Cytomegalovirus enterocolitis in a patient with common variable immunodeficiency: A capsule endoscopy-aided diagnosis

Enterocolitis por citomegalovirus en un paciente com inmunodeficiencia común variable Un diagnóstico asistido por cápsula endoscópica

Common variable immunodeficiency (CVID) is an antibody deficiency with a high variability in its clinical presentation. It is estimated to affect as many as 1 in 25,000 individuals.[1] According to the largest European database (including 902 patients),[2] the most common reported disorders were pneumonia (32%), autoimmunity (29%), splenomegaly (26%) and bronchiectasis (23%). The main features include respiratory tract infections and their associated complications, enteropathy, autoimmunity and lymphoproliferative disorders. Gastrointestinal disease is deemed to occur in 15% of the patients and despite clinical immunodeficiency, opportunistic infections are not a typical manifestation of CVID. The authors report a case of a 69-year-old Caucasian female with a previous diagnosis of CVID since 2002 (receiving intravenous Ig [immunoglobulin] on a three-week basis) and a non-specific interstitial pneumonitis (under systemic steroids – prednisolone 20 mg per day). She was admitted in our department with a chronic and severe watery diarrhea (8–10 bowel movements per day) lasting for 8 weeks and weight loss (7 kg in 8 weeks). At presentation, she denied fever, abdominal pain, visible blood or pus in the feces, recent travels or new drugs (namely nonsteroidal anti-inflammatory drugs). Upon physical examination, the patient was pale and dehydrated but afebrile and hemodynamically stable. A mild peripheral edema was noted. Labs demonstrated a marked increase in inflammatory parameters (leucocytosis [$19{,}900 \times 10^6$ cel/mm^3] with neutrofilia [91%], trombocytosis, elevated C-reactive protein [7.1 mg/dL] and erythrocyte sedimentation rate [38 mm/h), severe hypokaliemia (2.6 mmol/L), hypomagnesiemia (1.5 mg/dL) and hypoalbuminemia (2.4 mg/dL). Stool examinations for bacteria, *Clostridium difficile*, ova, cysts and parasites were negative. Cryptococcus and *Giardia lamblia* antigen and cultures were persistently negative. Human immunodeficiency virus (HIV), hepatitis B and C virus serologies were negative. Cytomegalovirus (CMV) serology was positive for IgG and negative for IgM. Upper endoscopy did not demonstrate any findings; however, biopsies taken from the duodenum revealed a mild villous atrophy and a chronically active duodenitis. Ileocolonoscopy observed in the right colon a continuous area of hyperemia and erythema without obvious ulceration (biopsies were performed). The observed mucosa of the terminal ileum was normal. Upon the absence of categorical findings for the chronic diarrhea, a capsule endoscopy was performed (Fig. 1). Starting at the distal part of the jejunum, multiple small and rounded ulcers were observed (Fig. 1A and B). More distally, linear and serpiginous ulcers were also observed (Fig. 1C and D). Later, biopsies taken from the right colon revealed the presence of multiple CMV inclusions (confirmed with immunohistochemistry; Fig. 2C) and small vessels vasculitis (Fig. 2D). In a patient with a chronic severe diarrhea with marked increase of inflammatory markers, the mentioned small-bowel findings and the anatomo-pathological findings from the right colon, a presumptive diagnosis of CMV enterocolitis was

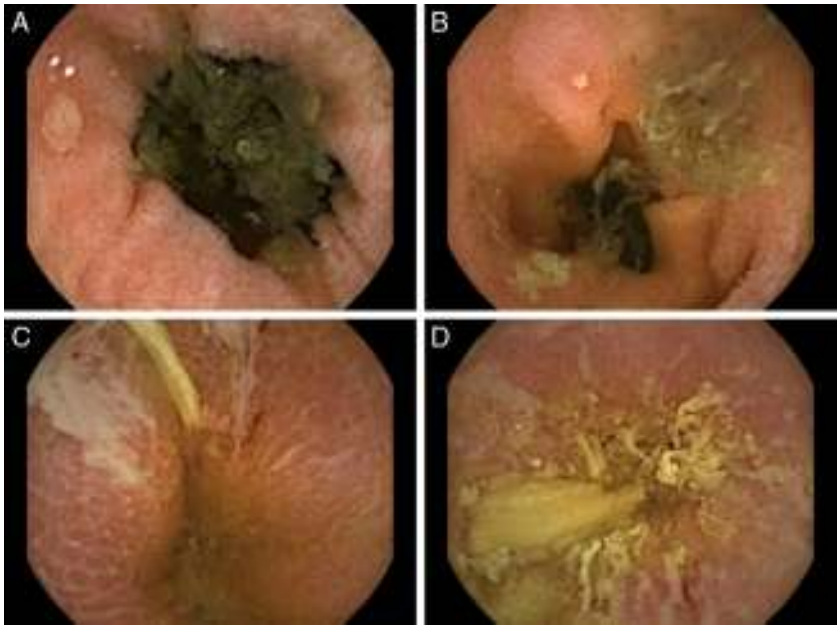

Figure 1 Capsule endoscopy findings. (A and B) Distal part of the jejunum, multiple small and rounded ulcers were observed. (C and D) In the ileum, linear and serpiginous ulcers were also observed.

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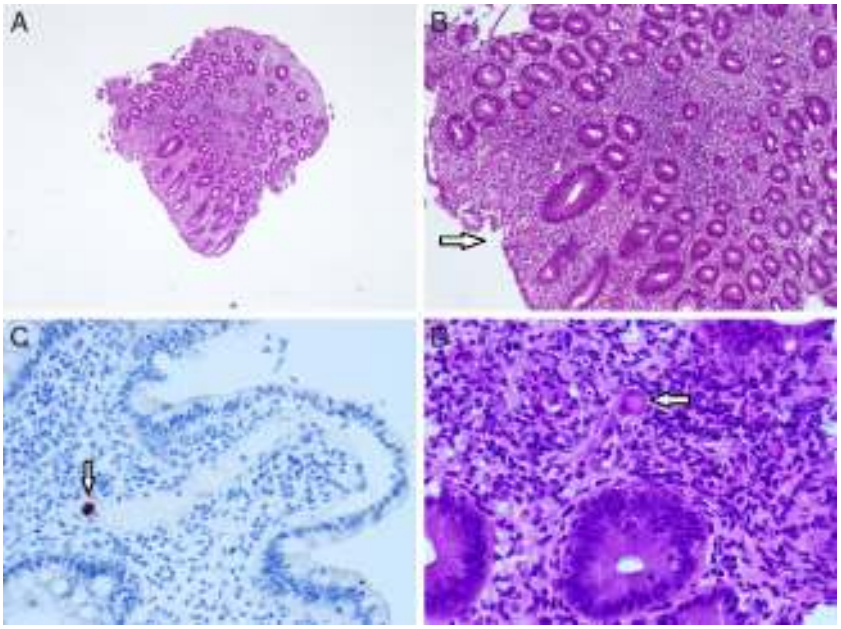

Figure 2 Histologic findings (right colon). Hematoxylin and eosin staining 4× and 10× magnification (A and B): marked inflammatory changes and an area of superficial ulceration (arrow). CMV immunostaining (C): immunohistochemically stained biopsy specimen showing a cytomegalovirus-positive cell (arrow); hematoxylin and eosin staining 40× magnification (D): small vessel vasculitis by a giant cell with inclusion body characteristic of CMV (arrow).

assumed and intravenous ganciclovir was promptly initiated. Oral steroids were reduced by half the dose. After 4 weeks of antiviral therapy, the patient was discharged, she had two bowel movements per day and her electrolytic imbalance was controlled.

The main gastrointestinal symptom in CVID is a transient or persistent diarrhea,[3,4] mostly due to *Giardia lamblia* persistent infection, norovirus, *Campylobacter jejuni* or *Salmonella*. Even thought, many gastrointestinal symptoms cannot be imputed to an infectious etiology. Inflammatory bowel disease remains an important differential diagnosis to be made, being present in 19–32% of those with persistent severe diarrhea, steatorrhea and malabsorption.[1] In fact, gastrointestinal disease in CVID displays so many features that can mimic lymphocytic and collagenous colitis, lymphocytic gastritis, celiac disease, granulomatous disease, acute graft-versus-host disease and inflammatory bowel diseases.[3] The standard of care in CVID is replacement Ig (300 mg/kg every 3 weeks or 600 mg/kg per month). This therapy greatly impacts on bacterial infections incidence.[5] However, it does not appear to have significant impact on other inflammatory complications like progressive lung disease, gastrointestinal and granulomatous disease, autoimmunity, lymphoid hyperplasia and lymphoma. Additionally to the most obvious risk factor (CVID) in our patient, we admit that despite following regular Ig administrations, long-term oral steroids have played an important role in this opportunistic gastrointestinal infection. CMV infection and disease is relatively common among HIV infected patients and among those with secondary immunosuppression (e.g., post-transplant). *Albeit* that, severe organ damage, even on those patients, is considered rare. Clinically, small-bowel involvement (due to infection of vascular endothelial cells) may range from mild anorexia to overt massive gastrointestinal bleeding and perforation.[6,7] Capsule endoscopy (CE) is widely accepted for small-bowel investigation. Its diagnostic yield in chronic diarrhea is considered to be low, ranging from 13 to 24%[8,9]; however, in the present case, this technology enabled us to establish the diagnosis of CMV enterocolitis without histological sampling of the small-bowel. Clinical, laboratorial and endoscopic resolution after proper antiviral treatment finally supported the initial diagnosis. In conclusion, this case illustrates the difficult diagnosis of CMV enteritis in an immunocompromised patient, only made possible after conserted endoscopic and pathological assessment.

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Peristomal pyoderma gangrenosum after rectal adenocarcinoma in the context of colonic and complex perianal Crohn's disease☆

Pioderma gangrenoso periestomal tras adenocarcinoma de recto en el contexto de enfermedad de Crohn de localización colónica y perianal compleja

Pyoderma gangrenosum (PG) is the second most common extra-intestinal cutaneous manifestation of inflammatory bowel disease (IBD), accounting for 1–3% of cases. Although more common in ulcerative colitis (UC) (5–12%) than in Crohn disease (CD) (1–2%), 2 recent Italian and Spanish retrospective multicentre studies appear to suggest a change in trend.[1,2] The peristomal variant (PGP) is undoubtedly one of the most feared complications affecting a surgical stoma, and while it is believed to occur in this location in 10–15% of all cases, it is probably underdiagnosed. Rapid detection of PG is essential in order to implement prompt therapeutic measures in a multidisciplinary setting. We report a difficult case that required unique management due to its severity and refractoriness to treatment, and because it occurred in the context of a recent neoplasm, which gave rise to a therapeutic dilemma.

The patient was a 43-year-old woman who had been diagnosed in 1993 with colonic (involving the rectum and left colon) and perianal CD according to standardised criteria (A2L2B1p). She commenced immunosuppression with azathioprine in 2000, due to corticosteroid dependence. However, owing to complications in the perianal disease (rectovaginal fistula plus several high transsphincteric fistulae) in 2004, infliximab was added at the beginning of 2005, following the usual induction and maintenance regimen; maximum escalation (shortening of the interval to 4 weeks) was required from the second year of treatment. The medical treatment was combined with multiple surgical interventions (abscess drainage, seton placement in fistula tracts and advancement flaps for the rectovaginal fistula), but the patient did not progress well, with severely limited quality of life, rectal stenosis and repeated perianal abscesses. Definitive terminal colostomy and left hemicolectomy with proctectomy was therefore proposed at the end of 2012 due to refractoriness to maximum medical and surgical treatment (colonoscopy with rectal stenosis biopsies in early 2012 showed no tumours). The patient initially refused to consider this option, preferring to exhaust all other alternatives and requesting inclusion in a clinical trial with intralesional stem cell injections. However, histological study of a lower rectum biopsy taken during a colonoscopy required as part of the inclusion protocol in the trial (June 2013) revealed adenocarcinoma.

At the end of July 2013, she underwent left hemicolectomy and abdominal–perineal resection, with construction of a definitive colostomy using the distal transverse colon, presenting 2 immediate postoperative complications: infection and partial dehiscence of the perineal and vaginal wall sutures. The surgical specimen showed a segment of large intestine severely affected by the CD, with extensive ulceration and transmural inflammation. At rectal level, there was a 2-cm moderately differentiated adenocarcinoma with a mucinous component of more than 50% that infiltrated the muscle layer without reaching the perirectal fat. Neither the surgical margins nor lymph nodes were affected (pT2N0MX). Abdominal-pelvic computed tomography (CT) did not reveal distant metastasis.

In September 2013, a large, ulcerated peristomal lesion with violaceous, anfractuous borders appeared, completely surrounding the stoma and causing intense local pain, retraction, and compromising its functionality, consistent with PGP (Fig. 1). Biopsies of the lesion were consistent with PGP, while cultures taken from the lesion were negative.

After joint evaluation by the dermatologist, surgeon, stoma care nurse and gastroenterologist, we decided on comprehensive and sequential management.

As a major part of the treatment, the patient's nutritional status was optimised and the pain caused by the pyoderma was controlled according to the World Health Organization pain ladder.

Local management in the stoma care unit consisted of cleaning the ulcers with sterile saline solution under

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