related as determined by the examinations performed in our hospital followed by analysis with the chi-square test.

We concluded that ESRD, which requires renal replacement therapy, may contribute to the increased prevalence of HZ.

Conflict of interest statement. None declared.

Department of Nephrology, Saitama Medical School, Saitama, Japan
E-mail: iromichi@saitama-med.ac.jp

Takahiko Sato
Tsutomu Inoue
Kei Endo
Yusuke Watanabe
Tomohiro Kikuta
Masahiro Tsuda
Jonde Arai
Kazuhiro Kobayashi
Naofumi Ikeda
Yoichi Ohno
Tsuneo Takenaka
Hiromichi Suzuki

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Hydrochlorothiazide-induced tubulointerstitial nephritis in a patient with Dent disease

Sir,

Dent disease is an X-linked renal tubular disorder characterized by low-molecular-weight proteinuria and combinations of hypercalciuria, nephrolithiasis, nephrocalcinosis and aminoaciduria. Some have progressive renal failure. It is caused by mutations in *CLCN5* gene encoding chloride/proton exchanger CLC-5 [1]. Nephrolithiasis and nephrocalcinosis increase risk of loss of renal function [2]. Hypercalciuria is a risk factor for stone formation. Thiazide diuretics reduce hypercalciuria and are recommended for treatment of Dent disease [3]. We describe acute renal failure (ARF) in a patient with Dent disease treated with hydrochlorothiazide.

Dent disease was diagnosed in a 12-year-old boy with rickets, short stature, renal insufficiency, hypophosphataemia, hypercalciuria, aminoaciduria, proteinuria and increased β_2-microglobulin excretion. *CLCN5* gene sequence analysis showed a G→C nucleotide substitution in exon 9 of the *CLCN5* gene. He was treated with angiotensin-converting enzyme inhibitor to reduce proteinuria and preserve renal function. This was complicated by increase in serum creatinine (sCr) and discontinued. For hypercalciuria, he was treated with hydrochlorothiazide (0.5 mg/kg/day) and citrate. At that time he was 13 years old, with sCr 1.4 mg/dl and estimated glomerular filtration rate 72 ml/min/1.73 m^2 (Figure 1). Eleven weeks later he was asymptomatic without fever, rash, arthralgia or oliguria. Physical examination, hydration and blood pressure were normal. sCr was 11.1 mg/dl, phosphorus 9.4 mg/dl, uric acid 9.7 mg/dl, potassium 4.0 mmol/l, bicarbonate 26 mmol/l and haemoglobin 9.8 g/dl. White blood cell (WBC) count was 9600/cm^2 with 4.1% eosinophils (count 394). Urinalysis showed one plus protein, 10–25 WBCs and negative stain for eosinophils. Renal ultrasound showed 0.3 cm stone in the upper pole of the left kidney, without renal oedema or enlargement. There was no history of drug allergies or use of nephrotoxic medications. Presumptive diagnosis was tubular interstitial nephritis (TIN) induced by hydrochlorothiazide, which was then discontinued. sCr decreased only to 10.1 mg/dl in the next 2 days, and therefore he was treated with methylprednisolone (10 mg/kg/dose) for 3 days followed by oral prednisone, 60 mg/day, for 5 days. sCr was 4.9 mg/dl at the start of corticosteroid taper. This resulted in near-complete restoration of renal function (sCr 2.3 mg/dl) (Figure 1). Therefore, a renal biopsy was not done.

Renal complications of thiazide diuretics are acute TIN and ARF, typically developing 4–10 weeks after starting therapy. Withdrawal of the medication, with or without corticosteroids, restored renal function in reported cases [4]. Thiazides are classified as sulfonamides, which can cause hypersensitivity reactions, such as acute TIN. Renal biopsies of patients with ARF associated with thiazides show acute TIN without immune complex or anti-tubular basement membrane antibody deposits [4]. The report on use of hydrochlorothiazide in children with Dent disease described muscle cramps, hypovolaemia, hypokalaemia and hyponatraemia [5]. Our patient developed ARF as a complication of treatment of hypercalciuria with a thiazide diuretic. This should be kept in mind when prescribing thiazide diuretic to these patients.

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Division of Pediatric Nephrology
The Children's Hospital of Philadelphia, 34th Street and Civic Center Boulevard,
Philadelphia
PA 19104, USA
E-mail: marsenico@email.chop.edu

Olivera Marsenic
Bernard S. Kaplan

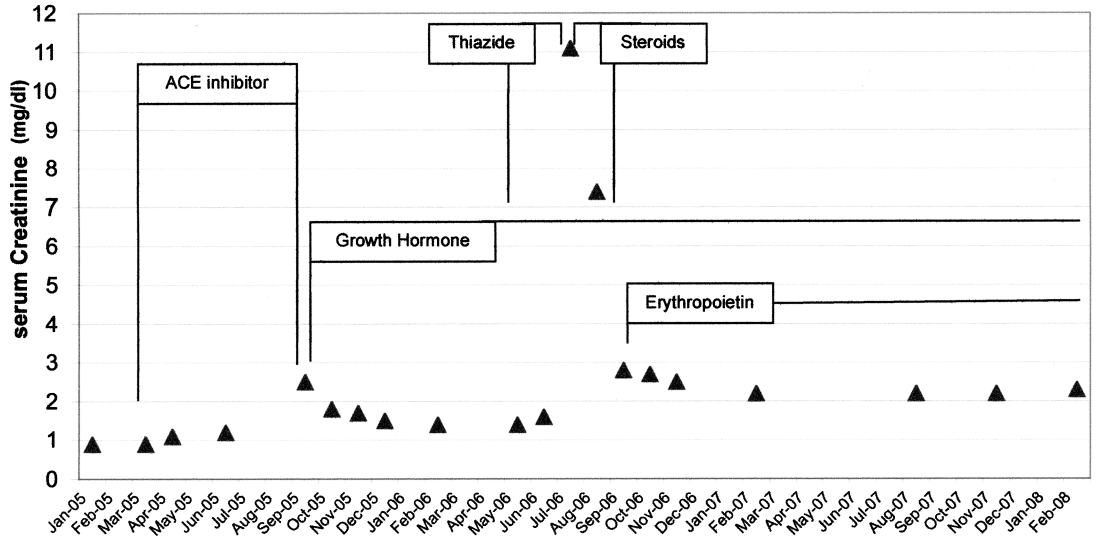

Fig. 1. Serum creatinine and treatment used in patient with Dent disease.

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Comment on: 'Lanthanum carbonate possibly responsible for acute liver failure in a patient with Child–Pugh stage A liver cirrhosis'

Sir,

De Leeuw and colleagues reported decompensation of existing liver disease in a patient with a complex history including alcohol-induced liver cirrhosis, pancreatitis and secondary diabetes [1]. The patient required hospitalization due to decreased consciousness and somnolence. The authors, noting a temporal association with lanthanum carbonate therapy, proposed that there was a causal relationship.

This patient report is highly confounded by a number of factors, including concomitant medication and hypophosphataemia, which are also credible explanations for the patient's presentation.

Firstly, the patient was taking lorazepam, which can cause coma in patients with reduced hepatic metabolism. Secondly, following dialysis the patient was profoundly hypophosphataemic. This is a recognized cause of irritability, paraesthaesia, confusion, convulsions and coma [2].

Evaluation of the published data on lanthanum carbonate (FOSRENOL®, Shire Pharmaceuticals, Basingstoke, UK) shows that the bioavailability is ∼0.001% and the small fraction of lanthanum absorbed is not metabolized. Animal studies have demonstrated that the presence of lanthanum in the liver is consistent with hepatic excretion via a lysosomal transcellular transport mechanism [3,4].

A long-term follow-up of clinical trial cohorts has included liver function tests and has not demonstrated any evidence of acute or chronic liver toxicity during 2 years of therapy compared to standard therapy. In uncontrolled studies, subjects have been exposed to lanthanum carbonate for up to 6 years [5,6]. In addition to over 5000 subjects in clinical studies, there is now over 60000 patient-years of post-marketing experience with lanthanum carbonate.

Although no specific studies were done in patients with liver impairment, there is insufficient evidence to assume that lanthanum carbonate may contribute to a worsening of liver function in this patient population.

Conflict of interest statement. M.S., B.G. and R.D.P. are employees of Shire Pharmaceuticals.

Editorial Note: Dr De Leeuw *et al*. had been invited to reply to this letter but we did not receive a response in time.

[1]Global Medical Affairs
[2]Pharmacovigilance, Shire Pharmaceuticals, Basingstoke, UK
[3]Research and Development, Shire Pharmaceuticals, Wayne, PA, USA
E-mail: msmyth@shire.com

Michael Smyth[1]
Birgitt Gellert[2]
Raymond D. Pratt[3]