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 anatomopathological findings from the right colon, a presumptive diagnosis of CMV enterocolitis was assumed and intravenous ganciclovir was promptly initiated. Oral steroids were reduced by half the dose. After 4 weeks of antiviral therapy, the

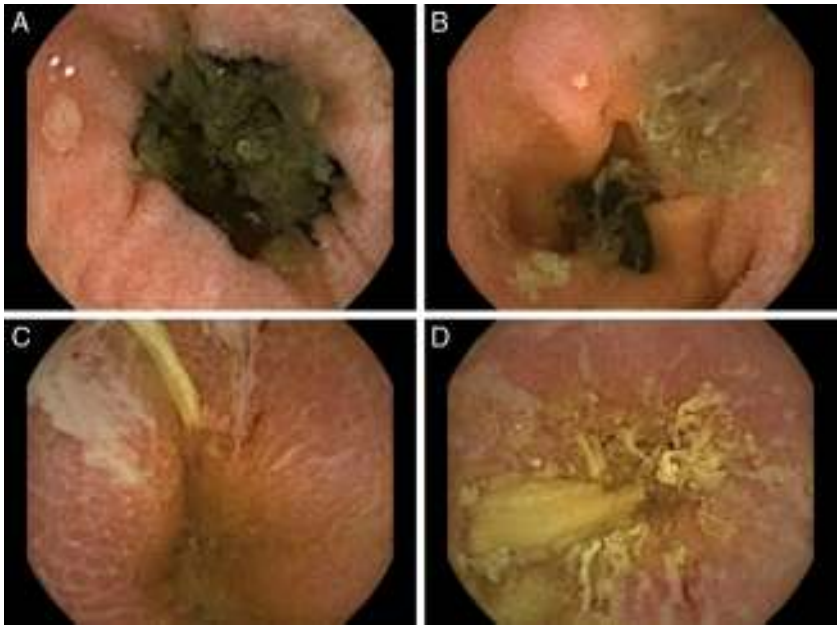

Figure 1 Capsule endoscopy findings. (A and B) Distal part of the jejunum, multiple small and rounded ulcers were observed. (C and D) In the ileum, linear and serpiginous ulcers were also observed.

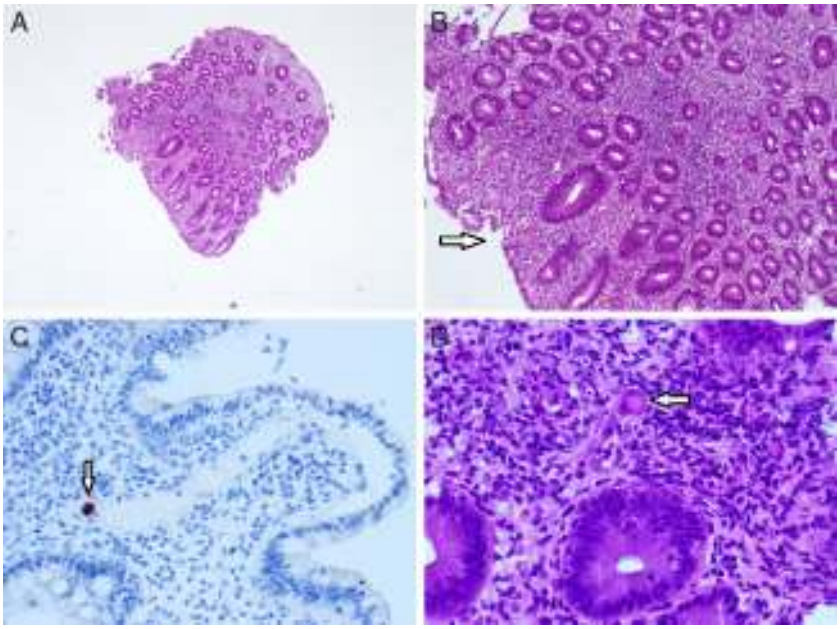

Figure 2 Histologic findings (right colon). Hematoxylin and eosin staining 4× and 10× magnification (A and B): marked inflammatory changes and an area of superficial ulceration (arrow). CMV immunostaining (C): immunohistochemically stained biopsy specimen showing a cytomegalovirus-positive cell (arrow);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

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

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

El pioderma gangrenoso (PG) representa la segunda manifestación extraintestinal cutánea más frecuente de la enfermedad inflamatoria intestinal (EII) (1-3% de casos). Más frecuente en colitis ulcerosa (CU) (5-12%), que en enfermedad de Crohn (EC) (1-2%), 2 recientes trabajos multicéntricos retrospectivos italiano y español parecen señalar un cambio de tendencia[1,2]. La variante periestomal (PGP), es sin duda una de las complicaciones más temidas de cuantas afectan a un estoma quirúrgico. Probablemente infradiagnosticado, supone un 10-15% del total de localizaciones de pioderma. Su rápido reconocimiento es clave para implementar de forma precoz medidas terapéuticas en un contexto multidisciplinar. Notificamos un caso de difícil y peculiar manejo por un doble motivo: su gravedad y refractariedad, y la contextualización en un ámbito de neoplasia reciente que ocasionó un dilema terapéutico.

Mujer de 43 años de edad actual diagnosticada en 1993 de EC de localización colónica (afectación de recto y colon izquierdo) y perianal según criterios estandarizados (A2L2B1p). Desde el año 2000 inicia inmunosupresión con azatioprina por corticodependencia. A partir de 2004 la enfermedad perianal se torna compleja (fistula rectovaginal más varias fístulas transesfinterianas altas), por lo que a inicios de 2005 se asocia infliximab según pauta de inducción y mantenimiento habitual precisando intensificación máxima (acortamiento de intervalo a 4 semanas) a partir del segundo año de tratamiento. El tratamiento médico se combina con múltiples intervenciones quirúrgicas (drenaje de abscesos, sedalización de trayectos fistulosos y colgajos de avance para la fistula rectovaginal). La evolución no es satisfactoria con limitación severa de la calidad de vida, estenosis rectal y abscesos perianales de repetición. Es por ello, que a finales de 2012 se plantea a la paciente colostomía terminal definitiva y hemicolectomía izquierda con proctectomía por refractariedad a tratamiento médico-quirúrgico máximo (la colonoscopia con toma de biopsias de estenosis rectal de inicios de 2012 no demostraba neoplasia). La paciente no contempló en primera instancia dicha opción y prefirió agotar otras opciones solicitando inclusión en ensayo clínico de inyección intralesional de células madre. En la colonoscopia previa del protocolo de inclusión en dicho ensayo (junio 2013) se biopsia recto inferior con resultado histológico de adenocarcinoma.

A finales de julio de 2013 se realiza hemicolectomía izquierda y resección abdominoperineal con confección de colostomía definitiva con colon transverso distal presentando 2 complicaciones postoperatorias inmediatas: infección y dehiscencia parcial de las suturas perineal y de la pared vaginal. La pieza quirúrgica evidenciaba un segmento de intestino grueso con severa afectación por EC con extensa ulceración e inflamación transmural. A nivel rectal, adenocarcinoma moderadamente diferenciado de 2 cm con componente mucinoso de más del 50% que infiltraba la capa muscular sin alcanzar grasa perirrectal. Los márgenes quirúrgicos no estaban afectos, así como ningún ganglio (pT2N0MX). La TC abdominopélvica no reveló afectación a distancia.

En septiembre de 2013 aparece lesión periestomal ulcerada de grandes dimensiones, de bordes violáceos y anfractuosos, que rodea en su totalidad al estoma provocando dolor local intenso, retracción y compromiso de su funcionalidad, compatible con PGP (fig. 1). Las biopsias de la lesión fueron compatibles con PGP y los cultivos tomados de la lesión negativos.

Tras la evaluación conjunta por dermatólogo, cirujano, estomaterapeuta y gastroenterólogo optamos por un manejo integral y secuencial.

Como parte importante del tratamiento, se atendió a la optimización del estado nutricional y control del dolor producido por el pioderma según escala de la OMS.

El manejo local en la unidad de estomaterapia consistió en la limpieza de ulceraciones con salino estéril bajo anestesia local, aplicación de agentes antibacterianos (peróxido de hidrógeno) y la colocación de apósitos absorbentes hidrocoloides (carboximetilcelulosa y película de poliuretano).

El tratamiento médico local se inició en octubre de 2013 con corticoides tópicos (clobetasol propionato 0,05%, 2 aplicaciones/día) objetivándose a las 2 semanas ausencia de mejoría de las lesiones, por lo que se cambió a tacrolimus