A Limited Form of Wegener’s Granulomatosis with Bronchiolitis Obliterans Organizing Pneumonitis-like Variant in an Ulcerative Colitis Patient

Shuichi Yano, Kanako Kobayashi, Kazuhiro Kato and Kengo Nishimura*

Abstract

A case of a 19-year-old man with ulcerative colitis (UC) developed multiple pulmonary nodular shadows with cavity formation, elevated perinuclear antinuclear cytoplasmic antibody (pANCA) and positive lymphocyte stimulation test by drug (DLST) for mesalazine suggesting mesalazine induced Wegener’s granulomatosis (WG). Transbronchial biopsy specimens were consistent with WG and thoracoscopic biopsy specimens were consistent with bronchiolitis obliterans organizing pneumonitis (BOOP). We diagnosed WG with BOOP-like variant, which was induced by mesalazine. To our knowledge, this is the first report of a limited form of WG associated with orally administered mesalazine.

On admission, white blood cell count was 8,300/mm³. Serum C-reactive protein was elevated (3.1 mg/dl). Serum perinuclear antinuclear cytoplasmic antibody (ANCA) by ELISA, pANCA (Anti-myeloperoxidase ANCA, SRL-INC. co, Japan) was slightly increased to 20 EU and cANCA (Anti-proteinase-3 ANCA, SRL-INC. co, Japan) was normal value. The lymphocyte stimulation test by drug (DLST) for mesalazine was positive (stimulation index 184%). Urinalysis was negative for protein, occult blood, sugar, cells and casts. Stool was negative for occult blood. Routine bacteriological, fungal, and mycobacterial cultures of sputum were negative. Plain chest radiograph and CT scanning revealed two tumors with cavity formation in bilateral B6 and a nodular shadow in right B4 (Fig. 1A). Spirometry revealed a forced expiratory volume in one second (FEV₁) of 4.78 l (105.3 percent of predicted), forced vital capacity (FVC) of 4.38 l (96.5 percent of predicted), and FEV₁/FVC ratio of 90.4 percent. The transbronchial biopsy specimen from right B6 showed that necrotic granuloma or basophilic necrosis with granulocytes surrounding by epithelioid cells (Fig. 1B). These findings were compatible with Wegener’s granulomatosis (WG). Resection of the right B4 nodule by thoracoscope was undertaken for the diagnosis. The thoracoscopic biopsy specimen showed typical polypoid granuloma formed from respiratory bronchiole to alveoli and the matrix contained variable numbers of lymphocytes, macrophages and eosinophils (Fig. 1C). These specimens were compatible with bronchiolitis obliterans organizing pneumonitis (BOOP). As we diagnosed a limited form of WG with BOOP-like variant, he was treated by adding prednisolone of 20 mg to mesalazine. Staining for acid-fast bacilli and fungi were negative in both the transbronchial and thoracoscopic specimens. After one month with prednisolone and mesalazine a chest radiograph showed no pulmonary lesions and serum pANCA was slightly decreased to 13 EU. Prednisolone was gradually tapered and discontinued in November 2001. However, one month later, the high grade fever of 38°C recurred and a plain chest radiograph revealed right lower infiltration. He was treated only with 20 mg of prednisolone, as we consid-

From Department of Pulmonary Medicine, *Department of Surgery, National Matsue Hospital, Matsue
Received for publication April 23, 2002; Accepted for publication July 18, 2002
Reprint requests should be addressed to Dr. Shuichi Yano, Department of Pulmonary Medicine, National Matsue Hospital, 5-8-31 Agenogi, Matsue, Shimane 690-8556

Internal Medicine Vol. 41, No. 11 (November 2002) 1013
Yano et al

Figure 1. A: Chest radiograph on admission showing multiple nodular shadow in bilateral lung field. B: The transbronchial biopsy specimen from right B4 showing necrotic granuloma or basophilic necrosis with granulocytes surrounded by epithelioid cells (HE stain, ×100). C: The thoracoscopic biopsy specimen of right B4 showing typical polypoid granuloma are formed from respiratory bronchiole to alveoli and the matrix contains variable numbers of lymphocytes, macrophages and eosinophils (HE stain, ×100).

Discussion

Pulmonary manifestations of UC are very rare, although a constellation of extraintestinal manifestations affecting various organs or organ systems has been described in association with IBD (1). Turner-Warwick pointed to the possible association of UC and respiratory disease (2), and Kraft et al reported that respiratory involvement was included on the list of established complications of IBD (3). Following these reports, several publications described similarly disabling bronchitis or bronchiectasis in patients with IBD. Later on, panbronchiolitis, BOOP and interstitial pneumonitis mimicking WG were reported in patients with inflammatory bowel disease (IBD).

Camus et al (1) reported two patients with UC mimicking a limited form of WG. They both had inactive UC, fever and positive pANCA. Stebbing et al also reported a case of UC mimicking a limited form of WG (4). All of these cases had positive immunofluorescence tests for pANCA. In our case, serum pANCA was also slightly increased. Up to 90% of patients with WG with active disease are ANCA positive. Although the majority are cANCA positive by immunofluorescence, a significant minority (10%) are pANCA positive. A substantial proportion of patients with IBD, particularly those with UC, also have ANCA. As with systemic vasculitis, the precise role of ANCA in the pathogenesis of IBD remains unclear.

Sulfasalazine (Salazopyrin) is widely used in the treatment of UC, although a high incidence of side effects has been reported. Jones and Malone reported a case of lung disease attributable to sulfasalazine hypersensitivity that resembles simple pulmonary eosinophilia (5). Salerno et al reported a patient with UC who developed pulmonary symptoms, peripheral nodular lung infiltrates, and an elevated cANCA suggesting...
WG (6). Sulfasalazine and 5-aminosalicylic acid are also known as mesalamine or mesalazine, which has been thought to be free of most side effects. However, even in mesalazine, bronchiolitis and interstitial infiltrates were reported. In these previous reports of sulfasalazine or mesalazine–induced lung disease, DLST was not performed except in one report (7). In this case, as the DLST for mesalazine was positive, we considered the possibility of mesalazine-induced lung disease. However, we continued the use of mesalazine since deterioration of UC was a major concern, and 20 mg of prednisolone was added. Because the lung disease recurred, we should have stopped mesalazine in the first episode and treated only with prednisolone.

The transbronchial biopsy specimen was thought to be consistent with WG, while the thoracoscopic biopsy specimen was thought to be consistent with BOOP or eosinophilic pneumonia. Uner et al (8) reported that the major pathologic findings in WG resembled BOOP and constituted a BOOP-like variant (9). Therefore, we diagnosed this patient as having a limited form of WG in UC. To our knowledge, this is the first report of a limited form of WG with BOOP-like variant that might be associated with orally administered mesalazine.

We conclude that adverse pulmonary reactions to mesalazine must be considered in the differential diagnosis of pulmonary involvement such as a limited form of WG in patients with UC receiving mesalazine therapy.

References