8. Astroza G, Faundes V, Nanjarí R, Fleiderman M, Rodríguez C. Appendiceal endometriosis differentially diagnosed from acute appendicitis. Chin Med J (Engl). 2010;123:1610–1.

Eduardo Reyna-Villasmil*, Duly Torres-Cepeda, María Labarca-Acosta

Servicio de Ginecología, Hospital Central «Dr. Urquinaona», Maracaibo, Estado Zulia, Venezuela

*Corresponding author.
E-mail address: sippenbauch@gmail.com (E. Reyna-Villasmil).

Acute pancreatitis secondary to partial multidrug resistance 3 p-glycoprotein deficit☆

Pancreatitis aguda secundaria a déficit parcial de multidrug resistance 3 p-glycoprotein

Increasing numbers of young patients are being seen for abdominal pain and laboratory findings suggestive of cholestasis. Even after ruling out infectious, metabolic and autoimmune disease, and performing radiological examinations, a conclusive cause is often not identified.

With the intention of highlighting a disease that has been emerging in the literature in the last 10 years, but with no cases reported in Spain, we present the case of an 18-year-old patient who presented symptoms of acute pancreatitis and cholestasis related to a partial deficiency of *multidrug-resistance P-glycoprotein 3* (MDR3).

The patient had no personal history of interest. His maternal grandfather had died of pancreatic cancer, while his mother had undergone cholecystectomy for acute cholecystitis at 30 years of age.

He was admitted for sudden onset epigastric pain, radiating to the lumbar region. He reported having presented similar but less intense episodes during the previous year.

Laboratory tests on samples taken in the emergency department showed cholestasis (bilirubin 5.79 [direct 2.22; indirect 3.57], aspartate aminotransferase [AST] 318, alanine aminotransferase [ALT] 671, alkaline phosphatase [ALP] 261 and gamma glutamyl transferase [GGT] 347) and high serum amylase levels (1763 IU). Complete blood count and coagulation parameters, acute phase reactants, lipid, thyroid and iron profiles were normal. Abdominal ultrasound performed in the emergency department showed liver parenchyma with no abnormalities, acalculous gall bladder with no signs of inflammation, and intra- and extrahepatic bile ducts of normal calibre and echogenicity.

The clinical picture was interpreted as mild acalculous acute pancreatitis, and the patient was discharged 72 hours later.

Before reassessment in outpatients, though, he was readmitted for a new episode of abdominal pain, with abnormal liver function tests in a cholestatic pattern but no elevated serum amylase. Autoimmune and immunoglobulin tests, as well as hepatotropic virus serology tests were negative. Repeat abdominal ultrasound was requested, with no findings of interest. Magnetic resonance cholangiography showed distal segmental dilatation of the intrahepatic bile duct, with contrast uptake in segments V, VI and VIII, with hepatic and pancreatic parenchyma of normal morphology and intensity. The gallbladder was acalculous with no signs of inflammation; the extrahepatic bile duct was normal in calibre and intensity.

He was discharged after 7 days and scheduled for endoscopic ultrasound (EU).

However, a few days later, his mother came to the clinic with clinical reports on 2 maternal first cousins who had recently been placed on the transplant waiting list as a result of liver cirrhosis secondary to familial intrahepatic cholestasis type 3, due to a complete deficiency of MDR3 secondary to a homozygous mutation in *ABCB4*.

Consequently, given the family history, a genetic test was requested for *ABCB4* gene expression in peripheral blood, isolating DNA from lymphocytes and then sequencing exon 4 of the *ABCB4* gene and the adjacent intronic regions. Results showed a heterozygous mutation in nucleotide 202, which involves the substitution of glycine 68 for arginine, consistent with partial MDR3 deficiency.

Treatment with urosdeoxycolic acid (UDCA) 12 mg/kg/day was started immediately; laboratory parameters returned to normal, except for bilirubin, which has fluctuated since then (1-year follow-up), with increases at the expense of indirect bilirubin, probably related with Gilbert syndrome. He has presented no new episodes of abdominal pain. Owing to the risk of fibrosis due to chronic cholestasis in these patients, liver elastography was performed, with a result of 5.5 kPa (F0–F1). Given the patient's improvement, the EU was postponed. So far, no genetic studies have been conducted in first degree relatives.

Over the last few years, several clinical cases and studies have been published highlighting the role of various hereditary disorders that affect membrane transport proteins in cholestatic syndromes.

MDR3 is a protein that has been isolated in the canalicular membrane of the hepatocyte. It acts as an ATP-dependent pump, releasing phosphatidyl choline to the small bile ducts which, together with cholesterol and bile acids, enables formation of mixed micelles.[1]

The *ABCB4* (7q21) gene has been identified as responsible for its synthesis, with more than 60 different mutations having been described,[2] both homozygous and heterozygous. These will result in truncated (*nonsense mutation*), immature or nonfunctional proteins (*missense mutation*) that will determine the severity of the deficiency.[3]

Bile salt-induced cholangiocyte damage has been observed in cases of MDR3 deficiency, as well as increased formation of calculi, both in the gallbladder and intra- and extrahepatic bile ducts.[4] This deficiency is currently

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related with the following syndromes: progressive familial intrahepatic cholestasis type 3, low phospholipid-associated cholelithiasis (LPAC) syndrome, intrahepatic cholestasis of pregnancy, transient neonatal cholestasis, drug-induced liver disease, as well as fibrosis and cirrhosis in adults.[5]

Our patient met 2 of the following criteria for LPAC syndrome: (1) onset of symptoms before 40 years of age; (2) chronic mild cholestasis; (3) intrahepatic hyperechoic foci, biliary sludge or microlithiasis; (4) low biliary phospholipid concentration, and (5) recurrence of biliary symptoms after cholecystectomy.[6,7] Once the mutation had been confirmed, the presence of complicated biliary colic and chronic mild cholestasis led us to believe that this was a compound heterozygous patient, resulting in synthesis of immature or nonfunctional — but not truncated — MDR3 protein.

It is important to assess this possible aetiology in young patients who present repeated episodes of biliary colic for several reasons: first, because genetic tests are available that can confirm the diagnosis and avoid invasive tests with their associated risks; second, because it is an entity with a high response rate to UDCA,[3] an inexpensive, well-tolerated drug; third, because patients can present complications, such as complicated biliary colic or progressive fibrosis[5]; and finally, given its genetic nature, screening can be performed in first and second degree relatives who present compatible symptoms.[2]

References

1. Eferink RP, Tytgat GN. Hepatic canalicular membrane 1: the role of MDR2 P-glycoprotein in hepatobiliary lipid transport. FASEB J. 1997;11:19–28.
2. Poupon R, Rosmorduc O, Boëlle PY, Chrétien Y, Corpechot C, Chazouillères O, et al. Genotype-phenotype relationships in the low-phospholipid-associated cholelithiasis syndrome: a study of 156 consecutive patients. Hepatology. 2013;58:1105–10.
3. Jacquemin E. Progressive familial intrahepatic cholestasis. Clin Res Hepatol Gastroenterol. 2012;36 Suppl 1:S26–35.
4. Strubbe B, Geerts A, van Vlierberghe H, Colle I. Progressive familial intrahepatic cholestasis and benign recurrent intrahepatic cholestasis: a review. Acta Gastroenterol Belg. 2012;75:75–80.
5. Davit-Spraul A, Gonzales E, Baussan C, Jacquemin E. The spectrum of liver diseases related to ABCB4 gene mutations: pathophysiology and clinical aspects. Semin Liver Dis. 2010;30:134–46.
6. Poupon R, Arrive L, Rosmorduc O. The cholangiographic features of severe forms of ABCB4/MDR3 deficiency-associated cholangiopathy in adults. Gastroenterol Clin Biol. 2010;34:380–7.
7. Wang D, Afdhal N. Sleisenger and Fordtran's Gastrointestinal Liver Disease. Feldman & Friedman & Brandt. Volume 2. Sección IX. Liver Chapter 65, p. 1100–1133.

Héctor Miguel Marcos Prieto, Daniel Pérez Corte, M. Concepción Piñero Pérez*, María Cristina Revilla Morato, Ana María Mora Soler, Rosa Virgina Acosta Materán, Andrea Jiménez Jurado, Valeria Calabuig Mazzola, Antonio Rodríguez Pérez

Servicio de Aparato Digestivo, Complejo Asistencial Universitario de Salamanca, Hospital Clínico, Salamanca, Spain

* Corresponding author.
E-mail address: conxipi@hotmail.com (M.C. Piñero Pérez).

Metastatic intestinal obstruction secondary to a primary lung tumour☆

Obstrucción intestinal por metástasis de cáncer de pulmón

Small bowel tumours are very rare, accounting for 1%–6% of all gastrointestinal (GI) cancers. Between 1% and 4% correspond to metastatic tumours, most commonly originating from malignant melanoma, lung cancer and colon cancer.[1]

Metastatic involvement of the small intestine is rare from a clinical point of view, but not so much from a histopathology perspective, with an incidence of 2%–14% according to autopsy series.[2]

The clinical manifestation of intestinal metastases is generally due to a complication of the disease, such as perforation, obstruction or active bleeding.[3] Presence of any of these is associated with poorer prognosis of the underlying disease, and requires urgent surgical treatment.

We present 2 cases of patients with primary lung cancer who presented intestinal obstruction due to metastasis.

The first case, a 78-year-old man, smoker of 40 pack-years, was diagnosed with squamous cell lung cancer T2aN0M1 (hepatic) and treated with chemo- and radiotherapy. Nine months later, he presented to the emergency department for symptoms of bowel obstruction. Abdominal X-ray and computed tomography (CT) revealed dilatation of loops to the mid-jejunum with change in calibre secondary to adhesion or internal hernia. The patient underwent surgery, during which an obstruction was found in the jejunum as a result of a stenosing tumour. Complete resection and anastomosis were performed. Histopathology classified the tumour as squamous cell carcinoma metastasis. The patient was discharged on postoperative day 8. He continued with chemotherapy but died due to disease progression 20 months after the surgery.

The second case, a 49-year-old man, smoker of 20 pack-years, was seen in the emergency department for abdominal pain. Abdominal CT (Fig. 1) showed a mass in the right iliac fossa with signs of necrosis and regional lymphadenopathies. Colonoscopy was performed due to suspected caecal cancer, with no evidence of lesions. However,

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