

Two renal biopsies were performed because of persistent proteinuria, however, there was no remarkable histologically changes. She was diagnosed with IGS in the light of this clinical picture. Anemia and neurological symptoms were improved with vitamin B12 therapy in the next few weeks. Mild proteinuria remains persist with normal kidney function and she is being still followed-up with periodically for proteinuria.

IGS was firstly described in 1960 by Olga Imerslund and more than 300 cases have been published to date. In IGS, vitamin B<sub>12</sub> is completely abolished and if untreated with parenteral therapy the disease is fatal. A recent study revealed a biallelic mutation either in cubulin or amnions less genes cause IGS.<sup>3</sup> Both proteins act as a receptor for intrinsic factor-vitamin B<sub>12</sub> complexes as well as cubulin is an albumin binding protein important for renal tubular albumine reabsorption.<sup>4</sup> Because of absence of glomerular damage in kidney biopsies progressive kidney disease is not usual. Broch et al enrolled 14 patients to a long term follow-up study and exhibited no deterioration in kidney function.<sup>5</sup> Limited numbers of cases have been observed almost 50 years and renal prognosis is excellent. We aimed to announce our case with IGS who has a good renal prognosis over 20 years follow-up.

### Conflict of interest

The authors declare that there is no conflict of interest associated with this manuscript.

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## Adverse reaction to intravenous iron: hypersensitivity or secondary side effect?

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### To the Editor:

The replacement of iron is necessary in patients on haemodialysis due to the chronic blood loss that occurs when this technique is employed.<sup>1</sup> The intravenous administration of iron is not, however, free from adverse effects. Amongst these, we distinguish certain predictable reactions (an undesired consequence of the pharmacological actions of iron, such as side effects) from unpredictable reactions (in subjects with sensitivity of the immune system or susceptible to reactions such as hypersensitive and anaphylactoid reactions).<sup>2</sup> The latter are less common and more serious, and may require sus-

pension of the drug. We describe the case of an adverse reaction to the intravenous administration of iron that manifested as a burning sensation of the tongue, an inadequately defined sensation of peribuccal hyperaesthesia and generalised pruritus.

The patient is a 42-year-old woman who began a haemodialysis programme by right jugular tunnelled catheter following bilateral nephrectomy due to hypernephroma. In the post-operative period, the patient required a transfusion of 2 units of packed red blood cells. Ten days later a test showed: haemoglobin: 9.6g/dl, haematocrit 28.4, mean corpuscular volume: 87.1fl; iron: 56µg/dl, ferritin 233ng/ml; transferrin saturation index: 18%; folic acid: 22ng/ml vitamin B<sub>12</sub>: 921pg/ml; C-reactive protein: <5mg/l; Kt/V: 1.7. She was treated with omeprazole, vitamin B complex, folic acid and 30µg of darbepoetin weekly. 100mg of iron sucrose (Venofer<sup>®</sup>) was administered intravenously an hour after haemodialysis. 15 minutes after starting infusion, the patient complained of generalised pruritus, a burning sensation of the tongue and peribuccal hyperaesthesia. Physical examination: blood pressure 100/60mmHg, heart and lung auscultation normal, no lesions of the skin. Iron administration was discontinued and the symptoms gradually disappeared. In the following attempt, the patient was premedicated with dexchlorpheniramine and paracetamol. The reaction was identical and also it occurred with ferric carboxymaltose (Ferinject<sup>®</sup>). The Allergy Service was consulted: the patch test was negative for both iron preparations; the episode was compatible with the side effect. Clinical manifestations reappeared in a weaker form with the successive administrations of iron without major implications.

The rate of adverse effects associated with the administration of various preparations of intravenous iron (high and low molecular weight iron dextran, ferrous gluconate, iron sucrose) is approximately 38 per million.<sup>3</sup> The pruritus associated with ferric carboxymaltose is de-

scribed as isolated and infrequent (1/100-1000 of patients);<sup>4</sup> it seems to be present upon the first administrations and subsequently disappears.<sup>5</sup> The symptoms described by the patient as a burning sensation of the tongue and peribuccal hyperaesthesia, although subject to subjective assessments, did not correspond to the neurological disorders commonly described as paraesthesia or taste disorders<sup>4</sup>. The clinical profile that our patient presented seemed to signal an anaphylactoid reaction which was not confirmed. Generally speaking, reactions secondary to intravenous iron have been attributed to rapid infusion with an oversaturation of transferrin and the release of free iron, which is responsible for toxicity and vasomotor reactions.<sup>6</sup> This limited the total dose of iron administered and the rate of infusion in older formulations. Although ferric carboxymaltose is in this sense better tolerated, there are few studies comparing it to the rest of the formulations.<sup>7</sup> Furthermore, the potential development of severe, even fatal adverse effects remains a source of concern. Many of these reactions have been associated with high molecular weight iron dextran preparations and seem to have an immunological base<sup>1,7</sup>. However, controlled clinical trials for different intravenous iron preparations are limited by design to detect rare adverse effects as they are conducted in a small number of patients over short follow-up periods.<sup>1,2</sup>

Given the manifestation of infrequent side effects, it is vitally important that the intensity and seriousness of the reaction be established since this may require the permanent suspension of the drug, with the resulting limitation of the therapeutic arsenal available.

### Conflicts of interest

The authors declare that they have no conflicts of interest related to the contents of this article.

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### Emphysematous cystitis

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#### To the Editor:

We present the case of an 86-year-old female with a history of poorly controlled type 2 diabetes mellitus, who sought care for an episode of arterial

hypotension, fever, dysuria, and acute renal failure in the context of sepsis of a urinary aetiology. Laboratory tests revealed the following values: leukocytes: 27 200x10<sup>3</sup>/μl; glucose: 170mg/dl; creatinine: 5.1mg/dl; urea: 217mg/dl; and C-reactive protein: 232mg/l. An abdominal x-ray revealed gas surrounding the urine bladder, indicative of emphysematous cystitis (Figure 1 A).

Cultures of tissue samples did not reveal microbiological growth. We started treatment with intravenous hydration, insulin, and antibiotics with meropenem, which, along with catheterisation of the urine bladder, produced an adequate response. The patient recovered after three weeks of antibiotic treatment, with no complications and with normalisation of renal function (Figure 1 B).

Emphysematous cystitis is a rare, progressive, and fatal disease if it is not detected early. More than 90% of cases of this disease occur in diabetic and immunodepressed patients. The most commonly involved microorganisms are *Escherichia coli* and *Klebsiella pneumoniae*. The mechanism through which gas is produced in emphysematous infections is not well understood. In diabetic patients, one reason could be the production of CO<sub>2</sub> by the microorganism through the glucose fermentation pathway, which occurs when glucose concentrations are high. The best diagnostic method is radiological imaging (simple x-ray or computed axial tomography). This potentially fatal and rare complication must be kept in mind during patient diagnosis, especially in elderly diabetic patients with urinary tract infections.

Conservative treatment with antibiotics and catheterisation of the bladder is generally successful, with a rate of complications <20%. This strategy reduces patient mortality without requiring surgical interventions, and aids in preserving renal function.