Nephroquiz
(Section Editor: M. G. Zeier)

Supported by an educational grant from AMGEN

Crystals from fat

Case

A 69-year-old man was admitted with acute renal failure. Past medical history included chronic pancreatitis caused by heavy alcohol intake, diagnosed in 1972, with an ensuing requirement for enzyme replacement therapy and development of non-insulin dependent diabetes mellitus. In February 1999 his serum creatinine (SCr) was 80 μmol/l. One month later, he stopped pancreatic enzyme therapy and experienced fatty diarrhoea. At the end of March 1999, hyperglycaemia required insulin therapy. SCr was 140 μmol/l, without microalbuminuria or haematuria. In October 1999 he received a 7-day course of beta-lactam for a lower respiratory tract infection. Two weeks later SCr reached 560 μmol/l.

On admission, moderate lower limb oedema and polypnea were noted. Laboratory tests disclosed metabolic acidosis (arterial pH 7.19, total CO₂ = 3.4 mmol/l), hyperkalaemia (5.3 mmol/l), hypocalcaemia (1.61 mmol/l), hypomagnesaemia (0.25 mmol/l), hypoalbuminaemia (28 g/l), and low vitamin K-dependent coagulation factors (II = 52%, VII = 53%, X = 39%). Urinalysis showed 1+ haematuria, mild proteinuria (0.27 g/d), sodium 98 mmol/l, pH 5. Renal ultrasonography was unremarkable. Non-enhanced CT-scan demonstrated pancreatic calcifications.

Fig. 1. Renal biopsy. Masson’s Trichrome (×400). Large clear crystals and epithelial necrosis in distal tubules.

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A renal biopsy specimen disclosed severe tubular obstruction and necrosis due to extensive deposits of large clear crystals in the distal convoluted tubules (Figure 1). Mild mesangial matrix accumulation and moderate interstitial fibrosis were present. Immunofluorescence studies were unremarkable.

**Question**

What is your diagnosis?
The renal biopsy finding of numerous crystals in the distal tubule was compatible with the diagnosis of acute oxalate nephropathy (AON). The crystals were birefringent under polarized light and were identified as calcium oxalate (whewellite) using Fourier-transformed infrared microscopy.

The patient denied ethylene glycol, naftidrofuryl or vitamin C intoxication [1]. Additional investigations showed hyperoxalaemia (77 μmol/l; mean value of a reference group of ten patients starting haemodialysis = 22.5 μmol/l (18.3–45)). Plasma glycolate level was similar to the levels found in the same reference group (6.56 μmol/l (5.3–8.6)). Glyceric acid was undetectable in the plasma. Massive steatorrhoea (30 g fat/24 h stool (normal below 6 g)) was found.

Pancreatic enzyme replacement therapy was resumed. High urine output was induced, and a low-fat, oxalate-free diet and oral calcium supplementation were instituted. However, renal failure progressed, requiring regular haemodialysis.

The aetiology of renal failure in this patient was initially unclear. Renal biopsy documented AON. Because exogenous intoxication by oxalate precursors was denied, endogenous hyperoxaluria was considered. Normal plasma glycolate level and the absence of glyceric acid in the plasma ruled out hereditary defects of oxalate metabolism (type I or II primary hyperoxaluria) [2]. Since malabsorption was demonstrated, we concluded that enteric hyperoxaluria (EH) in this patient was secondary to pancreatic insufficiency.

EH is a well-established metabolic complication of various gastrointestinal diseases including Crohn’s disease, ileal resection, jejuno-ileal bypass and chronic pancreatitis. Within the intestinal lumen, free calcium normally combines with oxalate and limits its absorption by colic and rectal mucosae. EH occurs when non-absorbed fatty acids combine to intestinal calcium forming insoluble soap. The ensuing decline in intraluminal calcium favours enhanced oxalate absorption along the colon.

Renal complications of EH include recurrent calcium oxalate urolithiasis and chronic tubulointerstitial renal damage. In contrast, acute oxalate nephropathy due to EH is uncommon. A single case of AON due to EH related to chronic pancreatitis has been previously reported [3]. Extracellular volume contraction and metabolic acidosis resulting from hyperglycaemia and diarrhoea potentially contributed to tubular deposition of calcium oxalate crystals in our patient. In addition, we suggest that the course of antibiotics may have exacerbated EH. Indeed, antibiotics may lead to a disequilibrium in the gut flora with ensuing eradication of Oxalobacter formigenes, an oxalate-degrading microorganism which reduces oxalate enteric absorption [4].

We recommend considering AON as a possible cause of rapidly progressive renal failure in patients with diabetes mellitus secondary to chronic pancreatitis.

References


Fadi Fakhouri
Dominique Chauveau
Malik Touam
Laure-Hélène Noel
Jean-Pierre Grünfeld
1Department of Nephrology
2Unité INSERM U507
Hôpital Necker
Paris
France
Email: fakhouri@necker.fr