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LETTER

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Asymptomatic interstitial pneumonitis induced by bucillamine in a patient with rheumatoid arthritis

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Bucillamine [BU; *N*-(2-mercapto-2-methylpropionyl)-L-cysteine] is an antirheumatic drug.[1] The chemical structure is almost the same as that of D-penicillamine. We treated a rheumatoid arthritis patient who had asymptomatic interstitial pneumonitis induced by BU. A 44-year-old woman presenting with polyarthralgia and morning stiffness visited our outpatient clinic in April 2003. At that time, chest X-ray was normal (Fig. 1a). The patient was diagnosed as having rheumatoid arthritis and was treated with BU 100 mg per day. Her serum C-reactive protein and erythrocyte sedimentation rate were 1.6 mg/dl and 29.2 mm/h, respectively. Her rheumatoid arthritis particle agglutination was 640×; total protein was 7.3 g/dl; and serum γ-globulin was 17.1%. From June 2003, she began taking 200 mg BU per day. Her condition improved 3 months after the initiation of BU administration. In May 2004, she underwent a regular health check where she was found to have an abnormal shadow in her lungs, detected by chest X-ray (Fig. 1b). She was admitted to the respiratory unit for further checks in June 2004. Chest computed tomography (CT) scan revealed diffused ground-glass opacity and multiple nodular shadows in both lobes (Fig. 2).

Laboratory data were normal except for serum KL-6 (1160 U/ml; normal range < 500 U/ml). Arterial blood gas pressures measured in rooms were PCO_2 48.1 torr, PO_2 82.7 torr, pH 7.4. Serum total protein and serum γ-globulin were 6.1 g/dl and 12.9%, respectively. Total cell count in the bronchoalveolar lavage (BAL) fluid was 1.28×10^5 ml and the percentage of lymphocytes was normal. Stains and cultures of BAL fluid and sputum showed no evidence of microbial infection. A lymphocyte stimulation test using BU was negative. Loose fibrosis and moderately small, round cell infiltration of the peri-bronchiolovascular alveoli and hyalinous fibrosis of the alveoli were observed by lung biopsy.

Since the abnormal shadows on chest CT regressed after the withdrawal of BU (Fig. 2), we diagnosed the patient as having BU-induced pneumonitis. The level of serum KL-6 decreased 519 U/ml after the withdrawal of BU. The patient has remained free of respiratory complaints during the 12 months of follow-up after discharge.

Drugs such as bucillamine,[2,3] gold,[4] D-penicillamine,[5] and methotrexate[6] have been reported to induce lung injuries. Inokuma et al.[3] reported 13 BU-induced lung injury cases. They concluded that the characteristics of BU-induced lung injury might be mottled infiltrates in the center of the lung that appeared concurrently with serum immunoglobulin decrease. In our case the serum γ-globulin level of the patient before BU administration was normal and when lung injury appeared, the serum γ-globulin level decreased. In addition, the chest CT showed mottled imaging. There was no sign of infection. Thus, this case is compatible with BU-induced pneumonitis. Most BU-induced pneumonitis requires treatment with corticosteroids. This was a rare case in that the shadows of chest CT improved only with the withdrawal of BU without needing corticosteroid treatment. Interestingly, the effect of BU on rheumatoid arthritis activity was excellent in most patients who developed pneumonia induced by BU.[2] The cell-mediated hypersensitivity reaction may have contributed to the development of lung injury associated with BU therapy.

We concluded that BU should be added to the list of drugs capable of causing pneumonitis. Regular chest X-ray may be useful to monitor BU-administered rheumatoid arthritic patients and to diagnose asymptomatic BU-induced interstitial pneumonitis.

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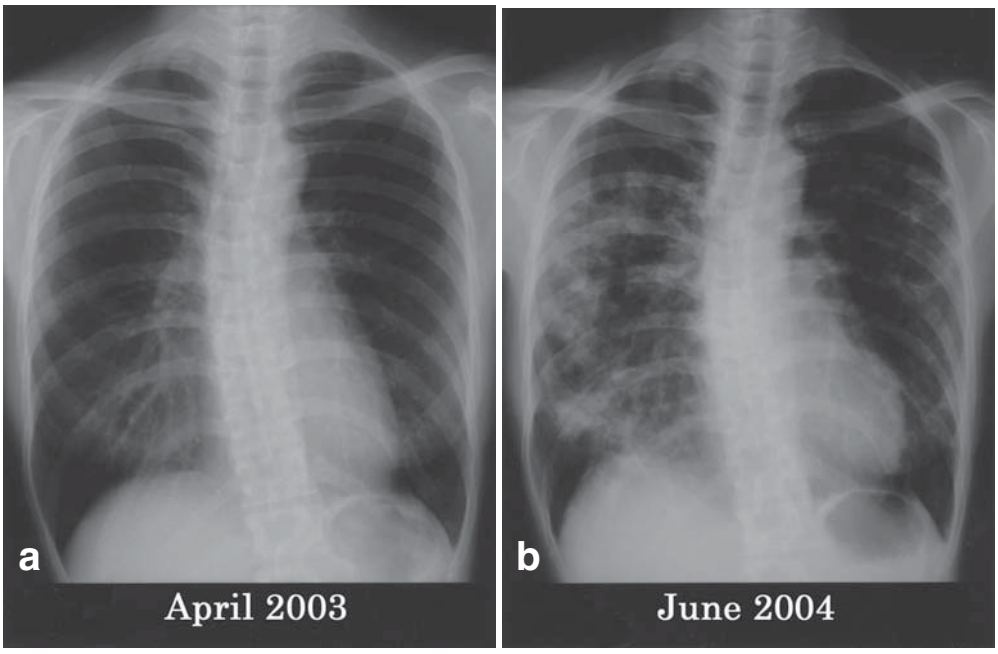

Fig. 1a,b. Chest X-rays. **a** April 2003. **b** June 2004

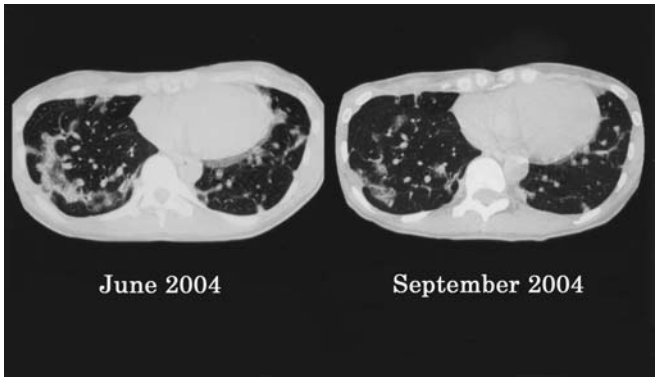

Fig. 2. Chest computed tomography scans done in June 2004 and September 2004

References

1. Ishikawa K, Sakaguchi M. SA 96 (N-(2-mercapto-2-methylpropanoyl)-L-cysteine) in rheumatoid arthritis. Scand J Rheumatol 1986;15:85–90.
2. Negishi M, Koga S, Kasama T, Hashimoto M, Fukushima T, Yamagata N, et al. Lung injury associated with bucillamine therapy (in Japanese). Riumachi 1992;32:135–9.
3. Inokuma S, Ikoma T, Inoue S, Ueda A, Urano Y, Satou T, et al. Bucillamine induced lung injury in rheumatoid arthritis (in Japanese). Riumachi 1996;36:34–42.
4. Winterbauer RH, Wilske R, Wheellis RF. Diffuse pulmonary injury associated with gold treatment. N Engl J Med 1976;294:919–21.
5. Camus P, Degat O, Justrabo E, Jeannin L. D-Penicillamine-induced severe pneumonitis. Chest 1982;81:376–8.
6. Cannon GW, Ward JR, Clegg DO. Acute lung disease associated with low-dose pulse methotrexate therapy in patients with rheumatoid arthritis. Arthritis Rheum 1983;26:1269–74.
7. Engelbrecht JA, Calhoon SL, Scherrer JJ. Methotrexate pneumonitis after low-dose therapy for rheumatoid arthritis. Arthritis Rheum 1983;26:1275–8.
8. Kremer JM, Alarcon GS, Weinblatt ME, Kaymakcian MV, Macaluso M, Cannon GW, et al. Clinical, laboratory, radiographic, and histopathologic features of methotrexate-associated lung injury in patients with rheumatoid arthritis. Arthritis Rheum 1997;40:1829–37.