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Endometriosis of the appendix☆

Endometriosis del apéndice

Extrauterine endometrial tissue is known as endometriosis, and is common in women of reproductive age.[1] Endometrial lesions are found in genital organs and the pelvic peritoneum, but are also observed in gastrointestinal organs such as the omentum, in surgical scars, and in the mesenterium; they are found more rarely in the kidney, lungs and skin, and very rarely in the nasal cavity.[2]

Endometriosis of the appendix (EA) has been identified in less than 1% of patients with pelvic endometriosis.[3] It is generally asymptomatic, and is associated with appendicitis, perforation and intussusception. An incidence of 0.05% in 71 000 appendectomy specimens has been reported.[4] We describe the case of a patient in whom EA was diagnosed during laparoscopy.

The patient was 38-years-old, gravida I, para I, and presented with a 9-month history of mild–moderate abdominal pain, which was constant, unrelated with the menstrual cycle and did not improve with common analgesics. Her menstruation was irregular-dysmenorrhoeic, and her last menstrual period was 12 days before admission. She reported no major medical or surgical history. Her general health was good, with normal vital signs. The abdomen was soft, palpable but painful on deep palpation predominantly in the right iliac fossa, and McBurney positive, with no frank evidence of peritoneal irritation; pelvic examination found no abnormalities. Plain abdominal X-ray showed no significant findings. Pelvic ultrasound revealed normal uterus and annexes. White cell count and percentage neutrophils were 8900 mm^3 and 67%, respectively. Urinalysis showed no pyuria or haematuria. Pregnancy test was negative.

The patient underwent diagnostic laparoscopy for the chronic pelvic pain, in which normal uterus, ovaries and Fallopian tubes were observed, with some endometrial foci at the bottom of the pouch of Douglas, which were treated with electrocautery. The appendix was observed to

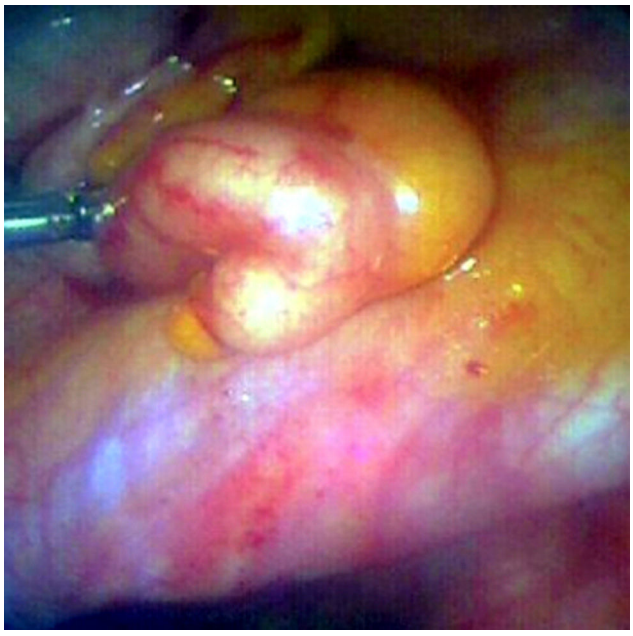

Figure 1 Irregular, distended and inflamed appendix.

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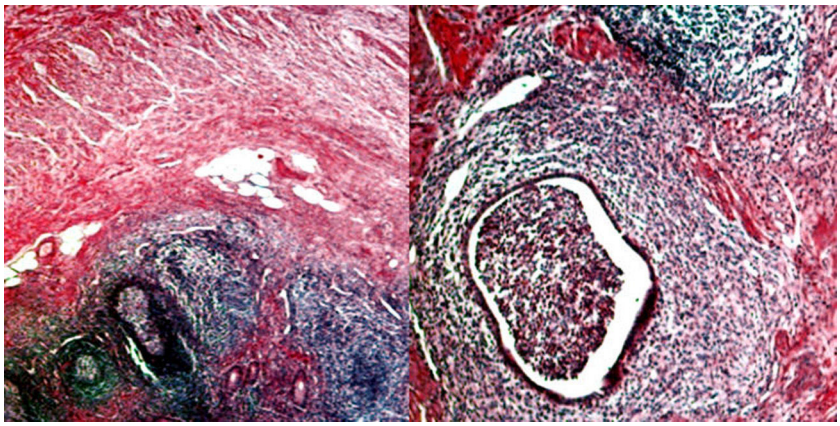

Figure 2 Endometrial glands and stroma in the seromuscular layer of the appendix.

be moderately congested, short, distended, irregular and oedematous, suggesting inflammation (Fig. 1), so appendectomy was performed. The patient was discharged on the third day. During her recovery, she reported a significant improvement in symptoms.

Histopathology analysis showed the presence of periglandular stroma consistent with endometrial stroma limited to the muscle and serosal layer (Fig. 2), confirming the diagnosis of EA.

EA is divided into primary and secondary forms. The primary form shows histopathological evidence of endometriosis within the appendix, with no clinical–pathological evidence of extra-appendicular endometriosis. The secondary form is associated with internal and/or external endometriosis. The majority of studies have pointed to similarities between appendiceal and tubo-ovarian endometriosis. Moreover, most patients diagnosed with EA suffer from menstrual irregularities and uterine myomatosis.[5,6]

Patients with EA can be divided into 4 groups, according to symptoms: patients with acute appendicitis, patients with invagination of the appendix, patients with atypical symptoms (abdominal pain, nausea and/or melaena) and asymptomatic patients. The most commonly observed group are patients who present with appendicitis, with the condition occurring mainly during menstruation.[6] Symptoms are caused by endometrial bleeding within the seromuscular layer followed by oedema, obstruction and inflammation, leading to partial or complete occlusion of the appendiceal lumen.[5]

Diagnostic options such as patient history, physical examination, blood tests (CA-125), colonoscopy, ultrasound, tomography and magnetic resonance imaging may be useful for making the diagnosis of endometriosis. There are no imaging findings pathognomic of endometriosis.[4] Definitive diagnosis is by biopsy of the endometrial implants. Although these are classically bluish-black lesions with variable degrees of pigmentation and peripheral fibrosis, most implants appear as non-pigmented lesions.[7]

The differential diagnosis of intestinal endometriosis includes inflammatory bowel disease, diverticulitis, ileocolonic tuberculosis, schistosomiasis, benign and malignant neoplasms and colonic ischaemia.[7]

Histopathological evaluation is essential for the diagnosis of EA.[8] Half of cases involve the body and the other half the tip of the appendix. The mucosa is generally not affected, while endometrial stroma and glands, like bleeding, are observed in the muscle and seromuscular layer in two-thirds of cases, and in the serous layer only in the other third.[6]

Treatment consists of surgery and hormone therapy based on the severity and type of symptoms. Preventing endometriosis is still not possible, so treatment begins with improving symptoms. Some patients are completely asymptomatic, and implants are found incidentally during surgery for other reasons. Laparoscopic surgery is useful in women with chronic abdominal pain, as in the present case, as it enables the entire peritoneal cavity to be explored and definitive diagnosis made. Laparoscopic appendectomy is the treatment of choice in these cases.[5] Further medical treatment should be considered following surgery in patients with symptomatic endometriosis.[7]

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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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