Nutrición Hospitalaria

Caso clínico

Atrophy of the intestinal villi in a post-gastrectomy patient with severe iron deficiency anemia

A. Lizarraga, C. Cuerda, E. Junca, I. Bretón, M. Camblor, C. Velasco y P. García-Peris

Nutrition Unit. Hospital General Universitario Gregorio Marañón. Madrid. España.

Abstract

Background & aims: Iron deficiency anemia is a common complication of gastric surgery that in certain patients can be refractory to treatment with oral iron and needs to be treated parenterally.

Methods: A 48-year woman underwent gastric surgery for a gastric ulcer. She was referred to the nutrition unit for the study and treatment of a 3-year iron deficiency anemia refractory to oral iron supplementation. Blood tests, endoscopy and jejunal biopsy were made to study the case.

Results: Intestinal villi atrophy in the absence of celiac disease was the result. She was treated with intravenous iron, resolving the villous atrophy and thus oral iron supplementation could be effective.

Conclusion: This case illustrates that iron deficiency may cause villous atrophy. In this setting, parenteral iron administration is necessary to correct the haematological and non-hematological alterations associated with this deficiency.

(*Nutr Hosp*. 2009;24:618-621)

DOI:10.3305/nh.2009.24.5.4493

Key words: *Intestinal villy atrophy. Iron deficiency. Gastrectomy.*

ATROFIA DE LAS VELLOSIDADES INTESTINALES EN UN PACIENTE POSTGASTRECTOMIZADO CON ANEMIA FERROPÉNICA GRAVE

Resumen

Introducción y objetivos: La anemia ferropénica es una complicación frecuente tras la cirugía gástrica que en algunos pacientes puede ser refractaria al tratamiento con hierro oral, siendo necesaria su administración por vía parenteral.

Métodos: Presentamos el caso de una mujer de 48 años intervenida de gastrectomía para tratamiento de una úlcera gástrica. Fue remitida a la unidad de nutrición para estudio y tratamiento de una anemia ferropénica de 3 años de evolución refractaria al tratamiento con hierro oral. Para el estudio del caso se realizó analítica y endoscopia digestiva alta con biopsia yeyunal.

Resultados: En el estudio realizado la paciente presentaba atrofia de la mucosa yeyunal en ausencia de enfermedad celíaca. Fue tratada con hierro intravenoso desapareciendo la atrofia intestinal, tras lo cual continuamos con suplementos de hierro por vía oral.

Conclusión: Este caso ilustra que la deficiencia de hierro puede producir atrofia intestinal. Si esto ocurre, es necesario la suplementación de este metal por vía parenteral para corregir las alteraciones hematológicas y no hematológicas asociadas a esta deficiencia.

(*Nutr Hosp*. 2009;24:618-621)

DOI:10.3305/nh.2009.24.5.4493

Palabras clave: *Atrofia intestinal. Deficiencia de hierro. Gastrectomía.*

Introduction

Iron is an essential element for so many basic functions in the organism that its intestinal absorption and losses are strictly regulated. The small intestine is the main organ responsible for the homeostasis of iron by controlling its absorption in response to changes in the amount of iron in the body. Iron deficiency directly influences the intestinal capacity of iron absorption. In iron deficiency there is an increase in the expression of proteins for iron absorption in the small intestine, such as divalent metal transport 1, mobilferrin, ferroportin-1, ceruloplasmin, and hepaestin.[1-3] Iron deficiency may also cause modification in intestinal morphology and function including villous atrophy,[4,5] reduced absorption of D-xylose,[4,5] decrease in intestinal disaccharidase,[6] and alteration in intestinal permeability.[7,8]

Correspondence: Cristina Cuerda.
Nutrition Unit.
Hospital General Universitario Gregorio Marañón.
Doctor Esquerdo, 46.
28007 Madrid.
E-mail: mcuerda.hgugm@salud.madrid.org

Iron deficiency and thus iron deficiency anemia is frequent after gastrectomy, diminished acid output and by-passed duodenum in certain techniques, are the principal physiopathological causes.[9] In patients who have developed villous atrophy secondary to iron deficiency, the treatment with oral iron will not be effective and an intravenous treatment must be implanted. In this case-report we focus on the role of the intestine epithelium integrity for the iron absorption to be efficient, in a post-gastrectomy woman with severe anemia to whom a celiac disease was put aside.

Case report

We report the case of a 48-year-old woman who underwent hemigastrectomy and gastrojejunal anastomosis (Roux-en-Y) in 2001 for the treatment of a gastric ulcer. Except for a hysterectomy due to a benign lesion, the patient had no medical or surgical history of interest.

In May 2006, she presented with a 3-year history of microcytic hypochromic anemia and was refractory to treatment with oral iron; she was taking 80 mg of elemental iron 3 times a day. She suffered hair loss, nail weakness, and fatigue. She had no melenic stools or weight loss. A blood test revealed a red cell count of 4,160,000/mm³, hemoglobin 9.1 g/dL, hematocrit 29.1%, mean corpuscular volume 69.8 fl, red cell distribution width 19.6%, ferritin 3 µg/L, blood iron 14 µg/dL, transferrin 396 mg/dL, and transferrin saturation index 3%. To rule out the presence of celiac disease, antitransglutaminase IgA and antigliadin IgA antibodies were analyzed, and both were negative. Endoscopy revealed a normal esophagus, gastric stump, anastomotic mouth, and jejunal intestine. Biopsy samples were taken from the jejunal intestine and revealed diffuse villi flattening —in some points the epithelium even disappeared— cylindric superficial epithelium, presence of isolated neutrophils, and nonspecific chronic inflammation in the lamina propria (fig. 1).

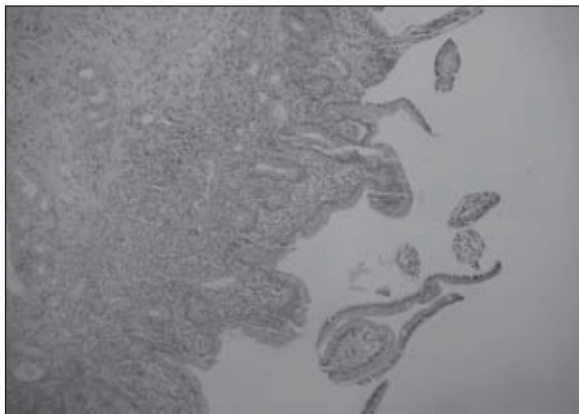In August 2006 the patient was sent to the nutrition unit for the study and treatment of iron deficiency anemia that could not be treated with oral iron. The iron deficiency was calculated to be 1,356 mg. Twelve 100 mg blisters of intravenous iron were administered over 4 weeks and folic acid was prescribed. The blood test was repeated and revealed a red cell count of 4,480,000/mm³, hemoglobin 11.3 g/dL, hematocrit 34.2%, mean corpuscular volume 76.4 fl, red cell distribution width 31.2%, ferritin 43 µg/L, blood iron 51 µg/L, transferrin 316 mg/dL, and transferrin saturation index 13%. As the anemia was improving, intravenous iron was interrupted and oral ferrous sulphate and folic acid were maintained.
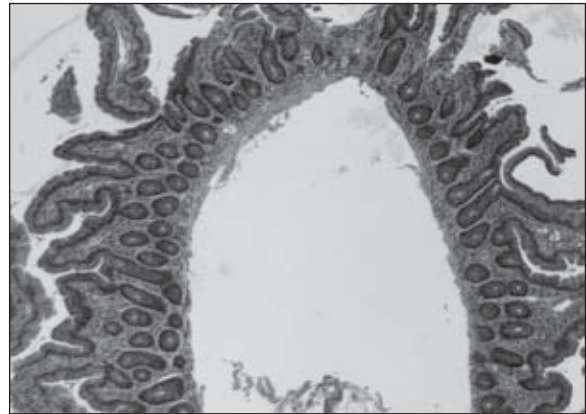
In November 2006, the blood test was as follows: red cells 4,780,000/ mm³, hemoglobin 14.1 g/dL, hematocrit 41.7%, mean corpuscular volume 87 fl, red cell distribution width 21.2%, ferritin 9 µg/L, transferrin 273 mg/dL, and transferrin saturation index 26%.

In January 2007, endoscopy was repeated, but showed no alterations. Another biopsy was taken and the jejunal mucosa showed no histological alterations. (fig. 2).

Treatment with oral iron was maintained until the levels of ferritin returned to normal.

Discussion

Iron is an essential mineral oligoelement that takes part in the synthesis of hemoglobin, transport of electrons for cellular metabolism, synthesis of DNA and in practically all oxidation and reduction processes. Therefore, a lack of iron alters the efficiency of cell proliferation and regeneration.[10] After bone marrow germinal blood cells, enterocytes have the second highest proliferation rate. Iron deficiency can have non-hematological manifestations, some of which may affect the gastrointestinal tract. Structural and functional abnormalities of the intestine including villous atrophy,[4,5] reduced absorption of D-xylose,[4,5] decrease in intestinal disaccharidase,[6] and alteration in intestinal permeability[7,8] have been previously reported. The mechanism by which these changes are produced is obscure.

Fig. 2.—Jejunal intestine biopsy after treatment.

Fig. 1.—Jejunal intestine biopsy at diagnosis.

The adult male has about 35-45 mg/kg of iron in the body. Women have smaller reserves. More than 2/3 is added to hemoglobin, the rest is stored in hepatocytes and macrophages.[11] Iron requirements are the amount of the element that has to be replaced to respond to the loss and requests of the organism. These vary according to age and sex.

The regulatory system for absorbing iron through the intestinal mucosa is essential for homeostasis. Regulated by direct and indirect mechanisms, the quantity absorbed depends on iron storage, erythropoietic activity, and the quantity and form of presentation of iron in consumed foods.[1] A European mixed diet offers about 6 mg per 1,000 calories —only 10% is absorbed. The form of iron in food is important because the heme form is more available (better absorption and usefulness) than inorganic non-heme iron. Indeed the heme form is not as affected by other components of the diet. In fact, the acid environment of the stomach improves the solubility of ferric ions (Fe^{3+}) and helps their conversion to the more easily absorbed ferrous ions (Fe^{2+}). The non-heme iron absorption rate depends on the presence of hydrochloric and ascorbic acid, glucides, and amino acids, which help the iron to be absorbed, and also on phosphates, phytates, oxalates, and tannates, which can inhibit absorption.[12]

Iron is mainly absorbed in the duodenal mucosa and the upper part of the jejunum. The rest of the intestinal tract can only absorb a residual part.

Iron loss is small and usually steady under normal conditions. It is lost through stool due to intestinal desquamation, through the skin, urine, and menstrual discharge.

This case study focuses on the role of the intestinal mucosa in the absorption of iron. Significant weight loss and anemia due to iron, vitamin B_{12} and folate deficiency have been documented after subtotal and total gastrectomy.[13-15] Iron deficiency anemia is very frequent after gastric surgery due to the decrease in acid output; therefore, the conversion to ferrous ions is diminished, and in techniques involving a duodenal bypass, the efficiency of absorption is greatly reduced.[9,16] The anemia is established in a period of years and the incidence in these patients reaches up to 30-50%.[9,17,18] They usually respond to treatment with oral iron; in fact, some authors recommend the use of prophylactic oral iron supplement in premenopausal women who undergo a Roux-en-Y gastric bypass to prevent the development of anemia.[19] In some patients, this treatment is not useful, probably because of the associated intestinal atrophy, and it must be administered parenterally.[20]

In people with celiac disease, intestinal atrophy of the proximal small gut is the mechanism involved in the pathogenesis of iron deficiency anemia, a well-known clinical manifestation of the disease.[21,22] However, it is important to remember that iron deficiency can induce intestinal atrophy in the absence of celiac disease, which can also impede iron absorption, thus worsening the iron deficiency.[4,5] Our case illustrates this mechanism very clearly and shows why in some patients the administration of parenteral iron becomes necessary to treat iron deficiency anemia that is refractory to oral iron.

Conflict of interest statement

None declared.

Acknowledgements

References

1. Morgan E, Oates P. Mechanisms and regulation of intestinal iron absorption. *Blood Cells Mol Dis* 2002; 29: 384-99.
2. Zoller H, Theurl I, Koch R, McKie A, Vogel W, Weiss G. Duodenal cytochrome b and hepaestin expression in patients with iron deficiency and hemochromatosis. *Gastroenterology* 2003; 125: 746-54.
3. Simovich M, Hainsworth L, Fields P, Umbreit J, Conrad M. Localization of the iron transport proteins mobilferrin and DMY-1 in the duodenum: the surprising role of mucin. *Am J Hematol* 2003; 74: 32-45.
4. Naiman JL, Oski FA, Diamond LK, Vawter GF, Shwachman H. The gastrointestinal effects of iron-deficiency anemia. *Pediatrics* 1964; 33: 83-99.
5. Guha DK, Walia BNS, Tandon BN, Deo MG, Ghai OP. Small bowel changes in iron-deficiency anaemia of childhood. *Arch Dis Child* 1968; 43: 239-44.
6. Prasad A, Prasad C. Iron deficiency: non-hematological manifestations. *Prog Food Nutr Sci* 1991; 15: 255-83.
7. Berant M, Khourie M, Menzies IS. Effect of iron deficiency on small intestinal permeability in infants and young children. *J Pediatr Gastroenterol Nutr* 1992; 14: 17-20.
8. Goto K, Chew F, Torún B, Peerson JM, Brown KH. Epidemiology of altered intestinal permeability to lactulose and mannitol in Guatemalan infants. *J Pediatr Gastroenterol Nutr* 1999; 28: 282-90.
9. Delgado del Rey M, Gómez Candela C, Cos Blanco AI, Iglesias Rosado C, Fernández Ibáñez MV, Castillo Rabaneda R et al. Nutritional assessment in patients with total gastrectomy. *Nutr Hosp* 2002; 18 (5): 236-9.
10. Adamson JW, Longo DL. Anemia y policitemia. En: Kasper DL, Braunwald E, Fauci AS, Heuser SL, Longo DL, Jameson JL, eds. Harrison, Principios de Medicina Interna, 16ª edición. Mexico DF: Interamericana. Mc Graw-Hill; 369-77.
11. Muñoz Hoyos A, Molina Carballo A. Hierro. En: Gil Hernández A. ed. Tratado de Nutrición, tomo I; Bases fisiológicas y bioquímicas de la nutrición. Sevilla: Grupo Acción Médica; 2005, pp. 927-72.
12. De Paz R, Hernández-Navarro R. Management, prevention and control of anaemia secondary to iron deficiency. *Nutr Hosp* 2005; 20 (5): 364-7.
13. Cuerda C, Camblor M, Bretón I, Velasco C, Parón L, Hervás E et al. Gastric surgery as a nutritional risk factor. *Nutr Hosp* 2007; 22 (3): 330-6.
14. Grant JP, Chapman G, Russell MK. Malabsorption associated with surgical procedures and its treatment. *NCP* 1996; 11: 43-52.

15. Tovey FI, Godfrey JE, Lewin MR. A gastrectomy population: 25-30 years on. *Postgrad Med J* 1990; 66: 450-8.
16. Stenson WF. The Esophagous and Stomach. In: Shils ME, Olson JA, Shike M, Ross AC, Eds. Modern Nutrition in Health and Disease, 9th edition. Baltimore: Williams & Wilkins; 1999, pp. 1125-33.
17. Harju E. Metabolic problems after gastric surgery. *Int Surg* 1990; 75: 27-35.
18. Calpena R, Bellot L, Pérez-Vázquez MT, Compan A, Del Fresno J, Serrano P et al. Metabolic disorders in the gastrectomized patient. *Rev Esp Enferm Dig* 1990; 78: 278-84.
19. Brolin RE, Gorman JH, Gorman RC, Petschenik AJ, Bradley LJ, Kenler HA et al. Are vitamin B_{12} and folate deficiency clinically important after roux- en- Y gastric bypass? *J Gastrointes Surg* 1998; 2: 436-42.
20. Stucki A, Grob JP, Chapuis G, Meyer A, Christeler P, Bachmann F. Biliopancreatic bypass and disorders of iron absorption. *Schweiz Med Wochenschr* 1991; 121: 1894-6.
21. Harper JW, Holleran SF, Ramakrishnan R, Bhagat G, Green PH. Anemia in celiac disease is multifactorial in etiology. *Am J Hematol* 2007; 82 (11): 996-1000.
22. Peláez-Luna M, Montaño-Loza A, Remes-Troche JM. Current concepts on celiac disease physiopathology. *Rev Invest Clin* 2003; 55 (5): 569-76.