Long-term efficacy and safety of maintenance therapy with azathioprine or cyclosporine for interstitial lung disease with diffuse cutaneous scleroderma

Sirs,

Several agents have been evaluated as treatments for scleroderma-related interstitial lung disease (SSc-ILD) (1-4). However, follow-up studies demonstrate that its effectiveness is not durable and regimens with long-term beneficial effects has never been reported (4-6). We describe two SSc-ILD patients who can be stabilised by long-term maintenance therapy with azathioprine (AZA) or cyclosporine (CYC).

Case 1: A 48-year-old woman presented with a two-year-period of cough, Raynaud’s phenomenon, and joint pains. Physical examination revealed hardening and scarring in her skin, and laboratory data included positivity for antinuclear, anti-topoisomerase I, and anti-centromere antibodies as well as an increase of sialylated carbohydrate antigen (KL-6, 1,250 pg/ml). Since a computed tomography (CT) scan of the thorax showed ground-grass opacities and consolidation in the bilateral lower lobes, we diagnosed diffuse cutaneous SSc with ILD. Until then, we had treated cutaneous lesions with oral prednisolone (PSL), but her % predicted value of vital capacity (%VC) had declined rapidly from 49.6% to 43.5% within two years. Her clinical manifestations such as dyspnea and hypoxemia had gradually worsened along with the pulmonary deterioration and presence of infiltrates visible by x-ray. Therefore, we started a treatment protocol with intravenous cyclophosphamide (CYC) for progressive ILD. Soon afterward, the patient’s symptoms lessened, and her %VC improved to 47.2% six months later. Six months after the foregoing initial treatment ended, however, her respiratory defects recurred; the chest x-ray findings confirmed a relapse, and %VC, which had been stabilised, again declined to 43.1%. At this point, we realised that drug withdrawal caused the recurrence and theorised that her previously improved clinical manifestations might be restored and sustained by maintenance therapy to inhibit the inflammatory response. After agreement with the patient and her family, we began maintenance therapy with AZA, 100 mg once daily. As a result, her clinical symptoms decreased and chest x-ray findings improved slightly. Subsequently, her %VC has been re-stabilised to the 43.0% level for more than four years, and no adverse events have recurred.

Case 2 (Fig. 1): The second SSc-ILD patient with anti-topoisomerase I antibody is included here to exemplify the effectiveness of CYA maintenance therapy. After two months of progressive dyspnea, this 53-year-old woman underwent imaging studies that revealed ground-glass opacities of peribronchovascular predominance in the bilateral lower lobes. The %VC had declined and KL-6 was increased to 3,040 pg/ml. Soon after we started oral PSL along with intravenous CYC pulse therapy, her symptoms and %VC lessened rapidly. One year after the discontinuation of CYC pulse therapy, however, her respiratory symptoms recurred; the %VC declined and the CT scan showed pulmonary deterioration. Based on this weakening clinical course, we began maintenance therapy consisting of oral CYA, 75 mg twice per day. As a result, her symptoms and %VC again improved slightly. Two years later, her pulmonary function and chest CT findings remain stable, and no adverse events are present.

In these two cases, our initial treatment regimens continued for one to two years, and the patients described here enjoyed a stabilised pulmonary function. However, one to two years after discontinuation of CYC-based regimens, the clinical manifestations resumed. These courses indicate that, although continuing CYC might be useful for the stabilisation of patients with SSc-ILD by inhibiting the inflammatory response, administering that agent could increase the risk of haematologic malignancies and bladder cancer (7, 8). Accordingly, maintenance with AZA or CYA after the CYC induction regimen ceases has the possibility of offering a novel treatment option. We expect to re-evaluate this protocol prospectively and are currently planning clinical trials to assess its safety and enduring efficacy.
Letters to the editor

K. ANDO\textsuperscript{1}, MD
T. NAKASHITA\textsuperscript{2}, MD
N. KANEKO\textsuperscript{1}, MD
K. TAKAHASHI\textsuperscript{1}, MD, PhD
S. MOTOJIMA\textsuperscript{2}, MD, PhD

\textsuperscript{1}Division of Respiratory Medicine, Juntendo University Faculty of Medicine and Graduate School of Medicine, Tokyo, Japan;
\textsuperscript{2}Department of Rheumatology and Respiratory Internal Medicine, Kameda Medical Center, Chiba, Japan.

Address correspondence and reprint requests to: Katsutoshi Ando, MD, Division of Respiratory Medicine, Juntendo University Faculty of Medicine and Graduate School of Medicine, 2-1-1 Hongo, Bunkyo-Ku, Tokyo 113-8421, Japan.
E-mail: kando@juntendo.ac.jp
Competing interests: none declared.

References


5. STEEN VD, MEDSGER TA Jr.: Case-control study of corticosteroids and other drugs that either precipitate or protect from the development of scleroderma renal crisis. \textit{Arthritis Rheum} 1998; 41: 1613-9.

