Hemorrhagic intestinal Henoch-Schonlein purpura complicated by cytomegalovirus infection

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Clinically significant cytomegalovirus (CMV) infection is uncommon in healthy adults. However, in immunosuppressed patients, it may cause considerable morbidity and mortality (1,2). We report a life-threatening case of gastrointestinal vasculitis due to Henoch-Schonlein purpura complicated by CMV ileitis.

CASE PRESENTATION
A 54-year-old man on hemodialysis for acute chronic renal failure and on corticosteroids for Henoch-Schonlein purpura developed massive hematochezia. After extensive clinical investigation, an ileal bleeding site was identified and surgically removed. Pathological examination of the diseased bowel segment revealed an extensive vasculitis with mucosal ulceration attributable to Henoch-Schonlein purpura as well as florid cytomegalovirus infection.

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oped a polyarthralgia involving the wrists, shoulders, ankles and knees, with sparing of the small joints of the hands and feet. He had no myalgias or 'flu-like symptoms. He had no personal or family history of rheumatological disease.

Palpable nontender but pruritic skin lesions then appeared over the shins and dorsum of his feet. Blood tests revealed an elevated erythrocyte sedimentation rate of 65 mm/h (reference values 0 to 10 mm/h). The serum level of C3 was within normal limits, and the serum levels of C4 and immunoglobulin (Ig) A were slightly elevated. Serum was negative for rheumatoid factor, antineutrophil cytoplasmic antibody and antinuclear antibody. A punch biopsy of his purpuric skin lesions revealed a necrotizing leukocytoclastic vasculitis; fresh tissue for IgA immunofluorescence was not available.

The patient’s presentation was consistent with Henoch-Schonlein purpura, and he was treated with intravenous immunoglobulin and methylprednisolone, followed by tapering doses of oral prednisone. The arthralgia and purpura resolved, but his renal function remained poor and he still had abdominal pain.

Eight days after starting steroid therapy, the patient complained of increased abdominal pain and had several episodes of hematochezia. White blood cell count was 32x10^9 cells/L (normal 4.0 to 9.0x10^9 cells/L) and blood hemoglobin was 30 g/L, and the patient was admitted to the intensive care unit and transfused with six units of packed red blood cells. No definable gastrointestinal lesions were found on upper and lower endoscopy. Initial technetium red blood cell scintigraphy and mesenteric angiography did not locate the site of the gastrointestinal bleeding.

The patient underwent a laparotomy with intraoperative endoscopy, but this was hindered by blood in the small bowel and failed to find the cause of his gastrointestinal hemorrhage. He continued to pass melena stools with occasional hematochezia requiring repeated packed red blood cell transfusions. A second technetium red blood cell scintigraphy was able to identify the site of active bleeding in the proximal ileum. Laparotomy revealed an edematous segment of ileum with congested, dusky serosa and creeping mesenteric fat. Flat mucosal ulcers were seen on enterostomy. The segment of diseased ileum was resected.

Pathological examination of the removed ileal segment revealed a moderate amount of blood in the lumen. The bowel wall measured up to 4 mm in thickness and showed multiple punctate mucosal ulcers covered with fibrinous exudate and separated by an edematous, viable mucosa (Figure 1). Histologically, a necrotizing leukocytoclastic vasculitis with recent and remote thrombotic occlusions was seen near the base of the mucosal ulcers (Figures 2,3). A large number of intranuclear inclusion bodies characteristic of CMV infection were observed in mesenchymal and endothelial cells. CMV infection was confirmed by immunohistochemical staining with anti-CMV monoclonal antibody (Chemicon International, California) (Figure 4). Fresh tissue for IgA immunofluorescence was not available.

The patient was treated with intravenous gancyclovir for his CMV infection, and his condition improved with no further intestinal hemorrhage postoperatively. He was discharged from hospital two weeks later and continued on hemodialysis for his end-stage renal disease.

**DISCUSSION**

Henoch-Schonlein purpura, a vasculitis of small arterioles and venules, affects multiple organ systems. It is thought to be an immune complex-mediated disease involving IgA (3). The disease is more common in children than in adults and is characterized by nonthrombocytopenic purpura, arthralgia, abdominal pain and glomerulonephritis. The renal lesion resembles that of Berger’s IgA nephropathy (3). Symptoms generally resolve spontaneously. Corticosteroids do not affect the natural history of the disease but are useful for symptom control (4).

Abdominal pain as a result of gastrointestinal vasculitis is
the most common presenting symptom in Henoch-Schonlein purpura and occurs in up to 70% of patients (4). Mucosal ischemia due to thrombotic vasculitic lesions may occur anywhere along the alimentary tract and result in diverse clinical manifestations. Rarely, intestinal infarction with necrosis, extensive hemorrhage and bowel perforation requiring surgical resection occur (5). The prognosis of gastrointestinal involvement is generally favourable but is occasionally fatal (6,7). In retrospect, our patient’s ulcerative esophagitis may have been due to Henoch-Schonlein purpura, but this was not evident in biopsied tissue. His crampy lower abdominal pain and hematochezia were, however, partly explained by ileal mucosal ulcers secondary to Henoch-Schonlein purpura vasculitis.

The differential diagnosis of gastrointestinal hemorrhage in our patient included ischemic enteropathy, inflammatory bowel disease, infectious enterocolitis, vascular ectasia, massive upper gastrointestinal bleeding and Meckel’s diverticulum. Colonic diverticular disease, which usually results in painless bleeding, and colonic neoplasms constitute the most common causes of bleeding in those age 50 years or more; these etiologies were ruled out by our patient’s recent normal colonoscopic examination (8). Surgical resection and histopathological examination were diagnostic.

CMV infection is common, and up to 80% of adults have anti-CMV antibody (9). In the majority of cases, the infection is mild; it rarely causes severe clinical manifestations in immunocompetent patients. Like other herpesviridae, CMV can reside quiescently in human tissue throughout a person’s life. Clinical disease occurs most commonly in immunocompromised patients from either primary infection or reactivation of latent CMV infection (2).

Serious CMV disease has been observed in recipients of heart, renal and bone marrow transplants, and patients with AIDS (2,10-12). The infection can involve any level of the gastrointestinal tract. Extensive mucosal ulceration with hemorrhage may be life-threatening and require surgical resection, and a fatal outcome is not infrequent (13). The pathogenesis of these mucosal lesions remains undetermined. In our patient, CMV inclusion bodies were present in endothelial cells, suggesting that these lesions may participate in a thrombotic process resulting in mucosal necrosis. Similar findings have been documented in previous reports (14,15).

Two factors predisposed our patient to an immunodeficient state and clinical CMV infection. First, corticosteroids are thought to impair cellular immunity by inhibiting cytokines and down-regulating RNA synthesis necessary for T lymphocyte proliferation (16). The association between iatrogenic immunosuppression and CMV infection has been well documented in transplant patients (10-12). Ileal hemorrhage due to CMV vasculitis in a patient being treated for Wegener’s granulomatosis, and fatal CMV colitis in a patient receiving low dose steroids have been reported (17,18). Second, end-stage renal failure is known to decrease T lymphocyte response to infection; the mechanism of this aberrant immune function is unknown but may be related to deficient levels of the cytokine interleukin-2, which is a growth factor for T lymphocyte proliferation and maturation (19). Hemodialysis does not appear to improve impaired immunity (19), and hemorrhagic CMV colitis requiring resection has been reported in a patient with uremia (20).

In our reported case, the massive intestinal hemorrhage was most likely caused by Henoch-Schonlein purpura and CMV infection. It is impossible to determine which of the two pathological processes was the dominant factor. Although surgery remains the ultimate treatment for intractable hemorrhage due to severe Henoch-Schonlein purpura or CMV infection, this case underscores the importance of differential diagnosis in the evaluation of patients receiving
corticosteroids. CMV infection of the gastrointestinal tract should be strongly suspected in patients with organ transplantation or AIDS who present with gastrointestinal symptoms. The same caution should be extended to apparently less immunocompromised patients to permit timely intervention with antiviral agents to reduce morbidity and mortality (21).

REFERENCES