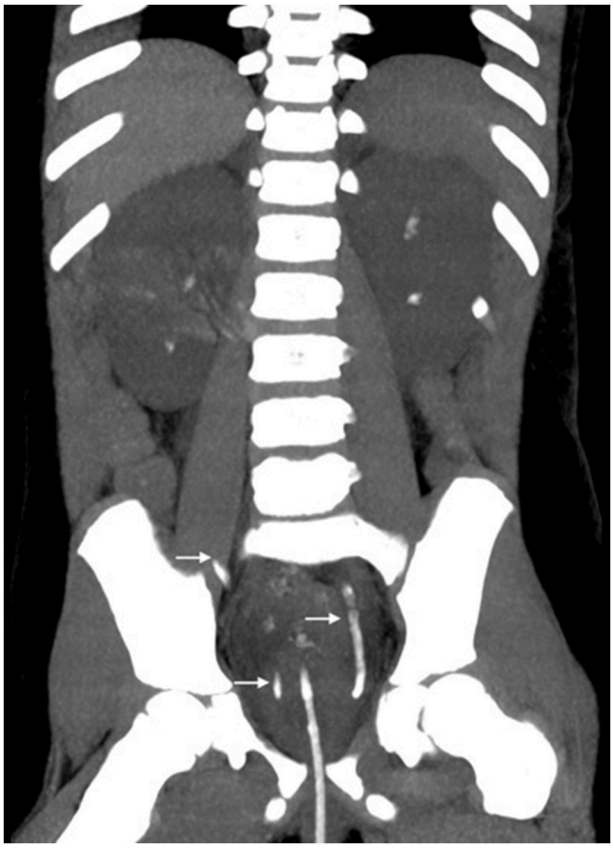

Fig. 2. Maximum Intensity Projection coronal non-contrast CT image demonstrating stones in bilateral renal pelvises and ureters (arrows).

potassium leaks back into the tubular lumen through the renal outer medullary potassium (ROMK) channels, increasing luminal charge and driving calcium back into the peritubular capillaries through the paracellular route. Increased plasma sodium modulates both of these transport proteins, ultimately leading to less calcium reabsorption and thus increased calciuria. We believe that her increased sodium levels could have led to her hypercalciuria.

Hypertonic saline has a pH of approximately 5.0, and as such would have induced an iatrogenic metabolic acidemia. Bone releases calcium and phosphate to buffer acidic loads through direct ion exchange and modulation of osteoclast/blast activity, as well as in response to immobilization, both factors found in this patient.[3] Corrected serum calcium levels remained within normal limits throughout her stay, but these would have underestimated her free serum calcium due to calcium-hydrogen exchange on the anionic albumin binding sites in acidemia. It seems reasonable that our patient with such a high salt load would develop calciuria through these mechanisms. Her stones were calcium phosphate, which forms in a high urinary pH, which corresponds to her pH of 9 that was previously mentioned.

Distal renal tubular acidosis (dRTA) is likely the underlying mechanism for her calcium phosphate stones. dRTA is caused by an inability to reabsorb bicarbonate, which leads to chronically alkaline urine. The proximal tubule responds by increasing citrate reabsorption, leaving an alkalotic urine low in citrate: a perfect milieu for calcium phosphate stone formation. This patient had no history of symptoms indicative of the hyperchloremic acidosis and severe hypokalemia often seen with dRTA (polydipsia, polyuria, weakness), which makes incomplete dRTA a potential diagnosis. Patients with incomplete dRTA only reveal their defect when challenged with an acid load, much like this patient.[4] Failure to acidify urine during acid loading is diagnostic for dRTA, and may prompt the initiation of potassium citrate supplementation to lower urinary calcium excretion and increase urinary citrate levels.[1]

An additional factor to consider in this patient is the levetiracetam

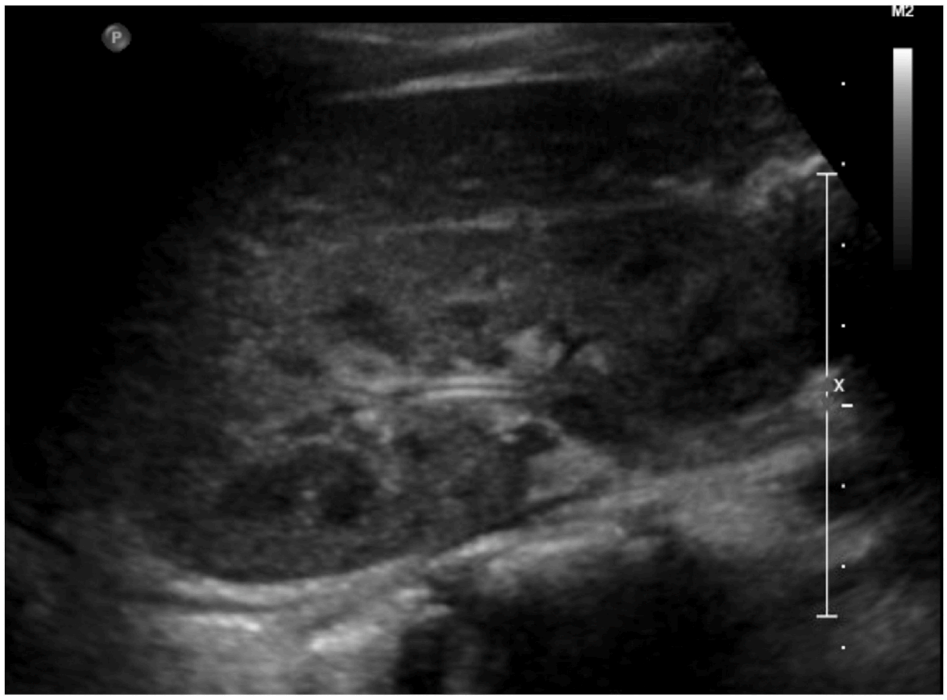

Fig. 3. Postoperative longitudinal ultrasound of the right kidney demonstating stent, resolution of caliectasis, and absence of debris.

she received. Some anti-epileptic drugs (AEDs) are known to increase stone risk. It is postulated that this is due to urine alkalization.[5] Our patient was on levetiracetam, which has not been studied regarding urinary pH or nephrolithiasis. It is reasonable, to suspect that her levetiracetam use may have increased her risk of stones by alkylinizing her urine, in the setting of a dRTA. It is also possible that partial precipitation of the drug may have caused the organic coagulum found at stent removal.

Conclusion

This case of HTS-induced obstructing nephrolithiasis presents a novel mechanism of iatrogenic stone formation and unmasking of RTA, and invites review of renal physiology and iatrogenic stone formation. Our patient returned for a follow-up with pediatric urology, at which time she continued to be stone-free with normal labs and blood pressure The patient will be periodically monitored by our multidisciplinary pediatric stone clinic to ensure she has no further stone episodes.

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