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Case report: Ampicillin-induced stone formation causing bilateral ureteral obstruction during pelvic surgery

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Introduction

Numerous medications can predispose patients to stone formation. Some induce metabolic changes that alter urine chemistries, such as topiramate, which can cause a mixed renal tubular acidosis. Others or their breakdown products form stones composed of the drugs themselves, like those that are renally excreted and become supersaturated in the urine in a favorable environment.[1,2] Like all stones, they can cause obstruction and infection.

Here we present a case of ampicillin stone formation in an 11-year-old girl during a pelvic reconstructive procedure, which required ureteral stenting to prevent obstruction from an institutional guideline's perioperative antimicrobial dosing. While there are many reports of amoxicillin and ampicillin crystalluria, there is only one account in the literature of an adult with resultant ureteral obstruction requiring intervention.[3–5] Our case is the first report, to our knowledge, in a child, and highlights the potential for significant crystal formation and if unrecognized, complete urinary obstruction. Since ampicillin is a commonly administered perioperatively, awareness of ampicillin stone formation during surgery is important.

Case presentation

An 11-year-old female with no prior medical history presented to the Emergency Department with 3-weeks of pelvic pain. MRI showed distal vaginal atresia with hematocolpos. She was subsequently taken to the operating room for cystoscopy, diagnostic laparoscopy, pelvic exploration, and flap vaginoplasty after admission the evening prior for bowel prep. Perioperative antibiotics included ampicillin, gentamicin, and flagyl. Ampicillin was administered at 35 mg/kg or 2000mg/dose every 2 hours per institutional guidelines. Gentamicin 120mg and flagyl 500mg were given once.

The procedure began with cystoscopy, which showed normal ureteral orifices with clear urine efflux and normal bladder mucosa. After the other portions of the case began, urine output through a foley catheter decreased. Given the bowel preparation a prerenal etiology was suspected and a fluid bolus given. However, urine output continued to decline with visible sediment in the urine along with new-onset hematuria; the decision was made to repeat cystoscopy at the end of the case. At that point, she had received 6000mg of ampicillin over a 5-h period. The remainder of the procedure continued without incident and a successful flap vaginoplasty was completed.

Cystoscopy revealed no evidence of injury, but numerous crystals floating within the bladder. Crystal chains were visualized from both ureteral orifices with bloody urine efflux. The chain emanating from the left ureteral orifice was grasped and removed; the crystal chain from the right ureteral orifice could not be grasped and the orifice remained obstructed (Fig. 1). Bilateral 6 Fr x 26 cm JJ stents were placed. Stone was sent for analysis and a Foley catheter was left in place. Postoperatively, the patient did well and her urine output normalized. A urinalysis sent 24 hours later showed a urine pH of 7.0. The patient's eGFR decreased initially from 105 to 78 mL/min/1.73m^2 but quickly returned to baseline. A urine culture from the OR was negative and her hematuria resolved.

On post-operative day seven she underwent cystoscopy and vaginoscopy and bilateral ureteroscopy with stent removal. Intravenous cefazolin was given. Flexible ureteroscopy was used to inspect both ureters and kidneys, showing no evidence of stone. Retrograde pyelograms showed good drainage bilaterally. A subsequent MAG3 renal scan was significant only for urine stagnation on the right side which responded promptly to lasix administration with a T ½ of 6.5 minutes on the left and 17 minutes on the right. The patient was discharged on post-operative day 9 from her initial procedure. Stone analysis returned sodium salt of ampicillin.

Discussion

Stone formation from antimicrobials is uncommon. During a pelvic reconstructive procedure, our patient developed bilateral obstructing ampicillin stones which required intraoperative manipulation and ureteral stenting. These developed within hours of starting the procedure. After adequate hydration and an eventual urine pH of 7.0, her urine

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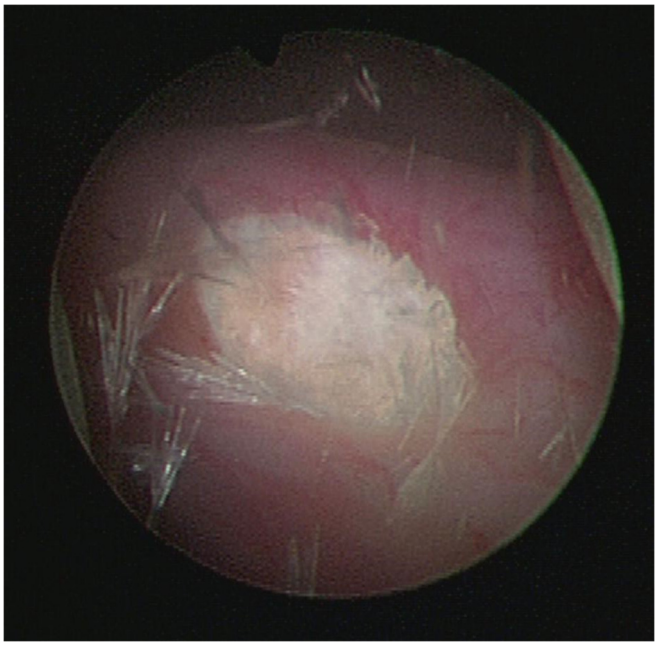

Fig. 1. Right ureteral orifice obstructed by ampicillin salt stone.

returned to normal within two days. Stones were not present on ureteroscopy seven days later. Although ampicillin crystalluria has been described, our case describes an acute process of obstruction that occurred in a patient during surgery, with cystoscopic view of obstruction of the ureteral orifice occurring at the time of stone formation.

Prior reports of ampicillin crystalluria focused primarily on microscopic crystal analyses, though some have addressed the possibility of acute renal failure and hematuria.[4] In these cases, ultrasound showed no hydronephrosis and conservative management pursued. When renal function is affected, the mechanism described is usually tubulointerstitial obstruction of crystals rather than ureteral obstruction.[4] Ours is the first report to our knowledge of ampicillin stones in a child and the first from surgical prophylaxis. Hematuria and oliguria were first noted during the surgery; re-evaluation cystoscopically for a post-renal etiology was possible intraoperatively. By stopping the agent and decompressing the upper tracts, deleterious effects were halted. Crystal dissolution and return to normal urine appearance within 1–2 days was concordant with prior reports with clinical improvement after cessation of the drug and hydration.[3]

Factors that favor crystalluria are ones that reduce urine solubility, including high drug levels, especially in pediatric patients, low diuresis, or an acidic pH.[3] Ampicillin crystals precipitate in acidic urine with a pKa of 2.5; it is possible that our patient had acidic urine since she was dehydrated. Her relative dehydration from bowel preparation and fasting prior to surgery is consistent with prior reports of ampicillin crystalluria which noted low fluid status in their patients.[3,5] Finally, the procedure was approximately 6 hours, resulting in ampicillin redosing per institutional guidelines. Our patient received 6g within six hours, or 35 mg/kg for three doses. However, this was a protocol dosing regimen, and åpatient factors likely played an additive role in facilitating stone formation. It is unknown if the patient would still have formed stones had she not been re-dosed.

Prevention of future similar events includes an institutional review of perioperative antibiotic dosing guidelines, taking into account procedure length and patient's hydration status at the time of surgery, and evaluation of alternative antibiotics.

Disclosures

The authors have no financial disclosures.

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