haematoxylin–eosin, PAS and Grocott-Gomori methenamine silver, or more specific stains, such as Mayer's mucicarmine (stains the capsule of the fungus magenta) and Fontana-Masson stain (stains melanin reddish-brown).[2]

Two forms of skin manifestations of *C. neoformans* infection have been described. Primary cutaneous cryptococcosis is caused by superinfection of a previous, usually isolated lesion on exposed areas of the skin. It is similar to PG in appearance, and systemic involvement is uncommon. Skin involvement secondary to haematogenous spread usually involves multiple lesions in both exposed and unexposed areas. The lesions appear as umbilicated papules and are accompanied by systemic symptoms. Irrespective of the appearance or characteristics of the skin lesions associated with *C. neoformans* infection, systemic disease must always be ruled out.[3]

C. neoformans infections have been described in patients with IBD[4] but no cases of PG and primary cutaneous cryptococcosis have been reported in any such patient. Given the high sensitivity of the culture, we believe that *C. neoformans* infected a previous PG lesion on the right forearm, although the possibility that a low concentration of cryptococci in the area chosen for the first biopsy precluded their detection in the initial culture cannot be completely ruled out. By the time the second biopsy was taken, cryptococci had multiplied due to the immunosuppressive action of prednisone and ciclosporin.[5] Either way, the practical conclusion is that before adding further immunosuppressants in patients with IBD, biopsy of PG lesions refractory to standard treatment should be repeated (histology, staining and culture) to rule out fungal and bacterial infections.

References

1. Rahier JF, Magro F, Abreu C, Armuzzi A, Ben-Horin S, Chowers Y, et al. Second European evidence-based consensus on the prevention, diagnosis and management of opportunistic infections in inflammatory bowel disease. J Crohns Colitis. 2014;8:443–68.
2. Gazzoni AF, Severo CB, Salles EF, Severo LC. Histopathology, serology and cultures in the diagnosis of cryptococcosis. Rev Inst Med Trop Sao Paulo. 2009;51:255–9.
3. Neuville S, Dromer F, Morin O, Dupont B, Ronin O, Lortholary O, et al. Primary cutaneous cryptococcosis: a distinct clinical entity. Clin Infect Dis. 2003;36:337–47.
4. Fraison JB, Guilpain P, Schiffmann A, Veyrac M, Le Moing V, Rispail P, et al. Pulmonary cryptococcosis in a patient with Crohn's disease treated with prednisone, azathioprine and adalimumab: exposure to chicken manure as a source of contamination. J Crohn's Colitis. 2013;7:11–4.
5. Zhu TH, Rodriguez PG, Behan JVV, Declerk B, Kim GH. Cryptococcal cellulitis on the shin of an immunosuppressed patient. Dermatol Online J. 2016;22:6.

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An uncommon cause of acute abdominal pain and diarrhoea in systemic lupus erythematosus

Una causa poco común de dolor abdominal agudo y diarrea en el Lupus Eritematoso Sistémico

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multisystem involvement, including the gastrointestinal tract.[1] Gastrointestinal symptoms such as abdominal pain are common in patients with SLE and can arise from multiple causes.[1] Lupus enteritis is a rare, poorly understood and potentially severe cause of abdominal pain in SLE.[2,3] Hydronephrosis is also a rare complication of SLE, usually associated with bladder and/or gastrointestinal involvement (63.3% of cases).[1,4]

An 18-year-old woman with a 1-year diagnosis of systemic lupus erythematosus (SLE) was under hydroxychloroquine (HCQ) 400 mg and prednisolone 5 mg daily. She was diagnosed with SLE based on cutaneous involvement (malar rash, diffuse hair loss, recurring nasal sores), arthritis, lymphopenia and positivity for antinuclear and anti-dsDNA antibodies. She was admitted with a 5-day history of lower abdominal pain and diarrhoea (5 bowel movements/day). Two weeks before admission, an acute pyelonephritis was diagnosis with bilateral hydronephrosis without no evidence of obstruction, treated with 8-day course of oral amoxicillin/clavulanic acid 875 mg/125 mg. Physical examination revealed abdominal tenderness in the lower quadrants. Laboratory analysis showed lymphopenia (600/mm^3), normocytic and normochromic anaemia (Hg-11.4 g/dL), and C-reactive protein of 2.35 (N<0.5 mg/dL). Antiphospholipid antibodies (anticardiolipin and anti-β2-glycoprotein I antibodies and lupus anticoagulant) were negative. She had a mild activity of SLE (SLEDAI: 4). Plain abdominal X-ray showed multiple air-fluid levels in the small bowel loops and abdominal ultrasonography revealed voluminous ascites, enlarged lymph nodes along iliac vessels and bilateral hydronephrosis. Urinalysis was negative for infection. Mononucleosis spot and pregnancy tests were

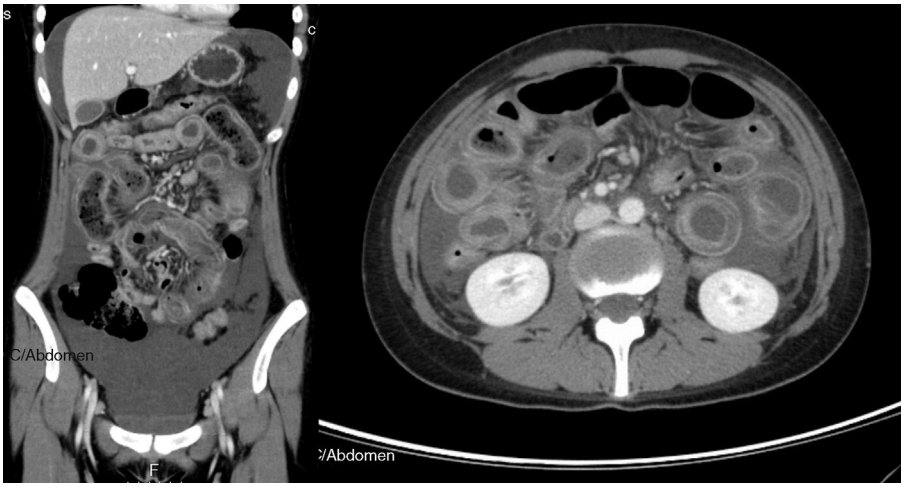

Figure 1 Contrast-enhanced abdominal-pelvic computed tomography scan showing voluminous ascites, diffuse and circumferential oedematous thickening of the small bowel wall with luminal dilation and parietal enhancement as ''target sign'', compatible with lupus enteritis (axial and coronal views).

negative. Diagnostic paracentesis was performed showing serum ascites albumin gradient <1.1 g/dL with negative culture. A provisional diagnosis of mesenteric lymphadenitis was presumed and the patient received antibiotic therapy with ciprofloxacin. Due to lack of improvement within four days, a contrast-enhancement abdominal-pelvic computed tomography (CT) was performed showing voluminous ascites, diffuse and circumferential oedematous thickening of the small bowel wall with luminal dilation and abnormal parietal enhancement as ''target sign'', compatible with lupus enteritis (Fig. 1). She started IV methylprednisolone (1 g/day for three days) followed by oral prednisolone 1 mg/Kg/day. Supportive measures were also attempted, including bowel rest, IV fluids, proton pump inhibitor and low-molecular-weight heparin. She had a dramatic improvement within three days. Oral prednisolone was rapidly tapered until 5 mg/day and continued daily HCQ 400 mg. Plain abdominal X-ray and abdominal ultrasonography within ten days of steroids therapy onset showed a resolution of the aforementioned lesions. No relapse was observed during 6-month follow-up.

Clinical features of lupus enteritis are unspecific, with abdominal pain being the major symptom.[1–4] CT scanning has become the gold standard for diagnosis of this condition, including bowel-wall thickening, bowel dilation, ascites and abnormal bowel wall enhancement, known as ''target sign''.[1–3] However, some other conditions may mimic lupus enteritis, such as pancreatitis, mechanical bowel obstruction, peritonitis, inflammatory bowel disease and intestinal ischemia. Bowel involvement is usually multisegmental, with jejunum and ileum being the most commonly involved sites.[1–4] Abdominal imaging is useful in diagnosis and ruling out other conditions with similar symptoms. Abdominal ultrasonography can be used as a simple and radiation-free imaging technique during follow-up to confirm clinical resolution.[2] This condition is typically steroid-responsive with an overall excellent prognosis.[1–4] A definitive diagnosis is based on clinical and imaging features, and the dramatic response to steroids.[2–5] Early diagnosis, prompt therapy and close surveillance for perforation and peritonitis are crucial to reduce morbidity and mortality.[2,4]

Author's contributions

Marta Gravito-Soares and Elisa Gravito-Soares contributed equally, writing the manuscript and reviewing the literature. Marta Gravito-Soares is the article guarantor. Manuela Ferreira and Luis Tomé critically reviewed the manuscript.

Informed consent

The informed consent was obtained for this case report.

Conflicts of interest

None to declare.

References

1. Fawzy M, Edrees A, Okasha H, El Ashmaui A, Ragab G. Gastrointestinal manifestations in systemic lupus erythematosus. Lupus. 2016;25:1456–62.
2. Janssens P, Arnauld L, Galicier L, Mathian A, Hie M, Sene D, et al. Lupus enteritis: from clinical findings to therapeutic management. Orphanet J Rare Dis. 2013;8:67.
3. Smith LW, Petri M. Lupus enteritis: an uncommon manifestation of systemic lupus erythematosus. J Clin Rheumatol. 2013;19:84–6.
4. Tian XP, Zhang X. Gastrointestinal involvement in systemic lupus erythematosus: insight into pathogenesis, diagnosis and treatment. World J Gastroenterol. 2010;15:2971–7.
5. Hong S, Kim YG, Ahn SM, Bae SH, Lim DH, Kim JK, et al. Clinical outcomes of hydronephrosis in patients with systemic lupus erythematosus. Int J Rheum Dis. 2016;19:1317–21.

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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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