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SCIENTIFIC LETTER

Diagnostic challenge of autoimmune pancreatitis in children: Utility of endoscopic ultrasound-guided biopsy



Reto diagnóstico de pancreatitis autoinmune en niños: utilidad de la biopsia guiada por ultrasonido endoscópico

Autoimmune pancreatitis (AIP) is a diagnostic challenge in the pediatric population due to its low prevalence, nonspecific clinical presentation, and heterogeneous biochemical characteristics and imaging results.¹ AIP is more common in adolescents, with a slight predominance in males (53%) and a median age at diagnosis of 13 years.² Despite the fact that it is an uncommon disease in pediatrics, its importance lies in the need for a histologic diagnosis before starting treatment with corticosteroids –a therapy not exempt from risks– and in the importance of preventing underdiagnosis that could delay adequate management.²

The diagnostic criteria established for adults, such as the 2010 International Consensus Diagnostic Criteria (ICDC) for AIP,³ include serology, histopathology, involvement of other organs, imaging study findings, and steroid therapy response, which may not be fully applicable in the pediatric population, given the variability of clinical manifestations and laboratory findings. In adults, elevated IgG4 levels are essential for diagnosing type 1 AIP (68–92%), whereas they are observed in only 22% of cases in children.²

From the imaging perspective, AIP can reveal overall or focal parenchymal enlargement, presenting as hypointense areas in T1-weighted images, as well as irregularities in the main pancreatic duct (64%).² However, none of those clinical or radiologic characteristics are specific for AIP, and so the differential diagnoses of pseudotumor and pancreatic tumor must be considered.⁴ Unnecessary surgical interventions, such as partial pancreatectomy or Whipple pancreatoduodenectomy, are reported in up to 17% of patients with AIP, underlining the importance of combining numerous diagnostic criteria and considering histopathologic diagnosis the gold standard.⁵ In such a context, obtaining tissue through ultrasound endoscopy (USE) has emerged as a basic tool, standing out for its high diagnostic yield and safety profile in the adult population.⁶ USE is the preferred method for pancreatic biopsy because it is less invasive, compared with laparoscopy, and it does not require the ionizing radiation used in computed tomography (CT)-guided percutaneous biopsy.⁷

A 13-year-old girl presented with recurrent acute pancreatitis (RAP), initially of idiopathic etiology, with three episodes of intense abdominal pain in the epigastrium and mesogastrium, accompanied by nausea and vomiting, but no fever or jaundice. During the acute episodes, elevated levels of amylase (340–1,120 U/l) and lipase (285–965 U/l) were detected. CT and magnetic resonance cholangiopancreatography (MRCP) identified a slight increase in the size of the pancreas, with no other significant alterations.

Etiologic study included measuring the levels of triglycerides, calcium, parathyroid hormone, and serum IgG4, and they were all within normal limits. Likewise, the genetic analysis ruled out the most frequent gene mutations (PRSS1, SPINK1, CFTR, CPA1, and PRSS2) associated with chronic pancreatitis.⁸ Due to the persistence of recurrent episodes and absence of obvious etiology, USE-guided biopsy of the pancreas was performed to obtain tissue.

The USE was carried out under general anesthesia, with a linear echoendoscope, enabling detailed evaluation of the pancreatic parenchyma (diffuse enlargement), main pancreatic duct, and contiguous organs (Fig. 1). Using a 22 G Franseen fine-needle biopsy needle, samples were obtained from the head of the pancreas, via the transduodenal approach, and the body of the pancreas, via the transgastric approach, preventing vascular damage through the Doppler technique (Fig. 2). One needle pass was carried out in each region, using the fanning technique, with the slow removal of the stylet to maximize the sample yield (Fig. 2). No intraoperative or postoperative complications were registered.

The histopathologic analysis of the samples revealed lymphoplasmacytic infiltration positive for IgG4, consistent with AIP, emphasizing the usefulness of the minimally invasive approach through USE for diagnostic accuracy, as well as for guiding adequate treatment. Treatment was started with prednisone (1 mg/kg/day) for four weeks, with reduced disease progression for the following month. The patient progressed favorably, with no new episodes of pancreatitis during a 15-month follow-up.

USE is an indispensable diagnostic tool in the context of pediatric AIP because it enables samples to be obtained that are adequate for histopathologic and immunohistochemical analyses. Even though there are challenges related to the availability of trained echo-endoscopists and the necessary infrastructure, the benefits in terms of diagnostic precision and safety profile justify its implementation at referral centers.

In conclusion, AIP should be considered in the differential diagnosis of recurrent pancreatitis in children,

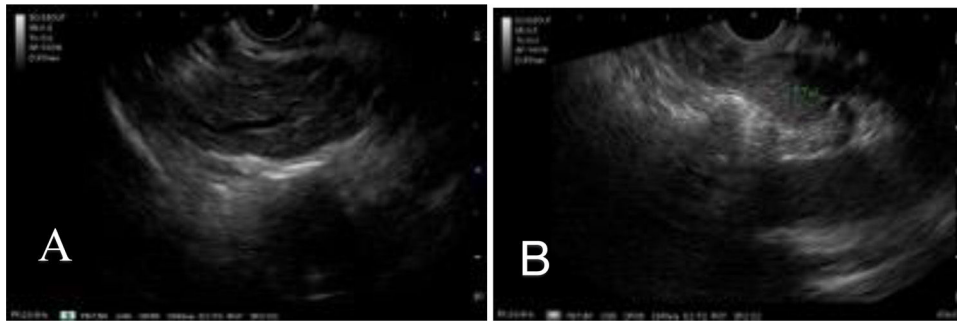


Figure 1 (A) Body and (B) tail of the pancreas with minor Rosemont criteria for chronic pancreatitis^{9,10} (hyperechoic traces with no acoustic shadow and hyperechoic enhancement of the walls of the main pancreatic duct).

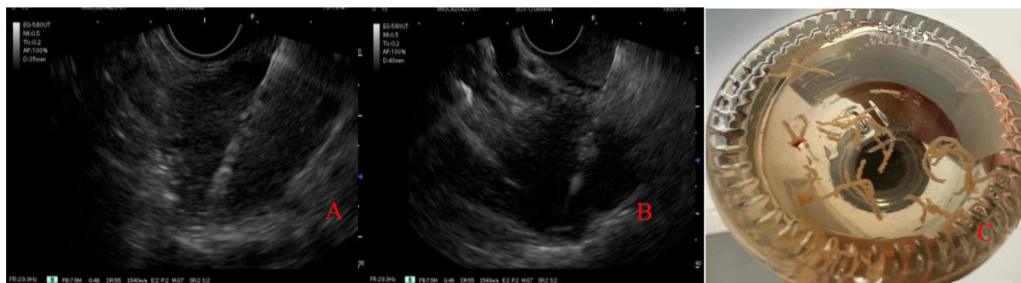


Figure 2 (A) Biopsy from the body of the pancreas obtained through the transgastric approach. (B) Biopsy of the head of the pancreas obtained through the transduodenal approach. (C) Pancreatic tissue obtained.

especially when clinical and imaging characteristics are inconclusive. USE-guided biopsy of the pancreas is a fundamental diagnostic support enabling histologic confirmation through a minimally invasive procedure, as well as preventing treatment with inadequate therapies that are not exempt from complications and underdiagnosis of the disease.

Ethical considerations

We declare we obtained written informed consent from the legal guardians of the patient to publish this article. This work is not an experimental or clinical study, but rather the presentation of a relevant clinical case. It contains no personal data that could identify the patient, thus additional consent was not required.

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Declaration of competing interest

The authors declare that there is no conflict of interest.

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Non-classical celiac disease with negative screening serology. Case report



Enfermedad celíaca de presentación no clásica con serología de escrutinio negativa. Reporte de caso

Celiac disease (CD) is one of the most common autoimmune enteropathies of the small bowel. It affects persons with a genetic predisposition and is derived from exposure to gluten, a protein present in wheat, barley, and rye. CD causes changes in the duodenal mucosa, characterized by intestinal villi atrophy, crypt hyperplasia, and lymphocytic infiltration, often producing malabsorption.¹

A 41-year-old woman had a past medical history of hypothyroidism and infertility (G2-A2), history of constipation and vomiting of 10-year progression, defecation pattern of <3 bowel movements per week with Bristol 1 and 2 stool consistency, and difficulty in passing the stools. She stated having no anal blockage sensation, incomplete evacuation, or digital manipulation. Stools had no mucus or blood, and bowel movements improved with fiber intake. She also stated having postprandial vomiting that contained bile and food, but no borborygmi, abdominal pain, or bloating. She said she experienced early satiety and postprandial fullness once or twice a week, triggered by fat and carbohydrate intake. She had no weight loss. Neurologic and abdominal physical examinations were unremarkable. Perianal inspection was postponed due to patient modesty.

Initial endoscopy reported Los Angeles grade A esophagitis, a 10 mm Forest III ulcer on the anterior surface of the greater curvature in the gastric antrum and flattening of the villi in the second and third parts of the duodenum. Gastric ulcer biopsies showed reparative epithelial changes, with no atypia, and were negative for *Helicobacter pylori*. There was mild villous atrophy, *Giardia* test was negative, and 50% of the CD3/CD8 intraepithelial lymphocytes (IELs) in the bulb and second and third parts of the duodenum were classified as MARSH 3A. Tissue transglutaminase IgA antibodies (tTg IgA) and serum IgA were both negative. Standard dose

esomeprazole for 12 weeks was the clinical management (Fig. 1).

Given the findings in the duodenum and the suspicion of CD versus seronegative enteropathy, testing for endomysial antibodies (EMA), deamidated gliadin peptide-IgA antibodies (DGP-IgA), and deamidated gliadin peptide-IgG antibodies (DGP-IgG) was ordered. CD was diagnosed by means of the positive DGP-IgA test finding and gluten restriction was started. After three months of treatment, the patient said her vomiting, constipation, and dyspeptic symptoms had improved (Table 1).

CD affects 1% of adults and the dietary restriction of gluten is the only efficacious treatment. Risk is higher in persons with autoimmune diseases, such as type 1 diabetes or autoimmune thyroiditis.² Prevalence of 0.5–0.7% is reported in Mexico, whereas it has reached 1.3% in Latin America, with greater frequency in Argentina and Brazil. According to its presentation, CD is classified into symptomatic, asymptomatic, and potential disease.

Symptomatic CD is characterized by the presence of classic, extraintestinal, or non-classic gastrointestinal symptoms. The classic manifestations are diarrhea, steatorrhea, and weight loss. Non-classic CD is characterized by the absence of malabsorption symptoms with the predominance of other manifestations, such as abdominal pain and bloating, borborygmi, constipation, vomiting, and anemia, among others. A high level of suspicion is essential, given that less than 50% of adults present with classic gastrointestinal symptoms. On the other hand, the asymptomatic variant is characterized by the absence of symptoms, with positive serology and altered duodenal mucosa, whereas potential CD presents in persons at risk of developing the disease, who have normal histology and positive serology.³

The testing for tTg IgA antibodies plus serum IgA is indispensable for making the diagnosis, with 78% sensitivity and 98% specificity. Due to the variable diagnostic accuracy, anti-IgA-endomysial antibody (EMA) and anti-DGP-IgA antibody tests are useful for diagnosing patients highly suspected of presenting with CD who have negative tTg IgA + serum IgA tests. The anti-IgA-EMA test has 94% sensitivity and 100% specificity, and the anti-DGP-IgA antibody test has 74% sensitivity and 95% specificity. In cases of selective IgA deficiency, determining IgG antibodies supports the diagnosis.⁴