painful and tense calf muscles. Serum laboratory evaluation showed serum creatinine (sCr) 7.5 mg/dL, urea 280 mg/dL, sodium 139 mEq/l, potassium 6.8 mEq/L, calcium 0.98 mmol/l, phosphorus 8.6 mg/dL and creatine kinase 602 234 IU/l. Haematological examination showed the presence of leucocytosis (16.7×10^9/l) only, with no anaemia (haemoglobin 13.7 mg/dl) or thrombocytopenia (456×10^9/l). Fractional excretion of sodium was 0.8% and the urinary excretion of potassium was 630 mmol/day. The patient needed dialysis support for 2 weeks (eight sessions) and evolved with a decrease in creatine-kinase levels and complete recovery of renal function (sCr, 1.2 mg/dL). Urine output was maintained during the entire hospital stay, with a mean output of 2.050 ml/day. Leptospirosis diagnosis was confirmed by positive serologic tests (ELISA IgM and microscopic agglutination test). Investigation for other infectious diseases (HIV, cytomegalovirus, toxoplasmosis and Coxsackie) was negative.

The pathophysiology of renal failure in leptospirosis involves proximal tubular dysfunction, augmenting distal sodium delivery and, consequently, potassium excretion by the intact distal tubule [2]. In the presented case, the presence of hyperkalaemia is explained by the rhabdomyolysis. However, the low fractional excretion of sodium and urinary potassium of the patient described is dissimilar to the findings described by Covic et al. [3]. These authors demonstrated, in a large series of ARF due to leptospirosis, a high fractional excretion of sodium (>1%) in all patients, even in those with volume depletion. Moreover, in the same series, 20/22 patients with hypokalaemia had a urinary excretion >1000 mmol/day.

On the other hand, the low urinary excretion of sodium and potassium observed in this case is in agreement with ARF due to rhabdomyolysis [4]. In conclusion, the absence of jaundice, normal platelet value and low renal excretion of sodium and potassium allowed us to conclude that the major renal lesion in this case was due to rhabdomyolysis, with no or minimal involvement of leptospirosis.

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Dialysis encephalopathy secondary to aluminum toxicity, diagnosed by bone biopsy

Sir,

Dialysis encephalopathy is a syndrome observed in chronic renal insufficiency patients on dialysis, characterized by dementia, speech alterations, myoclonias, asterixis and convulsions, associated with typical electroencephalogram alterations. These clinical findings show a poor prognosis, resulting in death in the majority of cases. The association with aluminum toxicity is indicated frequently as the underlying cause and described in the majority of the reports in the literature, although other etiologies cannot be discarded [1–5].

**Case.** A 40-year-old black male patient had chronic renal failure of undetermined aetiology, and was on haemodialysis for 5 years and without personal antecedents of aluminum use or exposure to heavy metals. After 3 years of dialysis therapy, he began to present clinical findings of slight mental confusion and shivering in his extremities after haemodialysis sessions, showing spontaneous improvement, but with a repetitive and progressive character. Hospitalized 30 days after the onset of symptoms, he presented an intense state of mental confusion, speech apraxia and myoclonias, evolving into a diminished level of consciousness (Glasgow <8) and the need for mechanical ventilation. On this occasion he presented the following serum biochemical results: serum creatinine, 10.3 mg/dl; blood urea nitrogen, 57 mg/dl; serum potassium, 4.0 mEq/l; serum calcium, 4.4 mEq/l and anaemia, with no signs of an infectious process (haematocrit, 27%; haemoglobin, 8.5 g/dl). A cerebral computed tomography scan was performed, which was normal. He had a normal liquor and negative toxicological exams. The electroencephalogram showed wide θ and θ-δ waves, often in a triphasic fashion, and diffuse slow spikes. Following support, clinical improvement was observed on the second day of treatment and the patient was discharged from hospital in good clinical condition. However, from this period onward, he began to present similar symptoms with variable intensity, always after haemodialysis sessions. An investigation for aluminum toxicity was begun. The dialysis unit presented reverse osmosis-treated water with normal levels of aluminum (<10 μg/l); the same occurred with the patient’s serum aluminum (47 μg/l), an exam confirmed twice on other occasions, normal up to 30 μg/l), as well as ferritin at 150 ng/ml (15–200 ng/ml) and parathormone at 150 pg/ml (7–53 pg/ml). The test for desferoxamine was not suggestive of aluminum toxicity. In spite of the lack of evidence, a bone biopsy was performed which showed numerous deposits of aluminum. Desferoxamine treatment was then initiated, with a progressive improvement in the symptoms until disappearance and normalization of the electroencephalogram.

**Comment.** Many studies have shown good results with desferoxamine following dialysis encephalopathy by aluminum toxicity, as well as treatment of the dialysis water by reverse osmosis, with electroencephalogram normalization [6,7]. However, in all the cases described, diagnosis was based on the verification of a serum aluminum level increase or a positive desferoxamine test. In our case, it was necessary to perform a bone biopsy for confirmation of the diagnosis.


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The data presented here suggest that a bone biopsy should be performed when investigating dialysis encephalopathy, principally in cases where the etiology remains undefined after less invasive examination.

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Comparison of the urine acidification tests of torsemide vs furosemide in healthy volunteers

Sir,

The gold standard test to assess the ability to lower urine pH has traditionally been based on orally administered ammonium chloride (NH₄Cl) [1]. The use of ammonium chloride for this purpose is not well accepted because the drug has unpredictable GI absorption when given in tablet form and has an unpleasant taste when administered in a powder form. Furthermore, ammonium chloride causes many unpleasant side effects such as abdominal discomfort, nausea and vomiting. An alternative drug used to assess the ability to lower the urine pH with increasing popularity is a loop diuretic, furosemide, which blocks the sodium–potassium–chloride co-transporter (NKCC) in the thick ascending limb of Henlé. One drawback of the furosemide acidification test is a low specificity (82–89%) [2,3]. The likely reason for the low specificity is the carbonic anhydrase inhibitory effect, which is attributed to the presence within the molecule of a sulfonamide moiety [4,5]; this latter effect would partially negate the stimulatory effect on acid secretion by furosemide. In contrast, another loop diuretic, torsemide, contains a sulfonylurea moiety, instead of a sulfonamide moiety, and therefore is devoid of the carbonic anhydrase inhibitory effect. For these reasons, it is hypothesized that torsemide would be more specific in detecting acidification defects than furosemide, and the following studies were carried out to test this hypothesis.

Studies were carried out in eight healthy male volunteers (aged 23–33 years) utilizing a single-blind randomized crossover format. Urine samples were collected immediately before oral administration of 40mg furosemide or 20mg torsemide, and then hourly for 4h after oral administration of the diuretic. Studies were repeated in the same subjects with the intravenous administration of the same medications in the same doses. pH measurements were made in all the urine samples, but only the baseline urine pH and the lowest urine pH following a loop diuretic were used for data analysis.

The baseline urine pH values were similar in all groups. The values with torsemide were 6.2±0.2 (mean±SE) with a range of 5.7–7.1 after oral administration and 6.2±0.2 with a range of 5.6–7.2 after intravenous administration. The values after furosemide were 6.3±0.3 with a range of 5.5–7.3 after oral administration, and 6.3±0.2 with a range of 5.6–7.4 following intravenous administration. However, urine pH after the administration of torsemide was significantly lower than that of furosemide (P<0.05), regardless of the routes of administration. The values for torsemide were 4.9±0.1 with a range of 4.5–5.2 after oral administration, and 4.9±0.1, with a range of 4.5–5.6 after intravenous administration. The values for furosemide were 5.6±0.2 with a range of 4.9–7.0 after oral administration, and 5.5±0.2 with a range of 5.0–6.5 after intravenous administration. For furosemide, urine pH remained >5.5 in four of eight subjects after oral administration, and two of eight after intravenous administration. For torsemide none had urine pH >5.5 after oral administration, and only one of eight subjects after intravenous administration. If we define urine pH <5.5 following a loop diuretic in normal subjects as a true normal result [6], the specificity of furosemide test was 50% with oral administration and 75% after intravenous administration, whereas for torsemide they were 100% after oral administration and 88% after intravenous administration, respectively. No subjects developed any significant adverse effects with either loop diuretic regardless of the routes of administration.

In conclusion, torsemide appears to be as safe and simple as furosemide in testing the maximum ability to lower the urine pH, with greater specificity than the latter. However, the sensitivity of this test needs to be determined in subjects with impaired urine acidification.

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1. Rozas VV, Port FK, Rutt WM. Progressive dialysis encepha
2. Alfrey AC, LeGendre GR, Kaehny WD. The dialysis encepha
5. Zatta P, Zambenedetti P, Reusche E et al. A fatal case of aluminium encephalopathy in a patient with severe chronic renal failure not on 
 aluminium from patient with dialysis encephalopathy. Lancet 1980; 27: 692–693
doi:10.1093/ndt/gf8072

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