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CASE REPORT

HYPOURICAEMIA AS A MARKER OF A GENERALIZED PROXIMAL TUBULAR DAMAGE IN ALCOHOLIC PATIENTS

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Abstract — **Aims and Methods:** Hypouricaemia is not frequently encountered in alcoholic patients. Described herein is the case of a 69-year-old alcoholic patient. **Results:** The patient presented with severe hypouricaemia (serum uric acid 95.2 μmol/l) due to renal urate wasting associated with a cluster of other metabolic abnormalities in the context of a reversible generalized dysfunction of the proximal tubules that mimicked Fanconi syndrome. **Conclusions:** The underlying mechanisms of this rare presentation are discussed.

INTRODUCTION

Increased serum uric acid levels are frequently encountered in alcoholic patients. However, hypouricaemia associated with uricosuria has been reported in patients with hepatic cirrhosis including patients with alcoholic liver disease (Michelis *et al*., 1974; Decaux *et al*., 1982). In such cases, a loss of hepatic xanthine oxidase activity due to severe hepatocellular injury may contribute to the pathogenesis of decreased serum uric acid levels (Michelis *et al*., 1974). Furthermore, in a carefully conducted study, De Marchi *et al*. (1993) showed that serum uric acid levels were slightly decreased in alcoholic patients compared with the control population (297.5 ± 71.4 vs 321.3 ± 107.1 μmol/l). Upon alcohol withdrawal, serum uric acid levels significantly increased to 321.3 ± 71.4 μmol/l ($P < 0.05$). On admission, seven patients (11% of the study population) exhibited hypouricaemia (serum uric acid concentration <190.4 μmol/l). Six of these patients had increased fractional excretion of uric acid (>15%). However, to the best of our knowledge, severe hypouricaemia (serum uric acid levels < 119 μmol/l) has not been reported in alcoholic patients. Here, we describe an alcoholic patient who developed severe hypouricaemia due to renal urate wasting associated with a cluster of other metabolic abnormalities in the context of a reversible generalized dysfunction of the proximal tubules that mimicked Fanconi syndrome.

CASE REPORT

A 69-year-old man was admitted to our clinic because of transient ischaemic attack (TIA). He was a heavy alcohol misuser (consuming ~200 g of alcohol per day for many years) and did not receive any drugs. On admission, the patient had severe hypouricaemia (serum uric acid 95.2 μmol/l), hypokalaemia, hypophosphataemia and hypomagnesaemia (Table 1). These metabolic abnormalities were accompanied by a profound renal urate, potassium, phosphate and magnesium wasting (see Table 1), as well as renal glucosuria (Bairaktari *et al*., 2001). Twenty-four-hour urine protein was 150 mg. There was no evidence of renal bicarbonate wasting; the arterial pH was 7.48, the serum bicarbonate concentration 21 mmol/l and the partial pressure of carbon dioxide was 30 mmHg. Renal and liver function tests (levels of serum creatinine, serum urea, alanine aminotransferase, aspartate aminotransferase, alkaline phosphatase, total bilirubin and prothrombin time) as well as serum sodium, chloride and calcium concentrations were all within the normal ranges. Oral supplements of potassium chloride and magnesium sulphate were given to the patient. Five days after alcohol withdrawal, a significant improvement in these metabolic parameters was noticed accompanied by a marked reduction in their tubular excretion (Table 1).

Table 1. Laboratory parameters on admission and after alcohol withdrawal

Parameter	On admission	Five days after alcohol withdrawal	Normal range
Serum uric acid (μmol/l)	95.2	178.5	202–476
FE of uric acid (%)	26.0	12.2	<10
Serum potassium (mmol/l)	3.0	4.9	3.5–5
FE of potassium (%)	44.0	11.5	9
Serum magnesium (mmol/l)	0.60	0.65	0.65–1.3
FE of magnesium (%)	5.4	3.0	<4
Serum phosphate (mmol/l)	0.45	1.26	0.81–1.61
FE of phosphate (%)	40	6	<20

FE, fractional excretion in urine.

Our patient reduced his alcohol consumption during a follow-up period of 6 months and did not present with the same cluster of metabolic disorders again.

DISCUSSION

The observed reversible non-acidotic proximal tubular damage could be due to the toxic effects of alcohol on renal

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tubules. In fact, it is known that alcohol misuse may result in a generalized reduction in the reabsorptive ability of the proximal tubular cells (De Marchi *et al*., 1993). This hypothesis is supported by studies indicating that ethanol interferes with the carrier function of these cells by decreasing the Na^+-K^+-ATPase activity (Parenti *et al*., 1991; Rodrigo *et al*., 1991; Rothman *et al*., 1992). Furthermore, it is possible that the acetaldehyde, produced after oxidation of ethanol by alcohol dehydrogenase, may inhibit the activity of several enzymes in renal tubules (Gonzalez-Calvin *et al*., 1983; Rothman *et al*., 1992). Finally, the oxidation of acetaldehyde by aldehyde dehydrogenase generates free radicals of oxygen reactive species that are capable of damaging cell membranes (Lieber, 1988).

Even though alcohol-induced increased electrolyte excretion could be the main underlying mechanism for the observed electrolyte abnormalities, other mechanisms may play a fundamental role in their pathogenesis. In fact, the coexistent respiratory alkalosis, the elevated adrenalin concentrations and increased insulin levels, commonly found in this population, can promote the movement of ions (potassium, magnesium and phosphate) into cells (Elisaf *et al*., 1994, 1998). Moreover, multifactorial origin electrolyte depletion, commonly encountered in this population, can interfere with a variety of renal functions, including renal urate and electrolyte excretion (Elisaf *et al*., 1994, 1998; Elisaf and Siamopoulos, 1997; Liamis *et al*., 2000).

We conclude that hypouricaemia in alcoholic patients should be considered either as a marker of liver cirrhosis or, in the absence of severe liver disease, as a marker of alcohol-induced reversible proximal tubular damage. This abnormality may be overlooked in everyday clinical practice, since serum uric acid measurements are infrequently carried out, and this may explain why this phenomenon has not been reported before.

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