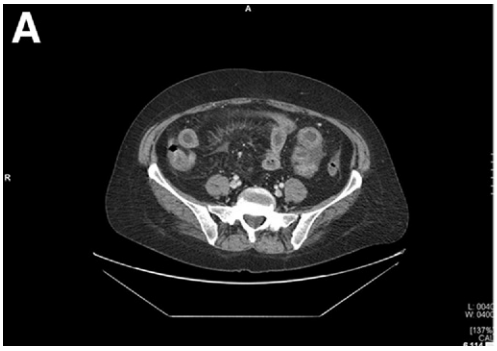
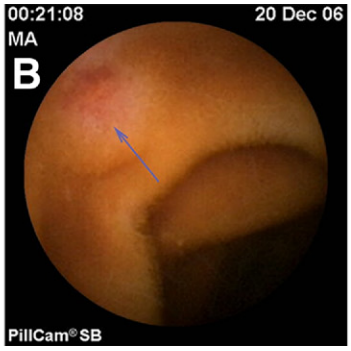
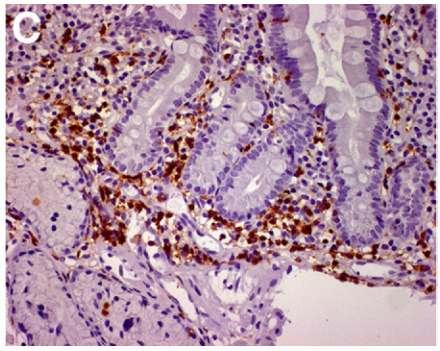
Intestinal HCV-Related Mixed Cryoglobulinemia







Question: A 58-year-old woman was admitted to the hospital because of a 3-month history of fever, diarrhea, abdominal pain, nausea, and vomiting. The patient had a 12-year history of hepatitis C virus (HCV) genotype 1b chronic infection, and an 8-year history of purpura and arthralgia, and had already withdrawn interferon treatment twice because of serious adverse effects. On physical examination, she seemed to be suffering and presented diffuse abdominal tenderness. Nausea and vomiting were not related to meals, and vomiting was often biliary. Diarrhea was watery, although during the last year the patient had experienced episodes of hematochezia. Blood test showed: aspartate aminotransferase, 36 U/L; alanine aminotransferase, 37 U/L; total protein, 5.5 g/dL; albumin 3.2, g/dL; total cholesterol, 97 mg/dL; C-reactive protein, 13.9 mg/dL (normal range, 0.1–0.8); and rheumatoid factor, 142 IU/mL (normal, <20). All autoantibodies were negative; C4 complement was 2 mg/dL (normal range, 16–38); and C3 complement, 79 mg/dL (normal range, 79–152). Bacteriologic and parasitologic stool tests were negative, but fecal occult blood test was positive. Contrast-enhanced computed tomography of the abdomen showed marked circumferential thickening of the entire small bowel wall; mesenteric haziness was also present (Figure *A*). Colonoscopy was normal. Esophagogastroduodenoscopy evidenced bilious stanching in the stomach and a focally erythematous duodenal mucosa. Capsule enteroscopy demonstrated numerous scattered mucosal lesions through the jejunum to the ileum (Figure *B*). Duodenal specimens were taken for histopathology and immunohistochemical studies. Histologic examination revealed villous blunting and a patchy lymphohistiocytic infiltrate in the lamina propria and in the epithelium. Immunohistochemical analysis for characterizing the lymphohistiocytic infiltrate showed that the inflammatory cells were mostly CD45RO$^+$ T lymphocytes focally surrounding and infiltrating lamina propria small vessels (Figure *C*). Initially, the patient was started on total parenteral nutrition, 1 mg/Kg IV methylprednisolone, IV metronidazole, and ciprofloxacin. After a few weeks, the patient did not show any significant improvement. Moreover, liver disease severely decompensated with the appearance of ascites, encephalopathy, renal failure, and severe arterial hypertension. Gastrointestinal picture was further complicated by subocclusive episodes that required nasogastric drainage.

What is the diagnosis?

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Conflicts of interest
The authors disclose no conflicts.

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Answer to the Clinical Challenges and Images in GI Question: Image 5: Intestinal HCV-Related Mixed Cryoglobulinemia

Cryoglobulins were searched in the serum and a cryoprecipitate of 7% was found; serum immunofixation showed that it was made of polyclonal immunoglobulin (Ig)G with a monoclonal IgM kappa protein. The patient was diagnosed having HCV-related mixed cryoglobulinemia (HCV-MC) with intestinal involvement. Because we could not continue with high doses of steroids and the complication of renal failure had also appeared, we started a 4-week treatment with the monoclonal anti-CD20 antibody rituximab, at the standard dose of 375 mg/m^2 once weekly. Six weeks after the 4-week rituximab treatment the cryocrit became negative and her clinical condition had dramatically improved. Gastrointestinal symptoms waned significantly. After 48 weeks of follow-up, the patient achieved a complete clinical and immunologic response, showing compensated liver disease and no gastrointestinal signs.

HCV-MC vasculitis mainly involves small vessels and may lead to common clinical manifestations as the classical MC syndrome (purpura, arthralgia, asthenia) or may lead to multiple organ involvement and life-threatening complications. Abdominal pain may occur in patients with MC[1] and can be attributed to inflammation of small-size vessels of the mesenteric district. Because endoscopic biopsies are superficial and often limited to the mucosa, the diagnosis of intestinal vasculitis in MC is difficult and requires a complex reasoning around clinical, endoscopic, and pathologic findings.[2] The complex pathogenesis of HCV-MC includes B-cell clonal expansion owing to chronic HCV infection and the role of T lymphocytes in mediating vessels injury. An abnormal T-cell pattern is present in peripheral blood of HCV-MC patients,[3] with an increase in memory (CD45RO$^+$) and activated T cells (HLA-DR$^+$) and a paucity of FoxP3$^+$, which are the cells involved in the control of autoimmunity. Moreover, the prevalence of T cells has been demonstrated in the liver and in peripheral nerves of patients with HCV-MC vasculitis. Because of the etiologic role of HCV chronic infection in MC vasculitis, HCV eradication should be considered the standard of treatment. Nevertheless, in patients presenting with severe disease or in whom antiviral treatment cannot be tolerated, rituximab must be considered the preferable option, because it was shown to restore B- and T-lymphocyte homeostasis, inducing clinical remission in patients with HCV-MC vasculitis.[3]

References

1. Gorevic PD, Kassab HJ, Levo Y, et al. Mixed cryoglobulinemia: clinical aspects and long-term follow-up of 40 patients. Am J Med 1980;69:287–308.
2. Case records of the Massachusetts General Hospital. Weekly clinicopathological exercises. Case 40-1984. A 33-year-old woman with cutaneous vasculitis, arthralgia, and intermittent bloody diarrhea. N Engl J Med 1984;311:904–911.
3. Saadoun D, Rosenzwajg M, Landau D, et al. Restoration of peripheral immune homeostasis after rituximab in mixed cryoglobulinemia vasculitis. Blood 2008;111:5334–5341.

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