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CASE REPORT

A case of cephalothin-associated urolithiasis

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Ivan WM Lim[1]
Peter JO Stride[1,2]
Robert L Horvath[3]

[1]Department of Medicine, Redcliffe Hospital, Redcliffe, Queensland, Australia; [2]University of Queensland School of Medicine, Redcliffe, Queensland, Australia; [3]Infectious Diseases Department, Prince Charles Hospital, Brisbane, Queensland, Australia

Abstract: We present a case of osteomyelitis requiring prolonged intravenous cephalothin complicated by symptomatic calcium oxalate urocalculi formation. Patients on long-term β-lactam antibiotics with lower urinary tract symptoms may have urolithiasis rather than a urinary tract infection.

Keywords: urolithiasis, urinary tract infection, cephalothin

Case report

A previously healthy 39-year-old male was admitted with right mid-tibial osteomyelitis, having sustained a 0.3-cm laceration in his right shin 2 months earlier from cut foliage while chopping pine trees. He neglected this lesion, did not seek medical advice, and developed an ulcer with surrounding cellulitis.

After 1 month, the lesion was ~0.5 cm in diameter, but his general practitioner predicted healing without specific treatment. After 2 months, the lesion enlarged further with ulceration and necrosis necessitating hospital referral. The patient had no significant past medical history and denied smoking, diabetes, recent travels, or any history suggestive of immunodeficiency.

On admission, computed tomography of the right tibia revealed a gas-containing soft-tissue defect eroding the anterior adjacent cortex of tibia compatible with a subperiosteal abscess with osteomyelitis (Figure 1).

The lesion was washed, debrided, and covered with a vacuum-assisted closure (VAC) dressing. He was treated empirically with intravenous cephalothin 1 g QID. Methicillin-sensitive *Staphylococcus aureus* (MSSA) was cultured from wound swabs. Six weeks of therapy was planned via a peripherally inserted central catheter line to expedite home therapy.

However, after 5 weeks of therapy, he developed intense dysuria, frank hematuria with the passage of clots, and intermittent fever up to 39.5°C, and then a widespread erythematous rash following commencement of gentamicin for a suspected urinary tract infection.

Investigations

Results of the diagnostic tests are shown in Table 1. Urinary tract symptoms persisted during 6 days of therapy with gentamicin and continued cephalothin. His symptoms finally resolved slowly over the next 3 days, when gentamicin and cephalothin were ceased and replaced with oral trimethoprim. The patient denied

Correspondence: Peter JO Stride
Department of Medicine, Redcliffe Hospital, University of Queensland School of Medicine, Anzac Avenue, Redcliffe, Queensland, Australia 4020
Tel +61 04 17039111/+61 04 38837777
Fax +61 04 38837214
Email peter_stride@health.qld.gov.au

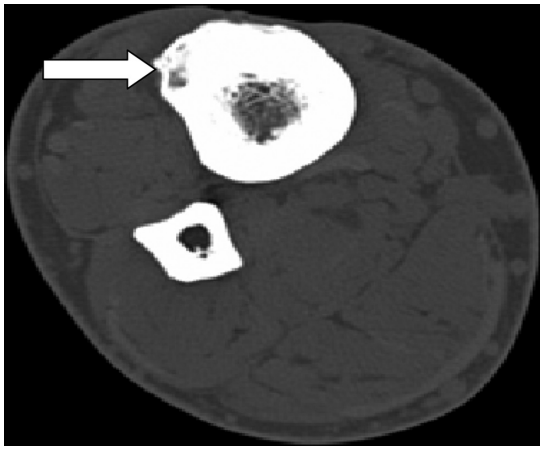

Figure 1 Osteomyelitis of the right tibia.

occurrence of sexually transmitted diseases in the past or any risky sexual behaviors and also said he had never suffered from urinary tract infections or renal calculi. The alternative diagnoses of cephalothin-tract infection were considered.

He then had a split skin graft over his improving wound site. Cephalothin was replaced with intravenous lincomycin for 2 days, and he was subsequently discharged with oral clindamycin.

Table 1 Diagnostic test results

Hemoglobin	143 g/L	RR: 135–180
White cell count	3.4×10^9/L	RR: 4.0–11.0
Neutrophils	1.77×10^9/L	RR: 2.0–8.0
Lymphocytes	0.85×10^9/L	RR: 1.0–4.0
C-reactive protein	42	n < 15
Hemolytic screen	Negative	
Blood urea serum electrolytes/creatinine/ liver function tests	Normal	
Urine protein creatinine ratio	470/5	
Midstream urine		
Red cell count	90	n < 10
White cell count	100	n < 10
Epithelial cells	<10	n < 10
Culture	Negative	
Urethral swabs	Negative	
PCR gonorrhea	Negative	
PCR chlamydia	Negative	
Urine cytology	Urothelial cells, eosinophils, no malignant cells	
Wound swab	Negative	
Blood culture	Negative	
Chest X-ray	Normal	
Renal ultrasound	Normal	

Abbreviations: RR, reference range; PCR, polymerase chain reaction.

At clinic review in 2 weeks, graft failure with an underlying infection necessitated admission and repeat debridement, washout, and VAC dressing. Intravenous cephalothin was started empirically postoperatively, and within 24 hours, he developed lower urinary tract symptoms again. Urine microscopy revealed white cell count >500, red cell count >500, no growth after 48-hour incubation, no casts, but presence of calcium oxalate crystals. The 24-h urine collection showed calcium 9.9 mmol/24 hours (reference range [RR]: 1.2–10.0) and phosphate 86.5 mmol/24 hours (RR: 11.0–32.0). Corrected serum calcium and phosphate were normal at 2.36 mmol/hour (RR: 2.15–2.55) and 1.24 mmol/hour (RR: 0.81–1.45), respectively, with epidermal growth factor receptor >90. Cephalothin was ceased and urinary symptoms resolved within 24 hours. Subsequently, *Morganella morganii* sensitive to cotrimoxazole and gentamicin.was cultured from an intra-operative bone specimen, expediting a therapy change to co-trimoxazole.

Discussion

Drugs may be responsible for 1%–2% of all renal calculi.[1] Although our patient had urinary calcium excretion at the upper limit of normal and long periods of bed rest, he only had nephrolithiasis while on intravenous cephalothin therapy, even though this was accompanied by an increased fluid intake from concurrent intravenous fluids. Drug-induced urolithiasis has two possible pathophysiological explanations. Firstly, poorly soluble drugs with high urinary excretion and concentration may precipitate as crystals. Secondly, following high-dose prolonged treatment, metabolic drug effects, such as alteration of urine pH, glomerular filtration rate, tubular reabsorption, and tubular secretion of drugs, may induce urolithiasis.[2] Cephalothin has not been associated with urolithiasis; however, its use outside Australia is less frequent, where ceftriaxone is the cephalosporin of choice. There have been case reports of ceftriaxone-induced nephrolithiasis and biliary calculi.[3,4] A prospective study of 51 children showed a 7-day course of normal or high-dose ceftriaxone resulted in 7.8% of children developing asymptomatic renal stones.[5] Mazhari and Kimmel suggested that all cephalosporins have the potential to induce urolithiasis.[6]

Summary

Physicians should be aware that patients on long-term cephalosporin have the potential to develop urinary calculi. They may well be the cause of lower urinary tract symptoms instead of a urinary tract infection and should be stopped.

Disclosure

The authors report no conflicts of interest in this work.

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