

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 feed-

back 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).

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.

1. Behrend M. Adverse gastrointestinal effects of mycophenolate mofetil: aetiology, incidence and management. *Drug Saf* 2001;24:645-63.
2. Zolezzi M. Mycophenolate Sodium versus Mycophenolate Mofetil: A Review of Their Comparative Features. *Saudi J Kidney Dis Transpl* 2005;16:140-45.
3. Selbst MK, Ahrens WA, Robert ME, Friedman A, Proctor DD, Jain D. Spectrum of histologic changes in colonic biopsies in patients treated with mycophenolate mofetil. *Mod Pathol* 2009;22:737-43.
4. Ponticelli C, Passerini P. Gastrointestinal complications in renal transplant recipients. *Transpl Int* 2005;18:643-50.
5. Placebo-controlled study of mycophenolate mofetil combined with cyclosporin and corticosteroids for prevention of acute rejection. European Mycophenolate Mofetil Cooperative Study Group. *Lancet* 1995;27:345:1321-5.
6. Davies NM, Grinyó J, Heading R, Maes B, Meier-Kriesche HU, Oellerich M. Gastrointestinal side effects of mycophenolic acid in renal transplant patients: a reappraisal. *Nephrol Dial Transplant* 2007;22:2440-8.
7. Arns W. Noninfectious gastrointestinal (GI) complications of mycophenolic acid therapy: a consequence of local GI toxicity? *Transplant Proc* 2007;39:88-93.

Goran Hauser¹, Ivan Bubic², Vera Vlahovic-Palcevski³, Josip Spanjol⁴, Davor Stimac¹

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

Nefrologia 2013;33(1):147-8

doi:10.3265/Nefrologia.pre2012.Aug.11661

Dear Editor,

Imerslund-Grasbeck syndrome (IGS) is a rare autosomal recessive disorder characterized by megaloblastic anemia due to selective vitamin B₁₂ malabsorption and asymptomatic proteinuria.¹ IGS occurs in the first 1-2 years of the life and megaloblastic anemia is responsive to parenteral vitamin B₁₂ 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 B₁₂ 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.

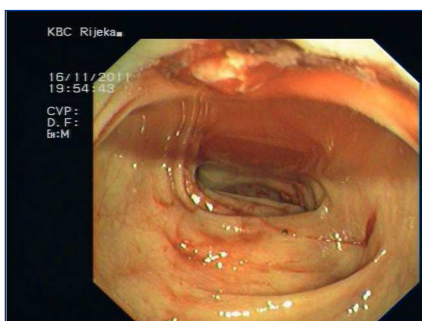


Figure 1.

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 B₁₂ 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 B₁₂ 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.

1. Imerslund O. Idiopathic chronic megaloblastic anemia in children. *Acta Paediatr Suppl* 1960;49(Suppl 119):1-115.
2. Bonfin C, Strapasson E, Dellê LA, Malvezzi M, Moreira VA, Netto AG, et al. [Imerslund-Gräsbeck syndrome: report of two cases]. *J Pediatr (Rio J)* 1999;75(6):477-80.
3. Fyfe JC, Madsen M, Højrup P, Christensen EI, Tanner SM, de la Chapelle A, et al. The functional cobalamin (vitamin B12)-intrinsic factor receptor is a novel complex of cubilin and amnionless. *Blood* 2004;103(5):1573-9.

4. Birn H, Fyfe JC, Jacobsen C, Mounier F, Verroust PJ, Orskov H, et al. Cubilin is an albumin binding protein important for renal tubular albumin reabsorption. *J Clin Invest* 2000;105(10):1353-61.
5. Broch H, Imerslund O, Monn E, Hovig T, Seip M. Imerslund-Gräsbeck anemia. A long-term follow-up study. *Acta Paediatr Scand* 1984;73(2):248-53.

Zafer Ercan¹, Mehmet E. Demir², Turgay Ulas³, Muharrem Ingeç², Mehmet Horoz²

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

Reacción adversa por la administración intravenosa de hierro: ¿hipersensibilidad o efecto secundario?

Nefrología 2013;33(1):148-9

doi:10.3265/Nefrologia.pre2012.Jun.11557

Sr. Director:

La reposición de hierro es necesaria en los pacientes de hemodiálisis debido a las pérdidas hemáticas crónicas que se producen con la técnica¹. La administración de hierro intravenoso no está, sin embargo, exenta de efectos adversos. De entre estos, distinguimos ciertas reacciones predecibles (consecuencia no deseada de las acciones farmacológicas del hierro, como son los efectos secundarios) de reacciones impredecibles (en sujetos con sensibilidad inmunológica o susceptibles tales como reacciones de hipersensibilidad y anafilactoides)². Estas últimas son más raras y más graves, y pueden obligar a suspender el fármaco.

Describimos el caso de una reacción adversa por la administración intravenosa de hierro manifestada como quemazón lingual, sensación mal definida de hiperestesia peribucal y prurito generalizado.

Se trata de una mujer de 42 años que inicia programa de hemodiálisis por catéter yugular derecho tunelizado tras binefrectomía por hipernefroma. En el posoperatorio la paciente requirió la transfusión de 2 concentrados de hemáties. Diez días más tarde se comprueba: hemoglobina: 9,6 g/dl; hematocrito: 28,4; volumen corpuscular medio: 87,1 fl; hierro: 56 µg/dl; ferritina: 233 ng/ml; índice de saturación de la transferrina: 18 %; ácido fólico: 22 ng/ml; vitamina B₁₂: 921 pg/ml; proteína C reactiva: < 5 mg/l; Kt/V: 1,7. Recibe tratamiento con omeprazol, complejo vitamínico B, ácido fólico y darbepoetina 30 microgramos semanales. Se pauta 100 mg de hierro sucrosa (Venofer®) a pasar por vía intravenosa en una hora poshemodiálisis. A los 15 minutos de iniciada la infusión, la paciente refiere prurito generalizado, sensación de quemazón lingual y de hiperestesia peribucal. Exploración física: tensión arterial 100/60 mmHg, auscultación cardíaca y pulmonar normales, no lesiones cutáneas. Se interrumpe la administración de hierro, con lo que cede paulatinamente la sintomatología. En el siguiente intento se premedica a la paciente con dexclorfeniramina y paracetamol. La reacción se repite de forma idéntica y se reproduce también con hierro carboximaltosa (Ferinject®). Se consulta al Servicio de Alergología: pruebas epicutáneas negativas para ambos preparados férricos; cuadro compatible con efecto secundario. Las manifestaciones clínicas reaparecen de forma atenuada con las administraciones sucesivas de hierro, sin mayores implicaciones.

La tasa de efectos adversos relacionados con la administración de diversos preparados de hierro intravenoso (hierro dextrano de alto y bajo peso molecular, gluconato férrico, hierro sucrosa) se sitúa en torno a 38 por millón³. El prurito asociado al hierro carboximaltosa se describe de forma aislada como poco frecuente (entre un 1/100-1000 de los pacientes)⁴;