An unusual cause of acute renal failure in systemic sclerosis
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LESSON OF THE MONTH
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Background: Scleroderma renal crisis is one of the most life threatening complications of scleroderma. Enteric hyperoxaluria complicates extensive disease or resection of the small intestine in the presence of an intact colon, and is associated with calcium oxalate nephrolithiasis. This cause of renal failure may be underestimated and should be considered in all patients with malabsorption and renal failure.

Case report: A 78 year old woman with systemic sclerosis affecting the bowel developed acute renal failure caused by oxalate nephropathy.

Results: The patient’s renal failure improved on an oxalate free diet.

DISCUSSION
The scleroderma pulmonary renal syndrome and the scleroderma renal crisis (SRC) are distinct syndromes with different clinical presentations, histopathological manifestations, treatments, and outcomes. The scleroderma pulmonary renal syndrome is an autoimmune vasculitis of kidney and lung associated with normal blood pressure. Treatment is supportive, and prognosis is dismal. In contrast, SRC is associated with systemic hypertension. The main pathological changes seen in scleroderma kidney are oedema and proliferation of intimal cells, glomerular changes with thickening, and obliteration of arteries, leading to decreased renal perfusion and increased rennin release. The use of angiotensin converting enzyme (ACE) inhibitors in patients with SRC is life saving.

Oxalate nephropathy is usually seen in patients with primary hyperoxaluria types 1 and 2 and in patients with end stage renal disease managed with long term dialysis. Enteric hyperoxaluria complicates extensive disease or resection of the small intestine in the presence of an intact colon, and is associated with calcium oxalate nephrolithiasis. Secondary hyperoxaluria is well recognised in malabsorption. It has been documented in Crohn’s disease, jejunal ileal bypass, but could be expected in all causes of malabsorption. Normally much of the oxalate in the gut lumen is complexed as insoluble calcium oxalate, but in malabsorption calcium becomes complexed with lumenal fatty acids, leading to increased levels of soluble and therefore absorbable sodium oxalate. Alterations in both the magnitude and direction of oxalate fluxes across the intestine can occur in systemic sclerosis as a result of the bowel abnormalities associated with this condition. This patient’s steatorrhoea will have contributed to the prolonged transit time through the “ileal brake”. This patient had confirmed that pyramids of both kidneys were prominent with increased reflectivity of the cortex, suggesting renal parenchymal disease. No evidence of collecting system dilatation or obstruction was seen, and both kidneys measured 11 cm in diameter. Renal biopsy showed tubular necrosis with associated crystal precipitation (fig 1). There was no demonstrable vasculitis or interstitial nephritis and, specifically, no glomerulonephritis.

She was maintained on a strict fluid regimen of 1.5 litres a day and a low oxalate diet, which requires excluding: strawberries, tea, coffee, chocolate, rhubarb, spinach, and beetroot. Repeat 24 hour urinary oxalate excretion after two weeks on this diet showed an improvement from 896 μmol/l to 402 μmol/l. At four weeks after discharge, she had no diarrhoea, felt well in her self, and her renal function had improved: sodium 135 mmol/l, potassium 4.7 mmol/l, urea 16.3 mmol/l, creatinine 315 μmol/l.

Abbreviations: ACE, angiotensin converting enzyme; SRC, scleroderma renal crisis

References:
1. Involvement of the small intestine is also common, reaching a 40–80% prevalence, and may occur in the absence of significant involvement of the skin. It often leads to life threatening complications. To our knowledge this is the first described case of a patient with systemic sclerosis and enteric hyperoxaluria who developed acute renal failure from oxalate nephropathy.

2. Primary hyperoxaluria types 1 and 2 and in patients with end stage renal disease managed with long term dialysis. Enteric hyperoxaluria complicates extensive disease or resection of the small intestine in the presence of an intact colon, and is associated with calcium oxalate nephrolithiasis. Secondary hyperoxaluria is well recognised in malabsorption. It has been documented in Crohn’s disease, jejunal ileal bypass, but could be expected in all causes of malabsorption. Normally much of the oxalate in the gut lumen is complexed as insoluble calcium oxalate, but in malabsorption calcium becomes complexed with lumenal fatty acids, leading to increased levels of soluble and therefore absorbable sodium oxalate. Alterations in both the magnitude and direction of oxalate fluxes across the intestine can occur in systemic sclerosis as a result of the bowel abnormalities associated with this condition. This patient’s steatorrhoea will have contributed to the prolonged transit time through the “ileal brake”.

3. No demonstrable vasculitis or interstitial nephritis and, specifically, no glomerulonephritis.

4. The scleroderma pulmonary renal syndrome is an autoimmune vasculitis of kidney and lung associated with normal blood pressure. Treatment is supportive, and prognosis is dismal. In contrast, SRC is associated with systemic hypertension. The main pathological changes seen in scleroderma kidney are oedema and proliferation of intimal cells, glomerular changes with thickening, and obliteration of arteries, leading to decreased renal perfusion and increased rennin release.

5. The use of angiotensin converting enzyme (ACE) inhibitors in patients with SRC is life saving.

6. Oxalate nephropathy is usually seen in patients with primary hyperoxaluria types 1 and 2 and in patients with end stage renal disease managed with long term dialysis.

7. Enteric hyperoxaluria complicates extensive disease or resection of the small intestine in the presence of an intact colon, and is associated with calcium oxalate nephrolithiasis. Secondary hyperoxaluria is well recognised in malabsorption. It has been documented in Crohn’s disease, jejunal ileal bypass, but could be expected in all causes of malabsorption.

8. Normally much of the oxalate in the gut lumen is complexed as insoluble calcium oxalate, but in malabsorption calcium becomes complexed with lumenal fatty acids, leading to increased levels of soluble and therefore absorbable sodium oxalate.

9. Alterations in both the magnitude and direction of oxalate fluxes across the intestine can occur in systemic sclerosis as a result of the bowel abnormalities associated with this condition.

10. This patient’s steatorrhoea will have contributed to the prolonged transit time through the “ileal brake”.

11. This patient had
pancreatic insufficiency and dilated loops of small bowel, which resulted in prolonged transit time. This further enhanced absorption of oxalate by the large intestine through increased permeability of a shunt conductance induced by malabsorbed bile salts and fatty acids.15

Crystals of calcium oxalate monohydrate and excess oxalate ions stimulate an array of responses, inducing localised injury and inflammation in the kidneys.15

Sloughing of the damaged necrotic tissue causes the interstitial crystals to ulcerate the papillary surfaces.16–18

Because anecdotal reports and short term studies have shown that ACE inhibition may preserve renal function in patients with scleroderma,19 treatment had been started with ACE-I for her hypertension. Oxalate nephropathy is a recognised cause of hypertension20 and might have contributed to this in her case. However, our patient did not have SRC, which in essence is characterised by the onset of new interstitial crystals to ulcerate the papillary surfaces. 16–18

The presence of diarrhoea, the use of ACE-I and diuretic contributed to the renal failure by potentially causing hypotension and dehydration, which provided the right environment for oxalate crystal formation. Renal failure from oxalate nephropathy resulting from enteric hyperoxaluria may be reversible if recognised and treated early by a low oxalate diet.6,21

This case emphasises that enteric hyperoxaluria should be looked for in patients with malabsorption caused by bowel scleroderma, and appropriate treatment started as soon as possible.

THE LESSONS

- In systemic sclerosis, enteric hyperoxaluria may be an easily overlooked complication.

- A high degree of awareness is necessary as oxalate nephropathy can potentially cause hypertension and acute renal dysfunction.

- 24 Hour urinary oxalate estimation in patients with bowel systemic sclerosis is a useful investigation to identify enteric hyperoxaluria.

- Management requires a simple low oxalate diet and careful fluid balance.

REFERENCES


