Multiple Hemorrhagic Gastric Ulcers due to Polyarteritis Nodosa

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A 73-year-old man developed refractory multiple hemorrhagic gastric ulcers. Emergent gastrectomy was performed, and the diagnosis of polyarteritis nodosa was made by histologic evaluation of the resected stomach. Although gastric ulceration is a relatively rare complication of polyarteritis nodosa, it should be considered in the differential diagnosis of refractory hemorrhagic gastric ulcers. Emergent surgery may be indicated in such cases.

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Introduction

Polyarteritis nodosa (PN) is a systemic inflammatory disease resulting from necrotizing angitis of the small to medium-sized arteries (1). Although gastrointestinal complications of PN such as abdominal pain, vomiting, and hematemesis have frequently been reported (2–6), severe gastric ulcers requiring surgical treatment are rare (7). We report a patient with multiple hemorrhagic gastric ulcers due to PN requiring gastrectomy.

Case Report

In April 1995, a 73-year-old man developed high fevers, arthralgias, myalgias, and temporal headache. On April 24, he was admitted to a local hospital. Two weeks after admission, he noted hematemesis and tarry stools without abdominal pain. Gastric endoscopy revealed a considerable amount of bleeding from multiple gastric ulcers (Fig. 1). The esophagus and duodenum were intact. Because the gastric bleeding was refractory to medical treatment and the patient’s hemoglobin concentration fell from 11.0 g/dl to 7.8 g/dl, an emergent total gastrectomy was performed on May 16. The resected stomach demonstrated multiple gastric ulcers (Fig. 2). Because the histologic diagnosis was suspected to be PN, he was referred to our hospital on June 6.

Physical examination on admission revealed severe emaciation (weight loss of 8 kg over the last 6 months), pale conjunctiva, an abdominal surgical scar, tachycardia (pulse 88/min), and diastolic hypertension (blood pressure 150/100 mmHg). The patient was drowsy and showed muscle weakness, wasting, and sensory disturbances in the distal portion of the lower extremities. All deep tendon reflexes were diminished. Neurologic features revealed mononeuropathy multiplex in the extremities.

Peripheral blood analysis revealed normocytic anemia (red blood cell count, 3.33x10^6/μl; hemoglobin, 10.1 g/dl; hematocrit, 33.0%), leukocytosis (white blood cell count, 15,610/μl with 83.9% neutrophils, 6.7% lymphocytes, 4.0% monocytes, 4.8% eosinophils, and 0.3% basophils), and thrombocytosis (platelet count, 51.3x10^3/μl). Urinalysis revealed microscopic hematuria with red cell casts. The erythrocyte sedimentation rate was 98 mm/h and the C-reactive protein (CRP) concentration was 20.28 mg/dl (normal, <0.3). The patient showed hypoalbuminemia (2.90 mg/dl) with hypergammaglobulinemia (γ-globulin, 21.2%) and severe renal dysfunction (serum creatinine, 4.27 mg/dl; urea nitrogen, 69.2 mg/dl). Liver function tests showed a total bilirubin concentration of 1.46 mg/dl, alkaline phosphatase of 541 U/l, and gammaglutamyl transferase of 48.2 U/l, with normal gluematic oxaloacetic transferase, glutamic pyruvic transaminase, and lactate dehydrogenase concentrations. Immunologic tests revealed elevated titers of anti-nuclear antibodies (1:160; normal, <1:20) in a speckled pattern. Anti-myeloperoxidase perinuclear anti-neutrophil cytoplasmic antibody was positive (MPO-ANCA, 20 EU; normal, <10), but tests for hepatitis B surface antigen, hepatitis C virus antibodies, rheumatoid factor, anti-DNA antibodies, cytoplas-
mic anti-neutrophil cytoplasmic antibodies (c-ANCA), anti-phospholipid antibodies, and anti-basement membrane antibodies were negative. Serum cryoglobulin was not detected. Arterial blood gas analysis during administration of 1 l/min O₂ revealed hypoxemia (PaO₂, 52 torr; PaCO₂, 25 torr; pH, 7.47). A chest radiograph showed diffuse hypolucency with cardiomegaly (cardiothoracic ratio of 69%) and bilateral pleural effusions. An electromyogram was consistent with mononeuropathy multiplex. A muscle biopsy taken from the left biceps showed mild neurogenic changes without angiitis. Pathologic findings from a biopsy of the superficial temporal artery revealed no inflammation of the artery, ruling out temporal arteritis.

Reevaluation of the microscopic examination of the resected stomach demonstrated that all ulcers were shallow and that the propionic muscular layers were intact. The majority of the medium- to small-sized arteries under the ulcerated fundus showed segmental fibrinoid necrosis and disruption of muscular walls with massive cellular infiltration (Fig. 3). There were no eosinophilic infiltrates. These findings were considered compatible with PN (8, 9).

After the diagnosis of PN, the patient was immediately treated with intravenous methylprednisolone 1,000 mg/day for 3 days, followed by 60 mg of oral prednisolone and 100 mg of cyclophosphamide everyday. His temperature returned to normal, and the CRP and serum creatinine concentrations gradually decreased (Fig. 3). On June 9, he had hemoptysis due to alveolar hemorrhage. On July 3, he developed abdominal
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Figure 3. Pathologic findings in the resected stomach (HE stain, x200). a) A small-sized artery in the proper muscle layer shows angiitis with segmental fibrinoid necrosis (arrowheads) and disruption of muscular walls. b) The arterial lumen is extremely narrowed by the proliferation of the endothelial cells, cellular infiltrates, and fibrinoid degeneration.

Discussion

The diagnosis of polyarteritis nodosa was made because our patient had a weight loss of more than 4 kg, myalgia, mononeuropathy multiplex, diastolic hypertension, elevated serum nitrogen and creatinine concentrations, and inflammation of the small- to medium-sized arteries in the resected stomach. These symptoms completely fulfill the diagnostic criteria for PN established by the Ministry of Health and Welfare of Japan in 1990 (8), as well as those advocated by the American College of Rheumatology in 1990 (9).

Polyarteritis nodosa is now divided into two separate clinical entities, classic polyarteritis nodosa (CPN) and microscopic polyangiitis (MPA) (10). MPA is a systemic necrotizing vasculitis affecting small-sized vessels without granuloma, and is associated with necrotizing glomerulonephritis and pulmonary capillaritis (11). MPO-ANCA is often positive in MPA but not in CPN. The present patient developed renal dysfunction and alveolar hemorrhage with positive MPO-ANCA, consistent with the diagnosis of MPA. However, postmortem examination failed to show crescent glomerulonephritis and pulmonary capillaritis, probably because they were transformed by the immunosuppressive therapy.

The most striking point of this report is that our patient presented with multiple hemorrhagic gastric ulcers one month after the onset of PN, and that the diagnosis was established by histologic evaluation of the resected stomach. In contrast, most instances of gastrointestinal involvement in PN occur during the late course of the disease, especially in patients who have received corticosteroids (6, 7). A few cases of PN have been diagnosed by pathologic examination of a gallbladder (12) or bowel segment (13) removed during surgery for abdominal pain; however, we could not find any case reports of PN diagnosed by examination of a resected stomach.

Gastrointestinal complications occur in more than 50% of all patients with PN (1). Symptoms vary and include abdominal pain, nausea, vomiting, diarrhea, and hematemesis (6, 7). The inflammatory changes in small-sized arteries found in MPA may lead to ulceration or bleeding of the gastrointestinal mucosa, whereas those in medium-sized arteries found in CPN and MPA may lead to necrosis, and perforation of the gastrointestinal tract. These changes are most frequently seen in the small intestine, with the stomach being the second most common site (7). The reason why our patient developed only the gastric ulcer without any involvements of the duodenum, small or large intestine was unclear.

Because the prognosis with complicating gastrointestinal symptoms is often poor, early diagnosis and aggressive therapy are essential. Matolo and Albo (7) reported that all four PN patients presenting with acute abdomen who underwent surgical treatment survived, while 6 of 10 patients who received medical treatment died. Zizic et al (14) reported that all five patients with PN and an acute abdomen required operative intervention. The present patient also underwent surgery successfully after developing refractory hemorrhagic gastric ulcers. However, his clinical outcome was poor because of other complications of PN, such as pseudomembranous colitis and generalized cytomegalovirus infection.

There are only a few reports of endoscopic and pathologic findings in ulcers due to PN. Williams et al (15) reported two
patients with PN who had endoscopically documented duodenal and jejunal ulcers. In both patients, deep, extensive, necrotic ulcers were seen. In contrast, the present patient exhibited broad-based, shallow gastric ulcers. These differences may reflect the extent of the ischemic area made by angiitis in the submucosal region.

In summary, PN should be included in the differential diagnosis of refractory hemorrhagic gastric ulcers. In such cases, emergent surgery may be indicated to improve outcome.

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References