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Gastrointestinal and hepatobiliary manifestations in patients with common variable immunodeficiency: In relation to three clinical cases☆

Manifestaciones gastrointestinales y hepatobiliares en pacientes con inmunodeficiencia común variable: a propósito de 3 casos clínicos

Common variable immunodeficiency (CVID) is a primary immune condition characterised by immunoglobulin deficiency. This leads to recurrent infections and, less commonly, autoimmune or skin manifestations, as well as a higher risk of cancer, particularly gastrointestinal and haematological types.[1] CVID affects one in 50,000, predominantly young people, and has no relationship with gender or race.[2]

Diagnosis is based on low IgG, reduction of at least one of the IgM or IgA isotypes and meeting three criteria: onset of immunodeficiency after the age of two; absence of isohaemagglutinins and poor response to vaccines; and exclusion of other causes of hypogammaglobulinaemia.[3] CVID presents with gastrointestinal symptoms in up to 60% of cases[4] and hepatic symptoms in 10%.[5]

We present three cases of patients with CVID and gastrointestinal symptoms. The first was a 46-year-old male who, in the context of acute hepatitis, had a liver biopsy which showed autoimmune hepatitis (AIH). He was managed with prednisone plus azathioprine with a good response. Blood tests revealed low immunoglobulins, but no previous recurrent infections. During follow-up, CVID was diagnosed. He is managed with monthly immunoglobulin replacement with a good clinical response.

The next case is that of a 33-year-old male patient with a history of CVID and recurrent respiratory infections, on therapy with monthly doses of immunoglobulin. Blood tests over the last 12 months showed a progressive decrease in total proteins (4.6 mg/dl) and albumin (2.9 mg/dl). He had normal prealbumin, no proteinuria, negative anti-transglutaminase antibodies and no weight loss.

Upper endoscopy showed antrum erosions, and colonoscopy resected colon polyps. Biopsies of the small intestine showed chronic duodenitis with subtotal villous atrophy and colon polyps with high-grade dysplasia. Nutrition was optimised without response, and protein-losing enteropathy was suspected and confirmed with the measurement of α1-antitrypsin in stools. The patient responded well to treatment with corticosteroids.

The last case is that of a 21-year-old male with a history of CVID and cyclic neutropenia, with recurrent infections, who occasionally receives doses of immunoglobulins. In the context of pruritus and abnormal liver function tests, primary sclerosing cholangitis (PSC) was diagnosed by magnetic resonance cholangiography. Secondary causes were ruled out and treatment was started with ursodeoxycholic acid, with a good response. The patient later presented with a six month history of intermittent diarrhoea with blood, but no other symptoms. Laboratory tests showed anaemia, neutropenia and normal faecal calprotectin.

Colonoscopy showed non-specific proctitis and two sigmoid polyps, which were resected. Biopsies showed non-specific chronic colitis. Immunoglobulins were prescribed monthly, improving the diarrhoea.

CVID is the most common primary immunodeficiency characterised by B cell dysfunction and low antibody production, leading to a poor response to infections and vaccines. In addition, dysregulation of T cell function is described, which determines some of the autoimmune manifestations.[4]

The first case has AIH; autoimmunity is common in CVID and autoimmune reactions have been described in the liver.[5] The diagnosis is complex, as IgG does not rise. In this case the Hennes criteria were applied for diagnosis, with the patient scoring a total of six points. Patients with CVID have a higher incidence of liver granulomas, nodular regenerative hyperplasia, PSC, primary biliary cholangitis and cryptogenic cirrhosis.[1–5]

The second case had hypoalbuminaemia and mononuclear inflammatory infiltration of the duodenal mucosa. In CVID, lymphocytic infiltration in the gastrointestinal tract is common,[6] resembling an autoimmune enteropathy, such as coeliac disease, which causes malabsorption, and this would explain the hypoalbuminaemia.[1] In these cases, anti-transglutaminase antibodies are negative and there is no response to a gluten-free diet; selected cases respond to corticosteroids.[7] The patient had several colon polyps. The presence of colon polyps is similar to the general population and there is no increased risk of colon cancer.[8]

The third patient presented with chronic diarrhoea and inflammatory involvement of the colorectal mucosa. Inflammatory bowel disease is more common in patients with CVID, but the detection of non-specific colitis is common and would explain the diarrhoea.[9] Immunoglobulin replacement does not generally resolve these symptoms, so corticosteroid therapy is required.[7] He also has PSC, which is more common

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in patients with CVID. Other gastrointestinal tract disorders include opportunistic infections that would cause chronic diarrhoea and *Helicobacter pylori* infection, associated with a 50-fold increase in the incidence of gastric cancer compared to the general population.[9]

Last of all, gastrointestinal and hepatobiliary manifestations are common in patients with CVID, and we therefore suggest that investigations be guided by the morbidity/mortality they represent.

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Microcytic anemia due to ileocolic anastomotic ulcer☆

Anemia microcítica secundaria a úlcera anastomótica ileocólica

Ileocolic perianastomotic ulcers are a late-onset, uncommon, and probably underdiagnosed complication of ileocaecal resections. They tend to present with diarrhoea, malabsorptive syndrome and occult gastrointestinal bleeding which can lead to chronic iron deficiency anemia.

We present the case of a 22-year-old male, who had been a preterm baby, with a history of right hemicolectomy and ileal resection of 23 cm in the first months of life due to necrotising enterocolitis, referred to the outpatient clinic at the age of 19 for severe iron deficiency anemia refractory to oral iron therapy. Initial analysis showed haemoglobin 10 g/dl, mean corpuscular volume 78.7 fl, cholesterol 76 mg/dl, triglycerides 49 mg/dl, albumin 4.12 g/dl and low ferritin levels of 11 ng/ml. Fibre optic gastroscopy with gastric and duodenal biopsies ruled out coeliac disease and *Helicobacter pylori* infection. After confirming the presence of faecal occult blood, fibre optic colonoscopy was performed, showing ileocolic anastomosis ulceration around the entire circumference. Biopsies were compatible with chronic ischaemia. An abdominal CT scan showed multiple gallstones and postoperative changes at the ileocolic anastomosis level.

Treatment was started with mesalazine, diosmin and glutamine. However, since there was no improvement, with the anemia persisting despite oral and parenteral iron replacement, it was decided to resect the ileocolic anastomosis and perform reanastomosis. The histology findings were compatible with chronic ischaemic ulcer (Fig. 1).

After 18 months of follow-up, the patient remains asymptomatic, with no anemia or iron deficiency.

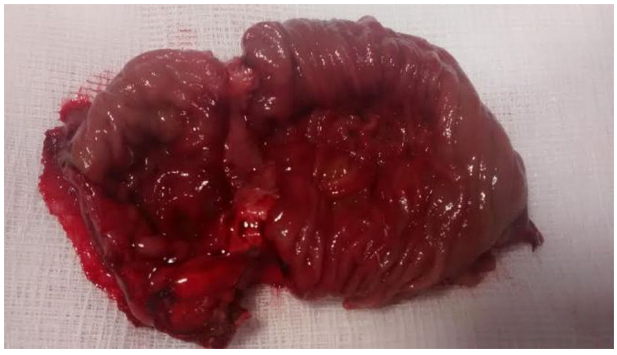

Figure 1 Resection segment from the ileocolic anastomosis showing circumferential ulceration.

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