Nephrocalcinosis in Shwachman's syndrome

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SUMMARY Nephrocalcinosis has been reported only infrequently in Shwachman's syndrome. We describe a case in which nephrocalcinosis occurred and speculate that this may be due to increased urinary oxalate excretion.

The syndrome of exocrine pancreatic insufficiency and bone marrow dysfunction was first described by Shwachman and colleagues in 1964, and subsequently other features such as bone dysplasia have been recognised.¹ In 1980, Aggett *et al* reviewed a series of 21 patients, one of whom was found to have nephrocalcinosis at necropsy.² We report another child with Shwachman's syndrome in whom nephrocalcinosis was an early feature.

Case report

A boy, weighing 3300 g, who was the second son of healthy, unrelated parents was born after a normal pregnancy, labour, and delivery. He was initially fed orally on a standard infant formula, but feeding became increasingly difficult and he failed to thrive. At 6 weeks of age, he was admitted to hospital, where he continued to gain weight poorly despite numerous feed changes.

Nasogastric feeding was therefore started at 10 weeks of age. Investigations showed intermittent neutropenia (the lowest concentration was $<0.2 \times 10^9$ neutrophils/l), persistently low serum immunoreactive trypsin (0–2 µg/l), and mildly raised plasma alanine transaminase and aspartate transaminase activities. Sweat sodium and chloride concentrations were normal. A radiograph of the chest showed broadened anterior ends of the ribs.

A diagnosis of Shwachman's syndrome was made and he was treated with pancreatic enzyme supplements from 4 months of age. Severe feeding difficulty and failure to thrive persisted, however, and at 7 months he was referred to us for further investigation. On admission his weight (5450 g), length (60 cm), and head circumference (42 cm) were all below the third centile. He had a narrow chest with Harrison's sulci, mild subcostal recession, increased tone in the legs with brisk reflexes and ankle clonus, and mild hirsutism. His liver was not

enlarged. Pancreatic enzyme supplements were withheld on admission. Shwachman's syndrome was confirmed by low bicarbonate production (maximum 16 mmol/l), low lipase activity (maximum 13 µmol/min/ml), and absent trypsin activity in duodenal fluid obtained after stimulation with secretin and cholecystokinin, together with intermittent neutropenia and typical radiological changes in the ribs. His transaminases were moderately raised (alanine transaminase 187 IU/l, and aspartate transaminase 122 IU/l). Immunological investigation showed poor neutrophil mobility. Further evaluation of the urinary tract was undertaken (see below) and pancreatic enzyme supplements were restarted at 8 months of age.

RENAL INVESTIGATIONS AND MANAGEMENT

Brightly reflective areas around the renal pyramids consistent with nephrocalcinosis had originally been observed in both kidneys on ultrasound examination at the age of 2½ months. At that time the urine was sterile and a spontaneous urinary pH of 5 was observed. Glycosuria or aminoaciduria were not present. The 24 hour urinary oxalate excretion was 0.31 mmol/1.73 m² surface area/24 hours (normal ≤ 0.46 mmol/1.73 m² surface area/24 hours). The 24 hour urinary calcium excretion was normal, as were the plasma urea and creatinine concentrations.

Further renal ultrasound examinations at the ages of 3 and 5½ months continued to show nephrocalcinosis, more noticeable on the left than on the right. At 7½ months, ultrasound examination showed nephrocalcinosis on the left side only; computed tomography of the abdomen performed at the same time confirmed the left sided nephrocalcinosis. Both investigations also showed dilatation of the right renal pelvis and ureter. A stone was visible in the right distal ureter on plain radiographs and computed tomograms.

The urine remained sterile, without aminoaciduria or glycosuria. Urinary calcium to creatinine ratio was 0.097 mmol/mmol (normal range 0.060–0.740 mmol/mmol), and oxalate excretion was 0.40 mmol/1.73 m² surface area/24 hours. At 8 months a right ureterolithotomy was performed. Analysis of the stone showed it to be 90% calcium oxalate.

At 11 months, after three months of continuous pancreatic supplementation, the urinary oxalate had

fallen to 0.23 mmol/1.73 m² surface area/24 hours and renal ultrasound showed a decrease in the left sided nephrocalcinosis. Urinary calcium to creatinine ratio was 0.10 mmol/mmol.

Discussion

Renal abnormalities have only rarely been recognised in Shwachman's syndrome. Aggett *et al*, in their review of 21 children with Shwachman's syndrome, described 10 children with intermittent and variable glycosuria.² Two children had mild, generalised aminoaciduria and one of these also had tubular acidosis. Marra *et al*, also described a patient with type I renal tubular acidosis.³ Nephrocalcinosis appears to have been reported only once previously and this was at necropsy; no data are available regarding this child's renal function during life.²

Hyperoxaluria and renal oxalate stone formation are common in adults with intestinal disease, particularly that of the ileum.⁴ Fat malabsorption is felt to be the basis of the hyperoxaluria seen in intestinal disease. Long chain fatty acids passing into the colon form soaps with calcium, depriving oxalate of its usual cation and thus increasing its absorption.⁵ Ogilvie *et al* measured urinary oxalate in 62 children with fat malabsorption. Five of the children had pancreatic dysfunction (two with cystic fibrosis, two with Shwachman's syndrome, and one with congenital isolated lipase deficiency). Both of the children with Shwachman's syndrome had hyperoxaluria; one of these was studied again after treatment with pancreatic enzymes and a low fat diet with added medium chain triglycerides, and his oxalate excretion was found to have returned to normal. In none of the children in that study were renal stones shown.⁶

Our patient showed nephrocalcinosis and produced a stone consisting largely of calcium oxalate. His urinary calcium concentration was normal and

he had no evidence of a renal tubular dysfunction or acidosis. Although hyperoxaluria could not be shown, excessive excretion of oxalate would appear the most likely cause of his calculi, and the fall in urinary oxalate on pancreatic enzyme supplementation with concomitant reduction in the degree of nephrocalcinosis supports this hypothesis. This case provides a link between the hyperoxaluria previously described in Shwachman's syndrome⁶ and the report of nephrocalcinosis discovered on necropsy.² The possibility of Shwachman's syndrome should be considered in a child with nephrocalcinosis and failure to thrive, and children known to have Shwachman's syndrome should have periodic urinary oxalate estimations and possibly also renal ultrasound examinations.

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References

- Shwachman H, Diamond CK, Oski FA, Khaw KT. The syndrome of pancreatic insufficiency and bone marrow dysfunction. *J Pediatr* 1964;**65**:645-63.
- Aggett PJ, Cavanagh NPC, Matthew DJ, Pincott JR, Sutcliffe J, Harries JT. Shwachman's syndrome: a review of 21 cases. *Arch Dis Child* 1980;**55**:331-47.
- Marra G, Appiani AC, Romeo L, *et al*. Renal tubular acidosis in a case of Shwachman's syndrome. *Acta Paediatr Scand* 1986;**75**: 682-4.
- Smith LH, Fromm H, Hofmann AF. Acquired hyperoxaluria, nephrolithiasis, and intestinal disease. *N Engl J Med* 1972;**286**: 1371-5.
- Silverman A, Roy CC. Malabsorption syndrome. *Pediatric clinical gastroenterology*. 3rd ed. St Louis: CV Mosby, 1983: 249-303.
- Ogilvie D, McCollum JPK, Packer S, *et al*. Urinary outputs of oxalate, calcium, and magnesium in children with intestinal disorders. Potential cause of renal calculi. *Arch Dis Child* 1976;**51**:790-5.

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Successful treatment after 'drowning' in sand

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SUMMARY A 30 month old boy who aspirated a large amount of dirty sand was successfully resuscitated and made a full recovery.

Sand and dirt aspiration as a result of accidental burial may be massive and fatal despite intensive treatment including intubation and bronchoscopy.^{1 2} Conservative treatment in sand aspiration has also been proposed.³ We present a case of a young child