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Case Report
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HYPERCALCIURIA: A RARE CONTRIBUTING CAUSE OF EXERCISE-INDUCED VISIBLE HEMATURIA

Wayne Barlow, Maitrey Darrad, Simon Fletcher, Raghuram Devarajan

University Hospitals Coventry & Warwickshire, UK.

Corresponding autor: mpsdarrad@gmail.com

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ABSTRACT

Exertional hematuria is a relatively common symptom. We present a case of exercise-induced hematuria in a long-distance runner with proven hypercalciuria. Our case report highlights that urothelial calcifications in patients with hypercalciuria have the potential to cause traumatic hematuria during high-intensity exercise. Whilst the diagnostic work-up of hematuria still applies, careful attention to the history in this specific group of patents has the potential to avoid further invasive investigations.

Exercise-induced hematuria is a common, transient, usually benign phenomenon, occurring in 10–25% of runners after a marathon.[1,2] Visible hematuria is rare and in a study by Reid et al accounted for only 3% of the 98 marathon runners investigated.[2] We present an unusual case of recurrent exercise-induced visible hematuria secondary to hypercalciuria.

CASE REPORT

A 58-year-old Caucasian male presented with recurrent episodes of painless visible hematuria precipitated by high-intensity running. He is a non-smoker with no significant past medical history. Clinical examination, urinalysis, blood biochemistry, and renal tract ultrasonography were unremarkable. Urine cytology showed atypical cells but was non-diagnostic. Flexible urethro-cystoscopy showed a small red patch which subsequent biopsies proved to be benign.

Due to persistent symptoms and atypical cytology he underwent a computed tomography (CT) urogram, rigid cystoscopy, and bilateral flexible uretero-renoscopy. On this occasion there was a single dystrophic calcified lesion adherent to the trigone in a crater-like lesion. Analysis showed this to be carbonate apatite. Histology of the underlying ulcer crater again showed no malignancy. A hypothesis was made that there might be an underlying metabolic cause and 24-hour urinalysis showed elevate calcium excretion. Bendroflumethiazide was suggested to reduce this. The patient was asked to report again if hematuria persisted and to reduce vigorous exercise with impact. After a period of improvement, the patient returned with visible hematuria induced by high intensity exercise with an empty bladder. He was reinvestigated with a CT urogram, which identified no urological abnormalities apart from small opacities in the bladder (Figure 1). Glomerular causes including exercise-induced haemolysis were excluded with a normal LDH Haptoglobin and blood films.

He subsequently underwent 2 flexible cystoscopies on the same day. On initial cystoscopy, we found 2 calcified lesions in the trigonal area but clear views (Figure 2). He went for a 5-mile run and had repeat cystoscopy. The views were bloody and opposite to the calcified lesions there were irregular raised erythematous areas, which were actively bleeding (Figure 3). Resection of the calcified areas which seemed to be in the line of ureteric jets was performed. Biopsies

FIG. 1 Cystoscopic appearance of calcified lesions in the trigone.

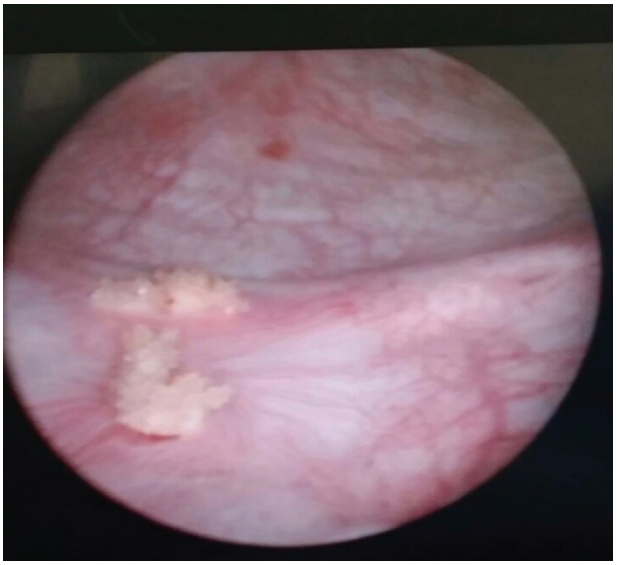


FIG. 2 Sagittal CT section displaying the calcified lesions seen on cystoscopy (red arrows).

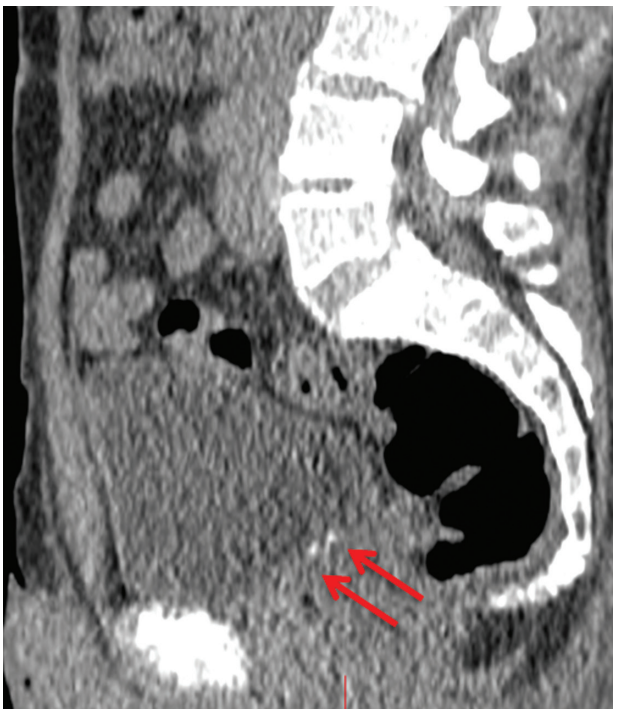
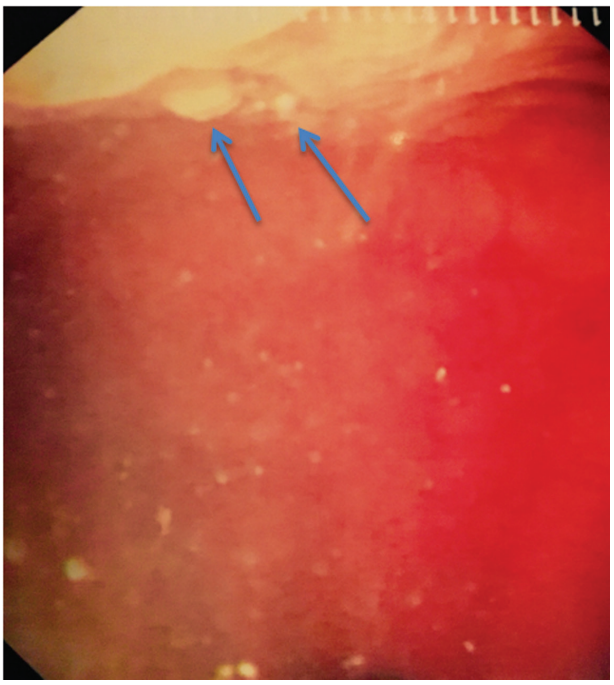


FIG. 3 Cystoscopic appearance following exercise displaying the abnormal bladder lesions in the anterior bladder wall (blue arrow) as a result of direct injury from the trigonal calcified lesions.



showed chronic urothelial inflammation with areas of fibrosis, oedema and calcium deposits in the lamina propria. There were no features of transitional cell carcinoma or carcinoma-in-situ. Parasitic and tuberculosis screens were negative. Stone analysis showed 70% calcium oxalate and 20% calcium phosphate.

We believe the cause of this patient's hematuria was as a result of urothelial trauma secondary to direct contact with the calcified trigonal lesions when the bladder was collapsed. We hypothesized that his persistent hypercalciuria was a predisposing cause leading to deposition of crystalline material in the line of ureteric jets.

Figure 1 demonstrates the calcified lesions in direct line with the ureteric urinary jets. This suggests a diagnosis of urolithiasis. A comprehensive serum and urinary metabolic work-up was undertaken. The summary of the results is shown in Table 1.

Table 1. Summary of the Biochemistry Analysis

Type of Fluid	Substance Tested	Result	Normal Reference Range
Serum	Creatinine	92 umol/L	65 – 105 umol/L
Serum	Uric Acid	366 umol/L	210 – 420 umol/L
Serum	Adjusted Calcium	2.43 mmol/L	2.10 – 2.58 mmol/L
Serum	Parathyroid Hormone (PTH)	3.4 pmol/L	1.1 – 4.2 pmol/L
24 hour urine	Urinary volume	1.628 L	-
24 hour urine	Calcium Excretion	11.9 mmol/collection	2.5 – 7.5 mmol/collection
24 hour urine	Phosphate Excretion	38 mmol/collection	15 – 50 mmol/collection
24 hour urine	Uric Acid Excretion	3.8 mmol/collection	2.8 – 4.4 mmol/collection
24 hour urine	Creatinine Excretion	15.4 mmol/collection	13.2 – 17.6 mmol/collection
24 hour urine	Urea Excretion		
24 hour urine	Oxalate Excretion	609 umol/collection	100 – 460 umol/collection
24 hour urine	Oxalate/Creatinine Ratio	42 umol/mmol creatinine	1 – 38 umol/mmol creatinine
24 hour urine	Citrate Excretion	5.83 mmol/collection	0.60 – 4.80 mmol/collection
24 hour urine	Citrate/Creatinine Ratio	0.40 mmol/mmol creatinine	0.04 – 0.33 mmol/mmol creatinine

Red = Pro-lithogenic factor/s
Blue = Anti-lithogenic factor/s

This patient was managed by increasing his fluid intake and started on bendroflumethiazide 2.5 mg once daily to treat hypercalciuria. To date, he has had no further episodes of exercise-induced hematuria.

DISCUSSION

Hypercalciuria is defined as urinary calcium excretion exceeding 200 mg/24 hours. There are many causes including absorptive hypercalciuria (intestinal hyperabsorption of calcium), renal hypercalciuria (impaired renal tubular reabsorption of calcium) and resorptive hypercalciuria (characterized by primary hyperparathyroidism). Less common causes include renal phosphate 'leak', primary enhancement of 1,25-$(OH)_2$D synthesis, and excessive production of prostaglandin E_2.

Hematuria is usually investigated by cystoscopic and radiological means to exclude neoplasm. When no cause is found, patients may be subjected to invasive tests. Our case report highlights the importance of a focused clinical history and diagnostic work-up to avoid unnecessary invasive investigations.

Different investigators have tried to localize the source of transient exercise-induced hematuria. Fassett found that this subset population had a higher incidence of dysmorphic red blood cells following exercise and suggested that the origin of symptoms was glomerular.[1] Others have suggested acidosis and hypoxia-related glomerular injury as the cause.[3] In contrast, Blacklock concluded that an empty bladder was more susceptible to trauma during running and demonstrated cystoscopic evidence of contusions of the trigone and posterior bladder wall.[4] Bladder wall calcification causing recurrent visible hematuria is documented in the literature. O'Sullivan reported encrusted cystitis (a rare inflammatory condition)

causing calcified plaques embedded into bladder mucosa leading to hematuria[5] These lesions were randomly located in the bladder. In contrast, we clearly found the bladder calcifications in our patient were in direct line with the urinary ureteric jets, which would favour urolithiasis as the etiology. Further evidence that our patient was in a pro-lithogenic state was obtained by the fact he had hypercalciuria and became asymptomatic with hydration and diuretic treatment. Our novel idea of pre and post exercise cystoscopies is a simple and reproducible technique to help aid the diagnosis of hematuria secondary to bladder wall calcifications.

In conclusion, exercise-induced hematuria deserves careful attention to history and consideration of factors such as lithogenesis.

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