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 sodium 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).

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
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 funda-
mental 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-
duced 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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