Mod Rheumatol (2002) 12:366–367

Letter

Serum KL-6: a useful marker for early detection of methotrexate-induced interstitial pneumonia

Tetsu Oyama, Nobuoki Kohno, Hiroko Oyama, Yasuaki Okuda, Shigeru Namba, Kiyoshi Takasugi

Key words KL-6 · Methotrexate (MTX)-induced interstitial pneumonia (IP) · Rheumatoid arthritis (RA)

To the Editor:

Interstitial pneumonia (IP) is the most significant adverse effect associated with methotrexate (MTX) therapy for rheumatoid arthritis (RA). The prompt evaluation of new respiratory symptoms in patients receiving MTX is critical for early recognition of this potentially life-threatening complication.[1] Unfortunately, because respiratory symptoms (including dry cough and exertional dyspnea) are nonspecific, it is often difficult to detect the complication before it becomes serious. KL-6,[2] a human MUC1 mucin preferentially expressed on type II pneumocytes, is a sensitive serum marker for alveolar damage due to IP. We experienced two cases of MTX-induced IP that were recognized by monitoring serum KL-6 levels before the emergence of chest radiographic abnormality.

When a 63-year-old woman with RA (Steinbrocker stage IV, class 2) began to receive MTX, her serum KL-6 level was 170 U/ml (normal <500 U/ml). MTX was initiated at 2.5 mg weekly and increased gradually to 10 mg/week during the next 8 weeks. Nine weeks after the initiation of MTX, she began to complain of a dry cough and dyspnea. Although lung auscultation and chest radiography revealed no abnormalities, the serum KL-6 level showed a slight elevation to 330 U/ml without abnormal elevation of lactate dehydrogenase (Fig. 1). Nineteen days later her dyspnea got worse, and a chest radiograph revealed ground-glass opacities in both lungs. Because serological and microbiological workups revealed no evidence of infection, and there had been no abnormality in the chest radiographs obtained before MTX treatment, she was diagnosed as having MTX-induced IP (by Searles and McKendry's,[3] criteria: possible).

In another case, an 83-year-old woman with RA (stage IV, class 2) was seen. When MTX (3.75 mg/week) was started, her serum KL-6 was 150 U/ml. Four months later, when she developed high fever and dyspnea, the serum KL-6 level was 240 U/ml. No abnormality was detected on a chest radiograph. Ground-glass opacities emerged in both lungs 2 days later. Because of severely impaired oxygenation, a high dose of methylprednisolone was administered.

Despite rapid alleviation of the respiratory symptoms and radiographic findings in both cases, the serum KL-6 level continued to rise (to 840 and 950 U/ml in the first and second cases, respectively). It took several months to return to normal. The persistent elevation of serum KL-6 might reflect the repair process in the damaged lung (i.e., replacement of damaged type II pneumocytes to type I pneumocytes and the prolonged damage to the air-blood barrie).[4]

The serum KL-6 level could be a useful marker for early detection of MTX-induced IP. Its assay requires no skills or tips, even when it shows only minimum elevation, within the normal range.

T. Oyama (✉) · H. Oyama
Oyama Medical Clinic for Rheumatic Disease, 10-10 Hakushimakitamachi, Naka-ku, Hiroshima 730-0001, Japan
Tel. +81-82-511-3535; Fax +81-82-511-3536
e-mail: fwna9858@mb.infoweb.ne.jp

N. Kohno
Second Department of Internal Medicine, Hiroshima University, Hiroshima, Japan

N. Kohno
Department of Molecular and Internal Medicine, Hiroshima University, Hiroshima, Japan

Y. Okuda · S. Namba · K. Takasugi
Dohgo Spa Hospital for Rheumatic Diseases, Ehime, Japan

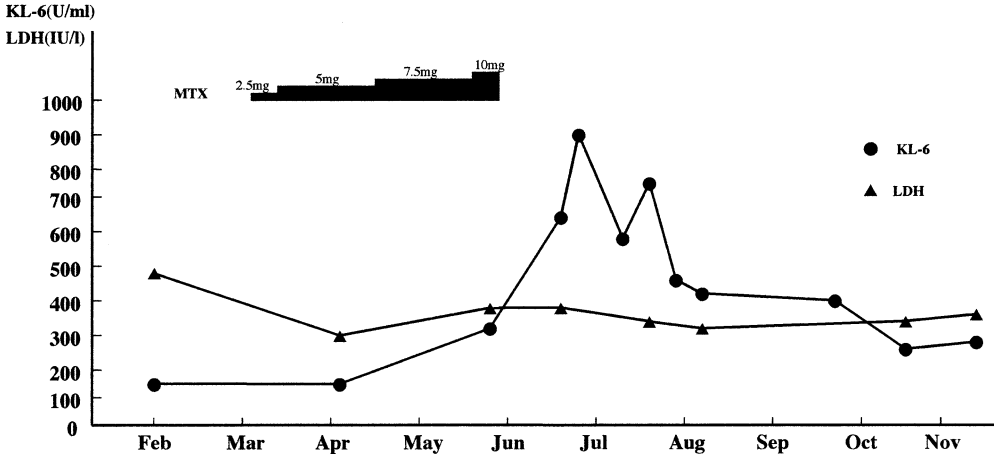

Fig. 1. Serum KL-6 levels were elevated at the onset of methotrexate-(*MTX*)-induced interstitial pneumonia. There were no significant changes in lactate dehydrogenase (*LDH*) levels

References

1. Van der Veen MJ, Dekker JJ, Dinant HJ, van Soesbergen RM, Bulsma JWJ. Fatal pulmonary fibrosis complicating low dose methotrexate therapy for rheumatoid arthritis. J Rheumatol 1995;22: 1766–8.
2. Kohno N, Kyoizumi S, Awaya Y, Fukuhara H, Yamakido M, Akiyama M. New serum indicator of interstitial pneumonitis activity: sialylated carbohydrate antigen KL-6. Chest 1989;96:68–73.
3. Searles G, McKendry R Jr. Methotrexate pneumonitis in rheumatoid arthritis: potential risk factors; four case reports and a review of the literature. J Rheumatol 1987;14:1164–71.
4. Inoue Y, Barker E, Daniloff E, Kohno N, Hiwada K, Newman LS. Pulmonary epithelial cell injury and alveolar-capillary permeability in berylliosis. Am J Respir Crit Care Med 1997;156:109–15.