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CASE REPORT

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Wegener's granulomatosis complicated with intestinal ulceration

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Abstract We report the case of a 32-year-old man who developed Wegener's granulomatosis complicated with refractory intestinal ulceration. In August 2001, he presented with a high fever, nasal bleeding, and bilateral leg numbness. These symptoms worsened, which prompted him to consult his home doctor on February 18, 2002. In spite of treatment with antibiotics, his symptoms did not improve. Furthermore, abdominal pain and melena occurred as additional symptoms in March 2002. He was admitted to our hospital on April 5, 2002. A deformed nose condition (the so-called saddle nose) was observed at this time. Laboratory data showed a high erythrocyte sedimentation rate (103 mm/h) and a high level of serum C-reactive protein (14.98 mg/dl), and hematuria and proteinuria were also observed. The patient was positive for an antineutrophil cytoplasmic antibody specific for proteinase-3 (PR3-ANCA). A chest computed tomography (CT) scan revealed multiple pulmonary nodules in the lung field. A biopsied-specimen from the nasal mucosa showed necrotizing granulomatosis with giant cells. Together with his symptoms and the laboratory and pathological findings, the patient was diagnosed as having Wegener's granulomatosis. A colon fiberscopy showed multiple ulcerations with bleeding from the terminal ileum to the ascending colon, and nodular lesions at the terminal ileum. We started a combination therapy of prednisolone (60 mg/day) and cylophosphamide (100 mg/day) orally. The patient's gastrointestinal symptoms disappeared and abnormal serological indicators improved. Although Wegener's granulomatosis complicated with refractory intestinal ulceration is rare, this case indicates that the gastrointestinal region is also a target organ of Wegener's granulomatosis.

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Introduction

Wegener's granulomatosis is a systemic necrotizing vasculitis of unknown etiology with distinct clinical and histological features. Histologically, it consists of necrotizing vasculitis affecting mainly small to medium-sized arteries, and sometimes involving venous or capillary vessels.[1] The disease typically involves the upper and lower airway, lungs, and kidneys. Although inflammatory involvement of the disease has been reported in other organs, a gastrointestinal complication is relatively rare except for scattered case reports.[2]

We present a case of Wegener's granulomatosis complicated with peripheral neuropathy and refractory intestinal ulceration, and then discuss the possibility that gastrointestinal involvement may be an inherent clinical manifestation of Wegener's granulomatosis.

Case report

A 32-year-old man developed a high fever, nasal bleeding, and bilateral leg numbness in August 2001. He consulted his home doctor, and was treated with an oral antibiotic. The high fever improved temporarily, but his symptoms worsened again in December 2001, when he noticed a macrohematuria. On February 18, 2002, he was admitted to a hospital where he was given a drip infusion of antibiotics. He was transferred to our hospital on April 5, 2002, because of abdominal pain and melena, in addition to the above symptoms.

In the course of a physical examination, his blood pressure was found to be normal and his heart rate was 82/min. A high fever (38.8°C) was observed. Surface lymph nodes were not palpable. A deformed nose condition described as

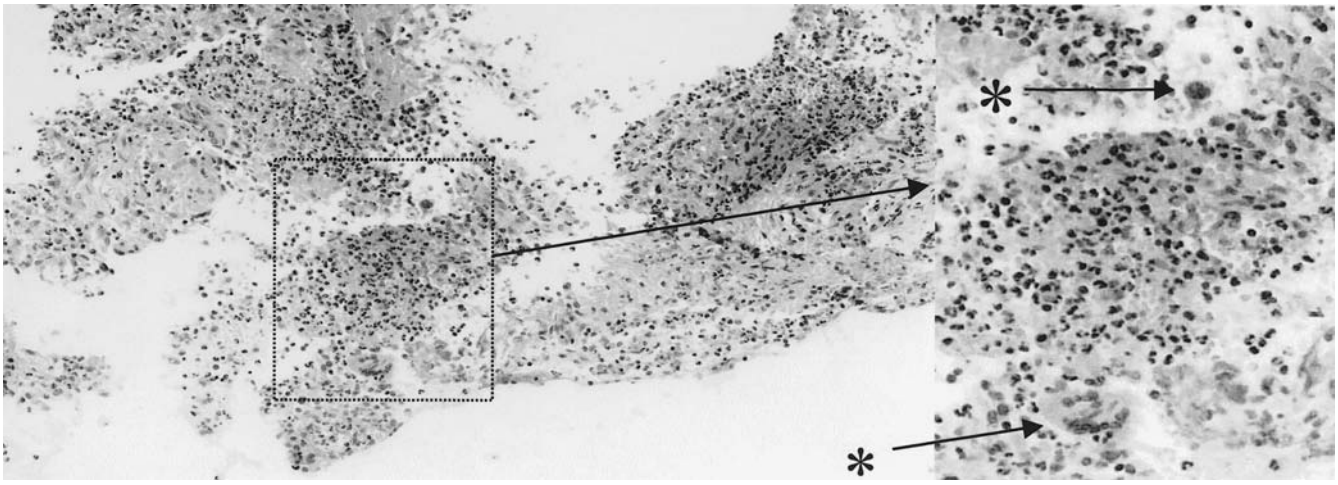

Fig. 1. The microscopic findings of nasal mucosa showing ulceration infiltrated with neutrophils and necrotizing granuloma with giant cells (*)

"saddle nose" was observed. His skin and conjunctiva were strikingly anemic. His heart and lung sounds were normal. Tenderness of the lower abdomen was found, but no organ enlargement or mass was palpable in the abdomen. Multiple sensory paralyses in his right and left feet, and the right-hand side of his face were observed.

Laboratory tests on admission revealed a leukocytosis (10300/μl) and normocytic anemia (6.9 g/dl). His erythrocyte sedimentation rate (ESR) was 103 mm/h and his serum C-reactive protein (CRP) level was 14.98 mg/dl. Although renal function (serum blood nitrogen and creatinine level) was normal, a microscopic hematuria and proteinuria (0.98 g/day) was observed. A mild elevation of serum transaminase levels (GOT 50 U/l, GPT 64 U/l) was found. In an examination for autoantibodies, antinuclear antibodies were found (40 dils) and an antineutrophilic cytoplasmic antibody (ANCA) specific for protease-3 (PR-3 ANCA) was positive (titer 102 EU.) However, an ANCA specific for myeloperoxidase (MPO-ANCA) and anti-ds DNA antibodies was not observed.

Several nodular shadows were revealed in the right upper and lower lobes on chest X-ray films. In a chest computed tomography (CT) scan, the nodular shadows in the lung were confirmed. In a head CT scan, the sinus and nasal mucosa were found to be infiltrated by the necrotizing granuloma. A biopsy of the nasal mucous membranes was performed and the microscopic findings of the specimen showed an ulceration, small to medium-sized vasculitis infiltrated with neutrophils, and necrotizing granuloma with giant cells in squamous epithelium and in stroma (Figs. 1 and 2).

A colon fiberscopy showed an elevated granulomatous lesion at the terminal ileum (Fig. 3A), and multiple, consecutive ulcerations with bleeding from the ascending colon to the terminal ileum (Fig. 3B–D). No ulcerations or granulomas were observed in the peripheral part of the small intestine, descending colon, and rectum. Microscopic findings from a biopsy specimen from the elevated lesion at the terminal ileum (Fig. 3A) showed nonspecific

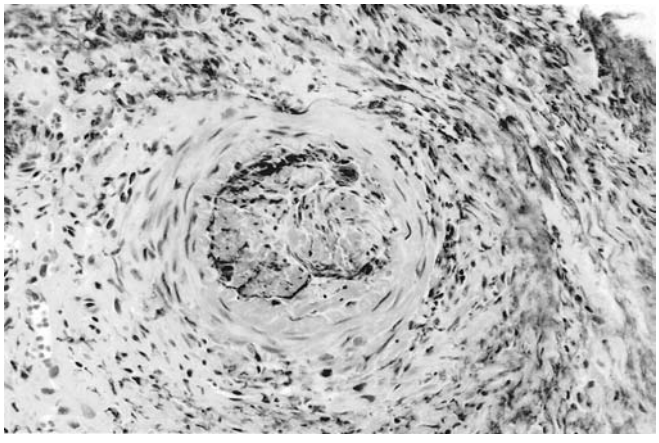

Fig. 2. The microscopic findings of nasal mucosa showing medium-size vasculitis.

inflammation with granulomatous lesion, giant cells, and vasculitis without necrosis (Fig. 4). We diagnosed the patient as having Wegener's granulomatosis with gastrointestinal organ complications.

We started oral medication with 60 mg/day prednisolone and 100 mg/day cyclophosphamide (Fig. 5). The melena stopped immediately, and after 2 weeks of treatment the ESR, the serum level of CRP, and a titer of PR3-ANCA had normalized. Although bilateral leg numbness and nodular shadows on both lungs (as shown by a chest CT scan) partly remained, the granulomatous mass in the sinus (shown by a head CT scan), the multiple ulcerations of the ascending colon, and the elevated lesion of the terminal ileum disappeared within 3 months of the onset of treatment.

The patient was discharged on July 21, 2002. Two years after discharge, the patient had no nasal symptoms or bilateral leg numbness. The nodular shadows on the bilateral lungs and granuloma of the sinus were significantly reduced. Moreover, no recurrence of intestinal ulceration was observed by fiberscopy.

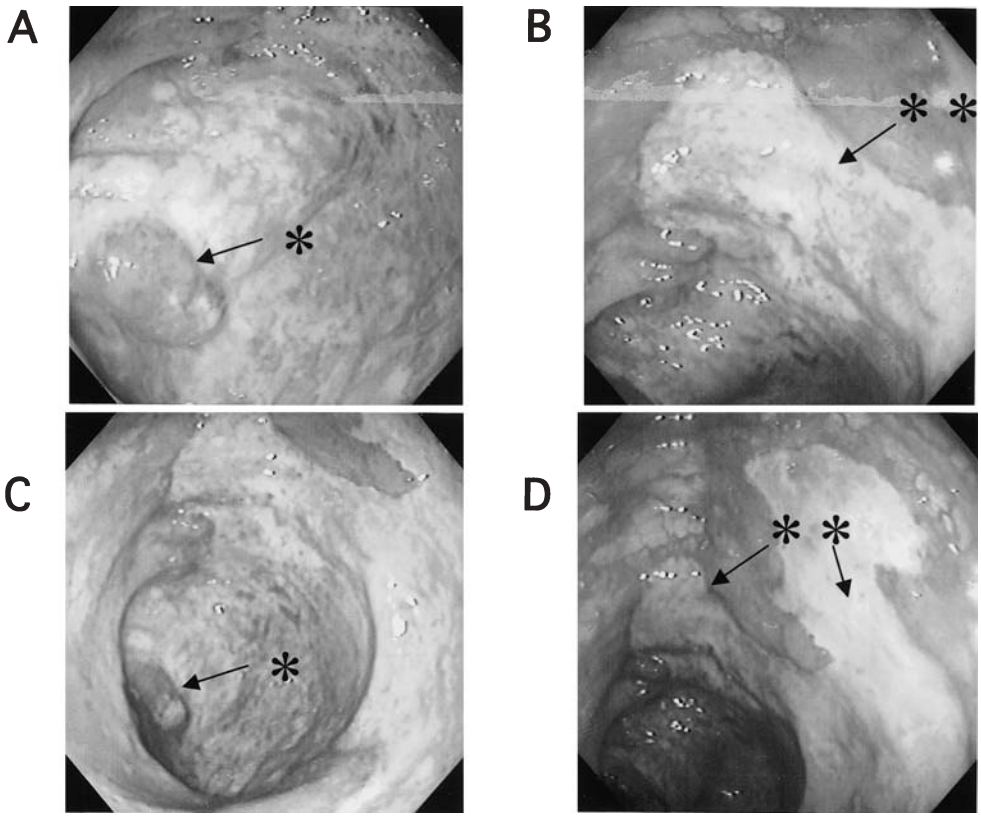

Fig. 3. Colon fiberscopy showing multiple ulcerations with bleeding (**) and elevated lesions (*) at the ascending colon.
A The terminal ileum.
B The descending colon
C Granulomatous lesion at the terminal ileum
D Nonconsecutive ulcer at the descending colon

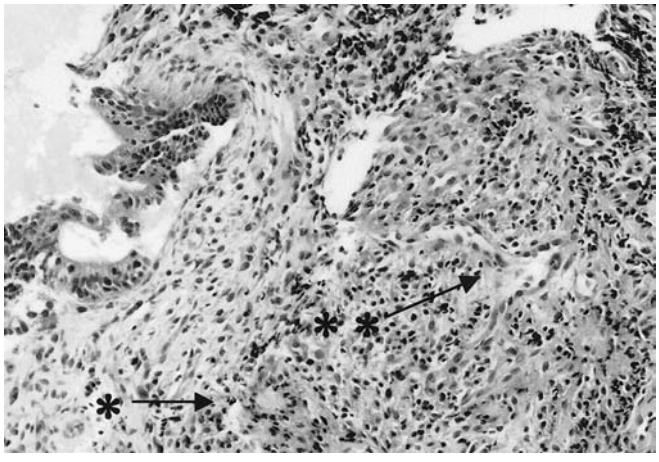

Fig. 4. The microscopic findings of the terminal ileum mucosa infiltrated with neutrophils and necrotizing granuloma with giant cells (*) and vasculitis without necrotizing lesion (**)

Discussion

Wegener's granulomatosis is a systemic granulomatous inflammatory disease which can affect a variety of organs. Histologically, it consists of necrotizing vasculitis affecting mainly small to medium-sized arteries, and sometimes involving venous or capillary vessels.[1] This granulomatous vasculitis involves primarily the upper and lower airway system, the lungs, and the kidneys. Since its description in the 1930s,[3,4] various sites of involvement have been identified, in a vast range of organ systems. The incidence of gastrointestinal involvement reported here is relatively rare.

Hashimoto et al.[5] reported that the initial symptoms of Wegener's granulomatosis in Japanese cases were nasal occlusion (51%), nasal bleeding (45%), and pyrexia (27%). Gastrointestinal symptoms were not referred to in this report. Moreover, in a study of 158 patients with Wegener's granulomatosis seen at the National Institute of Health, no gastrointestinal manifestations were reported.[2] Storesund et al.[6] reported that they found only six cases of Wegener's granulomatosis in the available medical literature that presented with severe intestinal involvement. In this report, any gastrointestinal involvement occurs in an earlier period of the Wegener's granulomatosis, and in most of the reported cases the disease had an active status. The intestinal involvement appears in any region of the large intestine, with skipped lesions which sometimes lead to perforation. Under microscopic examination, some of the cases showed ischemic changes and vasculitis in addition to ulcerations.[7–10] On the other hand, granulomatous lesions or typical necrotizing vasculitis are not usually recognized in this complication.

In our case, a biopsied specimen from the elevated lesion from the ascending colon showed nonspecific inflammation

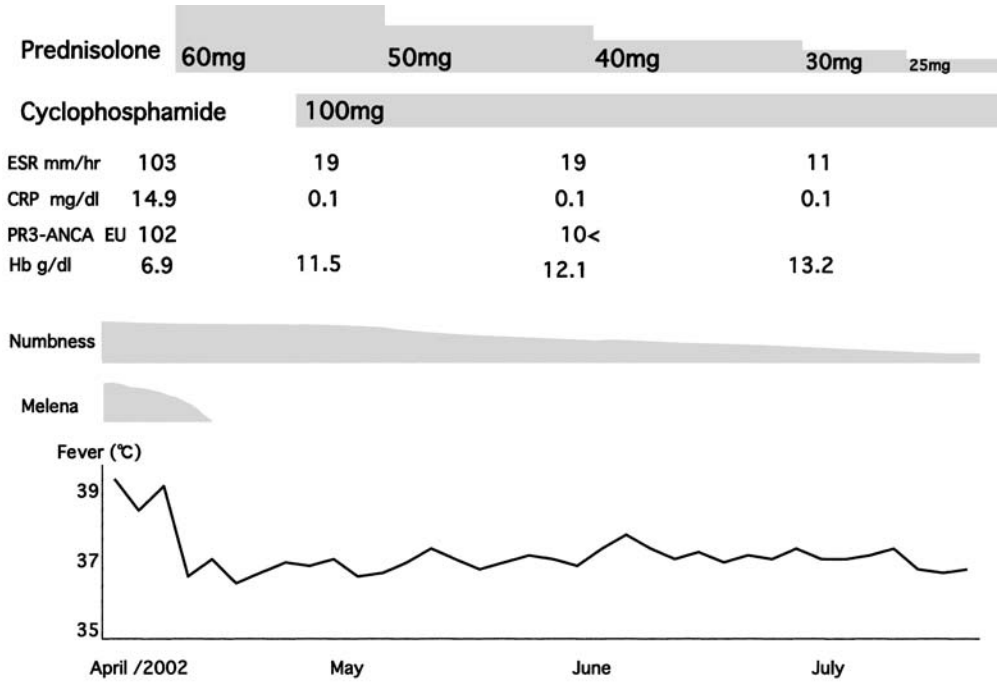

Fig. 5. Clinical course on admission. *ESR*, erythrocyte sedimentation rate; *CRP*, C-reactive protein

with granulomatous lesions, giant cells, and vasculitis without necrosis. The most important differential diagnosis in our case is the overlapping of other inflammatory bowel diseases such as Crohn's disease. One case of the overlapping of Wegener's granulomatosis and Crohn's disease has been reported.[11] It is important to differentiate between our case and Crohn's disease. Typical visible colonoscopic features of Crohn's disease are liner ulcer, nonconsecutive ulcer, small intestinal ulcer, cobble stoning, and inflammatory pseudopolyposis.[12] In our case, these typical findings for Crohn's disease were lacking. Furthermore, in our case, a vasculitis and giant cells, not usually seen in Crohn's disease, occurred histologically, although there was no necrotic vasculitis. Therefore, in our case, the overlapping of Wegener's granulomatosis and Crohn's disease is not the same. Unfortunately, typical histological findings in the gastrointestinal tract for Wegener's granulomatosis are uncommon. In only one case, described by Richard and William,[13] has the presence of typical necrotizing vasculitis been found in a biopsy specimen.

PR-3 ANCA, as well as the colonoscopy findings, will be useful to differentiate Wegener's granulomatosis from other inflammatory bowel diseases.[6,11,14] Together with visible colonoscopic features, pathological findings in the colon biopsy specimen, and a positive titer of PR3-ANCA, we diagnosed Wegener's granulomatosis complicated with intestinal ulceration. Although some cases with perforation had poor prognoses, this gastrointestinal complication has usually been curable in most reported cases.[6,8,13,15] In our case, the patient has remained in remission for more than 2 years.

In conclusion, gastrointestinal involvement is a rare event in Wegener's granulomatosis. However, our case and some cases in the literature indicate that the gastrointestinal region is one of the target organs in Wegener's granulomatosis in the initial stages of the disease.

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