Case Report

Irreversible tubulointerstitial nephropathy associated with prolonged, massive intake of vitamin C

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Introduction

Oxalate nephropathy is caused by a variety of conditions including hereditary hyperoxaluria, intestinal overabsorption of oxalate, ethylene glycol intoxication, and anesthesia with methoxyflurane. In addition to exogenous sources such as the latter two items, an overdose of ascorbic acid (vitamin C) has also been listed [1]. In this case, previous reports [2,3] describe an acute and often reversible form of oxalate nephropathy presenting with acute renal failure derived from intratubular precipitation of oxalate crystals. We report a patient who developed chronic, irreversible tubulointerstitial nephritis after a prolonged, massive intake of vitamin C, in which the interstitium was loaded with oxalate granules.

Case report

A 70-year-old woman was admitted to our hospital in November, 1995 because of increasing azotemia.

Since about 5 years prior to admission, the patient had been followed in another hospital for hypertension and hepatitis. The blood pressure had been controlled with Ca-antagonist and β-blocker. There were intermittent elevations of hepatic enzymes, usually in a mild degree, for which the diagnosis of hepatitis was given and followed. On the other hand, over the past 10 years she had privately taken daily three tablets, each allegedly containing 1000 mg, of vitamin C, which was supplied by her daughter who resided in the USA. There was no history of renal stone or relating symptoms. The urine and levels of serum creatinine (0.6 mg/dl) had been normal until March, 1994, when trace proteinuria and haematuria began to appear intermittently. Six months later, serum creatinine increased to 1.0 mg/dl, and another year later, to 2.9 mg/dl, which doubled in the following month, when she was referred to our hospital.

On admission, vital signs were stable with a blood pressure of 172/98 mmHg. Height was 146 cm, and weight 42.9 kg. Physical examination was unremarkable except for bilaterally palpable kidneys. The liver edge was also felt below the costal margin with smooth and non-tender surface.

The urine gave ++ test results for protein and ++ result for glucose; the sediment contained red blood cells of 10–15 per high-power-field (×400) and white blood cells of 30–40, and a few granular casts. Urinary excretion rates of protein were <0.9 g/24 h with urine volumes ranging from 700 to 1000 ml/24 h. Glycosuria was later confirmed to be of renal origin. A urine culture was negative. A urinary excretion of β₂-microglobulin was 980 µg/l (normal range: 5–253). An X-ray film of the chest and ECG were unremarkable. A CT scan of the abdomen revealed bilaterally enlarged kidneys (axis length 13–14 cm) due to the diffusely swollen parenchyma. There was no nephrocalcinosis or urinary calculi. The liver and spleen showed minimal enlargement without other abnormalities.

The white blood cell count was 7700/µl with a normal differential, red blood cell count 339 × 10⁹/µl, haemoglobin 10.9 g/dl, haematocrit 31.8% and platelet count 16.0 × 10⁹/µl. Pertinent laboratory data were as follows: serum creatinine 6.3 mg/dl, urea-nitrogen 55 mg/dl, uric acid 5.7 mg/dl, Na 137 mEq/l, K 3.5 mEq/l, Cl 106 mEq/l, Ca 9.3 mg/dl, iP 4.1 mg/dl, total protein 7.8 g/dl, albumin 4.5 g/dl. Hepatic enzymes were such that GOT was 33 IU/l (normal: 8–40), GPT 19 IU/l (normal: 5–35), LDH 498 IU/l (normal: 150–450), ALP 318 IU/l (normal: 70–230), γ-GTP 136 IU/l (normal: 6–30), LAP 150 IU/l (normal: 30–80). Serological examinations including anti-streptolysin-O titre, hepatitis viruses A, B and C, anti-nuclear factor, complement components, immunoglobulin levels, M-protein in the blood and Bence Jones protein in the urine were all negative or normal.

Percutaneous renal biopsy was performed at day 14...
Chronic interstitial oxalate nephropathy after admission. According to its findings (see below), a urinary excretion rate of oxalate was measured at day 34, and was 38.8 mg/24 h (normal: 16.2–53.3). In an attempt to improve renal function, the pulse therapy of methylprednisolone (1 g given intravenously on three consecutive days) was started, which was followed by 60 mg of prednisolone by mouth per day that was gradually tapered over 2 months and stopped. There was no beneficial effect on renal function, and for increasing azotemia, the patient was placed on dialysis therapy, and has been maintained on thrice weekly haemodialysis.

Renal biopsy findings

The specimen contained 10 glomeruli, of which two exhibited global sclerosis of ischaemic type, and the remaining eight appeared to be unremarkable. A major alteration was that of chronic tubulointerstitial nephritis; the interstitium was markedly widened due to mainly fibrosis and partly oedema with relatively scanty cell infiltration. The tubules had in general a degenerative appearance with flattened epithelial cells. Small arteries and arterioles showed intimal thickening and luminal narrowing (Figure 1).

On occasions, crystalline materials were also observed of polyhedral or rhomboidal shape arranged often in a rose fashion in tubular lumina, but their distribution was apparently less frequent than that seen usually in acute oxalate cast nephropathy. One of crystals accompanied a reactive giant cell (inset of Figure 2). When examined under half-polarized light, the crystals revealed birefringence, being consistent with oxalate. In addition, the same birefractile granules were diffusely deposited in the broadened interstitium (Figure 2). The crystals, i.e. oxalate, were also present along the walls of small artery and arteriole. Immunofluorescent studies were negative and electron-microscopic examinations were unavailable.

Discussion

Recently, two examples [2,3] of acute oxalate nephropathy due to an overdose of ascorbic acid (vitamin C) were reported. One deals with a fit 23-year-old male who ingested ~420 mg/day of vitamin C (over 10-fold the reference nutrient intake of 40 mg/day). The second is a cancer patient given massive intravenous injection of vitamin C. In these subjects, the cause of resultant acute renal failure was the precipitation of oxalate in the renal tubules, i.e. oxalate cast nephropathy. In the case of other exogenous sources of oxalate such as ethylene glycol, methoxyflurane (a precursor of oxalate) and a newly added agent, naftidrofuryl oxalate, a vasodilator [4,5], the same pathogenesis is working for acute renal failure. Therefore, if oxalate casts were washed out, acute renal failure could be reversibly recovered.

To the contrary, the present patient exhibited irreversibly progressive renal failure and severe tubulointerstitial nephritis. Although exact amounts of daily ingested vitamin C were not determined, it is highly probable that the daily quantity was excessive. It is indeed known that in hereditary hyperoxaluria, the renal parenchyma is disorganized by intense diffuse interstitial fibrosis, often with nephrocalcinosis which grates on the knife on section [6]. In this case, there was oxalate loading along the walls of intrarenal small vessels. Hepatic dysfunction observed in our patient may have been induced by...
oxalate infiltration in the liver. This was not confirmed since liver biopsy was not carried out.

Hereditary [6] or prolonged hyperoxaluria due to intestinal overabsorption [7] often complicates nephrolithiasis or renal stone excretion. However, the present patient never had such episode.

In our patient the prolonged and excessive intake of vitamin C was based on the superstition that it prevents cancer. Rapidly progressive interstitial renal fibrosis has been developed in young women in association with slimming regimen including Chinese herbs [8]. Continuous social education will be necessary to prevent these avoidable complications.

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References


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