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Case report

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Polyarteritis nodosa with mesenteric aneurysms demonstrated by angiography: report of a case and successful treatment of the patient with prednisolone and cyclophosphamide

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Abstract: Polyarteritis nodosa is a necrotizing angitis that predominantly affects small and medium-sized arteries. The prognosis of untreated polyarteritis nodosa is very poor. Since symptoms are diverse and no serologic test is specific for polyarteritis nodosa, the diagnosis is difficult and often delayed. We describe a patient with polyarteritis nodosa who had gastrointestinal involvement with multiple aneurysms of the inferior mesenteric artery; only abdominal angiography provided a conclusive diagnosis. Alleviation of symptoms and regression of aneurysms were observed after combination therapy of an immunosuppressive agent, cyclophosphamide, and prednisolone. We emphasize the importance of early diagnosis by angiography and aggressive therapy in patients in whom physical signs indicating definite polyarteritis nodosa are not present.

Key words: aneurysm, angiography, cyclophosphamide, polyarteritis nodosa, vasculitis

Introduction

Kussmaul and Maier described the syndrome of polyarteritis nodosa (PAN) in 1866.[1] PAN is an uncommon disease in which necrotizing inflammation extends through the walls of small and medium-sized arteries. PAN should be suspected in patients with fever, chills, weight loss, fatigue, and signs of multiple-system involvement. Gastrointestinal involvement has been reported in 23%–70% of cases of PAN.[2,3] However, early diagnosis is not easy. Because symptoms are diverse and no serologic test is specific, the diagnosis of PAN is frequently delayed. As the prognosis of untreated polyarteritis is poor, with a 5-year survival rate of less than 15%, correct and prompt diagnosis is very important.[3] We present a patient with abdominal symptoms in whom abdominal angiography demonstrated typical findings of PAN in an early phase of the illness and in whom timely treatment with a corticosteroid and cyclophosphamide was successful.

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Case report

A 51-year-old man presented with complaints of abdominal pain, high fever, and weight loss beginning in February, 1998. He had no remarkable past medical history. A local doctor had been treating him with fasting and total parenteral nutrition. No abnormality of the upper or lower gastrointestinal tract was demonstrated by upper gastrointestinal and barium enema radiography. After the fever had been alleviated and the abdominal pain had lessened, the patient consulted our hospital for evaluation of an ill-defined illness on March 23, 1998. On admission his complaints were mild abdominal pain, fatigue, and weight loss (8 kg over a period of 2 months).

On physical examination, the patient's height was 176 cm and weight was 66.2 kg. His pulse rate was 60 beats/min, blood pressure was 108/86 mm Hg, and his temperature was 36.8°C. Neither anemia nor jaundice was observed. No abnormal cardiopulmonary findings were appreciated. The abdomen was soft, but tender to palpitation. Signs of peritoneal irritation were absent. Neither bruit nor vascular murmur was present. No localizing neurologic signs were noted. No evidence of orchitis or epididymitis was present. Results of hematologic, biochemical, and endocrine examinations included a white blood cell count of 6600/mm,[3] an erythrocyte sedimentation rate (ESR) of 70/h, a C-

reactive protein (CRP) concentration of 0.09 mg/dl, a serum alanine aminotransferase (ALT) concentration of 114 U/l, a serum aspartate aminotransferase (AST) concentration of 53 U/l, a blood urea nitrogen concentration of 23.1 mg/dl, a serum creatinine concentration of 1.2 mg/dl, and a serum creatine phosphokinase concentration of 36 U/l. Urinalysis revealed no abnormality. Plasma renin activity was 3.72 ng/ml per h (normal range, 0.2–2.7 ng/ml per h), and serum aldosterone concentration was 107 pg/ml (normal range, 56.9–150.3 pg/ml). Serum concentrations of sodium and potassium were normal. Assays for hepatitis B virus surface antigen, anti-hepatitis B core antibody, anti-hepatitis C antibody, rheumatoid factor, and anti-nuclear antibody were all negative. A serum immune complex determination was within normal limits. Antineutrophil cytoplasmic antibodies and anti-cardiolipin antibodies were absent. Occult blood was absent from the stool. Abdominal ultrasonography revealed no abnormalities, including the kidneys. Esophagogastroduodenoscopy revealed chronic gastritis. Full-length colonoscopy and radiographic examination of the small intestine revealed no abnormality. Sensory disturbance and muscular pain in both legs developed soon after the patient's admission. The pain and paresthesia of the lower extremities continued, but neither motor nor sensory deficits appeared. The abdominal pain continued. Although we suspected a vasculitic syndrome, nerve biopsy was deferred due to the mildness of the symptoms. Other accessible tissues, such as skin, kidneys, or testes, were not involved in this patient. We therefore performed a muscle biopsy of the biceps to confirm vasculitis histologically. However, vasculitis was not demonstrable histologically in the specimen. Therefore, abdominal angiography was performed; while renal and hepatic arteriographies revealed no abnormality, the inferior mesenteric artery showed multiple stenoses and microaneurysms (Fig. 1a). According to the 1990 American College of Rheumatology criteria,[4] the patient was diagnosed with PAN, based on the findings of weight loss, polyneuropathy, and an arteriographic abnormality.

Oral prednisolone therapy (40 mg/day) and intravenous cyclophosphamide therapy (1000 mg) were administered. The patient's abdominal symptoms gradually become alleviated, but the sensory disturbance remained. The serum CRP concentration remained normal and the ESR decreased to normal. Serum concentrations of ALT and AST were normalized. Renal function and urinary analysis remained normal, although plasma renin activity was mildly elevated. Occult blood remained absent from the stool. Hypertension was not observed. At 37 days after the initiation of prednisolone therapy (also 37 days after the administration of intravenous cyclophosphamide), abdominal angiography was repeated; on the inferior mesenteric arteriogram, microaneurysms were much less prominent (Fig. 1b). The dose of prednisolone was tapered, and the patient has been followed in our outpatient department. Except for pain and paresthesia of the lower extremities, the patient has remained asymptomatic, and serum concentrations of CRP and the ESR have been normal.

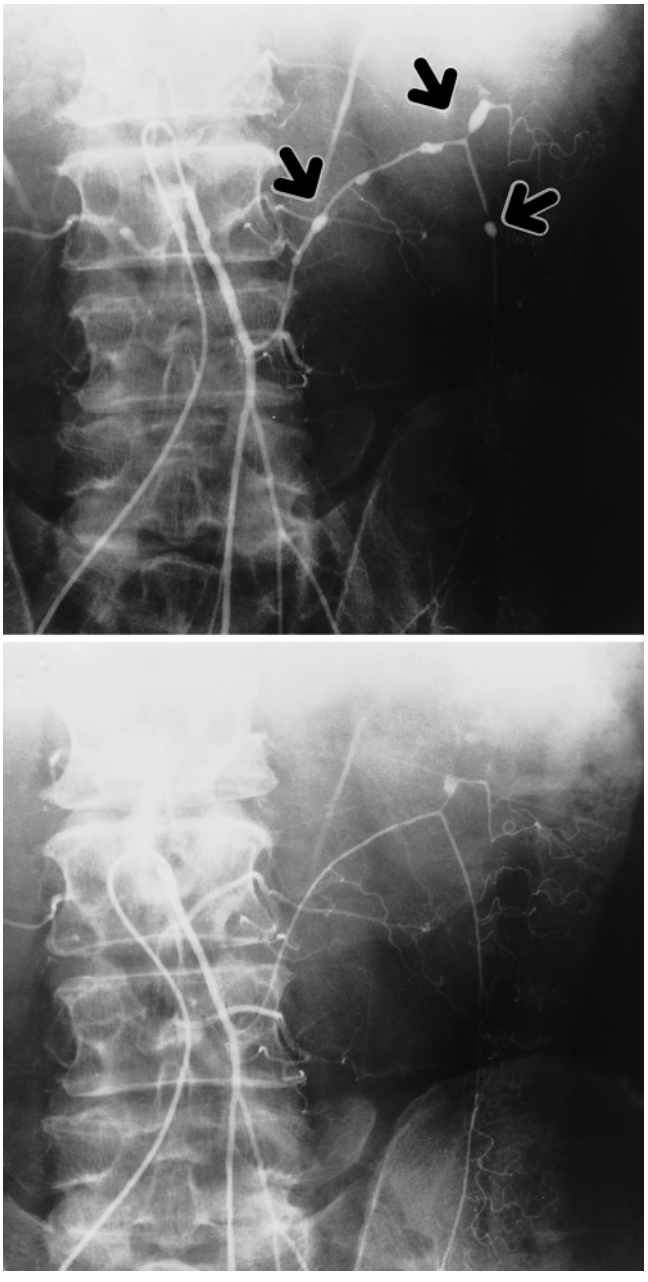

Fig. 1a,b. Angiograms of the inferior mesenteric artery **a** before and **b** after treatment. Segmental narrowing and multiple aneurysms (*arrows*) were observed before the treatment (**a**), and these findings disappeared after the treatment (**b**)

Discussion

Features of gastrointestinal involvement in PAN include abdominal pain, diarrhea, intestinal hemorrhage, and abnormal liver enzyme test results.[3] Our patient had abdominal pain and high fever that decreased with fasting and total parenteral nutrition, apart from any glucocorticoid or cytotoxic therapy. Therefore, we first considered other gastrointestinal diseases. The early improvement deserves attention, because bowel rest is important in both PAN and ordinary ischemic colitis. Improvement with fasting does not eliminate the possibility of PAN. Assessment of vascular abnormalities should be performed in patients whose abdominal symptoms are accompanied by symptoms in other organs such as nerve, skin, muscle, or kidney, or when the abdominal symptoms cannot be explained by more usual gastrointestinal diseases.

The prognosis of untreated PAN is poor, and the 5-year survival rate is less than 15%. Most deaths of patients with PAN occur within the first year of diagnosis of the disease,[5] and usually occur because of uncontrolled vasculitis, resulting from delay in diagnosis. Therefore, early diagnosis and appropriate therapy are very important. Visceral angiography is useful in the diagnosis of classic PAN.[6] Esophagogastroduodenoscopy in our patient revealed only mild chronic gastritis, and complete colonoscopy was negative. Missed observations were unlikely, as several expert endoscopists were involved together. Guillevin et al.[2] described endoscopy to be of limited value in the diagnosis of gastrointestinal manifestations of PAN. In addition to the failure of endoscopy to reveal any abnormality, neither radiographic examination of the small intestine nor abdominal ultrasonography revealed any abnormality in our patient. Gastrointestinal manifestations of PAN may be severe in some patients; hematemesis, melena, and hematochezia are caused by vasculitis of the upper or lower gastrointestinal tract, most commonly the small bowel.[3] If ischemia occurs but is limited to the mucosa or submucosa, mucosal ulceration and bleeding may occur. When transmural ischemia develops, infarction may occur and may progress to perforation. The paucity of pertinent physical signs in the present patient was probably due to the early phase of the illness. Visceral aneurysms have been encountered not only in PAN but also in such diseases as systemic lupus erythematosus, renal carcinoma, temporal arteritis, fibromuscular dysplasia, Wegener's granulomatosis, atrial myxoma, thrombotic thrombocytopenic purpura, bacterial endocarditis, diabetes mellitus, and segmental arterial mediolysis.[7,8] Therefore, angiographic findings should be carefully interpreted in conjunction with clinicopathologic information.

We administered oral prednisolone (40 mg/day) and intravenous cyclophosphamide (1000 mg) to our patient. Because his abdominal symptoms and fever had partially responded to previous treatment with fasting, we chose an intermediate dose of prednisolone. The prognosis of PAN has improved over the past 30 years. Thirty years ago, treatment of PAN consisted of corticosteroids alone, and the 5-year survival rate was 48%.[9] Since 1979, combination therapy of an immunosuppressive agent, cyclophosphamide, and corticosteroids has improved the outcome.[10,11] Multiple inferior mesenteric artery aneurysms in our patient resolved with such therapy. Regression of aneurysms has been reported in renal,[7,10,12–16] and hepatic[7,10,13,16] arteries in patients with PAN. Sellke et al.[17] described a patient with PAN in whom there was regression of multiple aneurysms of the middle colic artery after surgical ligation and prednisolone therapy. Aggressive treatment of PAN should be carried out when patients are in an early and acute phase, even though symptoms may still be mild, because aneurysms can lead to fatal complications. In patients in such early phases, we believe that angiography is a key to the timely diagnosis of PAN, especially when histological demonstration can be difficult.

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