studies up to 40%[5] of renal transplant recipients. Such adverse events can extend along the entire GI tract, and can vary in severity from those which are mild (nausea, discomfort, appetite loss) and do not require altering immunosuppressive regimen to those which are more severe or even life threatening (severe diarrhea, GI tract ulcerations, hemorrhage and perforations).[4,6]

The etiology of GI disorders following transplantation is not well understood. Because of enterocyte dependency for *de novo* purine synthesis MMF exposure could thus restrict the ability of intestinal epithelial cells to maintain normal barrier function, or decrease their capacity to recover from damage.[7]

Our patient has experienced a life threatening, severe lower GI bleeding which reoccurred within 2 days upon initial stabilization while on a stable immunosuppressive regimen. Upon dose reduction, the bleeding had stopped, indicating the possible adverse effect of MMF.

A database from the United States Food and Drug Administration's (US FDA) Adverse Event Reporting System (AERS), containing more than 4,000,000 adverse events reported between 2004 and 2011, has a record of 9 cases of haematochezia (0.02%) associated with MMF treatment (www.drugcite.com; accessed Feb 1, 2012).

We have reported this case to the Croatian National Drug Agency and in feedback letter have been informed that it is a serious, unexpected adverse drug reaction, possibly associated with MMF treatment. A total of 16 cases have been reported to the WHO Adverse Drug Reaction Monitoring Center with two fatal outcomes (WHO, UMC VigiBase, 29th November 2011).

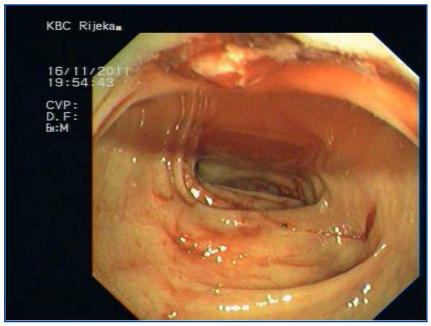

Figure 1.

Clinicians should be aware of possible, rare, but life threatening, lower GI bleeding associated with MMF treatment in renal transplant patients. Special caution should be given to patients with digestive system disease even if asymptomatic.

Conflict of interest

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

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Goran Hauser[1], Ivan Bubic[2], Vera Vlahovic-Palcevski[3], Josip Spanjol[4], Davor Stimac[1]

[1] Department of Gastroenterology. Clinical Hospital Centre. Rijeka (Croatia).
[2] Nefrology Department. Clinical Hospital Centre. Rijeka (Croatia).
[3] Department of Clinical Pharmacology. Clinical Hospital Centre. Rijeka (Croatia).
[4] Department of Urology. Clinical Hospital Centre. Rijeka (Croatia).

Correspondence: Goran Hauser
Department of Gastroenterology, Clinical Hospital Centre. Kresimirova 42. 51000, Rijeka, Croatia.
ghauser@medri.hr

A long-term follow-up of an Imerslund-Grasbeck syndrome patient with proteinuria

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To the Editor:

Imerslund-Grasbeck syndrome (IGS) is a rare autosomal recessive disorder characterized by megaloblastic anemia due to selective vitamin B_{12} malabsorption and asymptomatic proteinuria.[1] IGS occurs in the first 1-2 years of the life and megalablostic anemia is responsive to parenteral vitamin B_{12} treatment.[2] It is thought that proteinuria is benign in IGS; however, there is no sufficient number of follow-up series in IGS.

Case report

A 22-year-old woman had been referred to our pediatric outpatient clinic with the complaints of pale skin, loss of appetite, ataxia and diarrhea-constipation periods when she was 2-year-old. The clinical examination and laboratory studies revealed pallor of conjunctiva, megaloblastic anemia with vitamin B12 deficiency (serum vitamin B_{12} level <150pg/ml, hemoglobin: 6.5g/dl, MCV: 104fl and peripheral blood smear with hypersegmented neutrophils) and mild proteinuria (less than 0.5g/day) with absence of kidney function abnormality.

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_{12} 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.[3] Both proteins act as a receptor for intrinsic factor-vitamin B_{12} complexes as well as cubulin is an albumin binding protein important for renal tubular albumine reabsorption.[4] 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.[5] 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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Zafer Ercan[1], Mehmet E. Demir[2], Turgay Ulas[3], Muharrem Ingec[3], Mehmet Horoz[2]

[1] Department of Nephrology. Yildirim Beyazid Training and Research Hospital. Ankara (Turkey).

[2] Department of Nephrology. Harran University, School of Medicine. Sanliurfa (Turkey).

[3] Department of Internal Medicine. Harran University, School of Medicine. Sanliurfa (Turkey).

Correspondence: Mehmet E. Demir
Department of Nephrology. Harran University, School of Medicine, Yenisehir campus. 63300 Sanliurfa, Turkey.
demirmehmetemin@hotmail.com

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.[1] 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).[2] The latter are less common and more serious, and may require suspension 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 postoperative 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_{12}: 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®) 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®). The Allergology 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.[3] The pruritus associated with ferric carboxymaltose is de-