Acute Eosinophilic Pneumonia Induced by Minocycline: Prominent Kerley B Lines as a Feature of Positive Re-Challenge Test

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We report herein a case of acute eosinophilic pneumonia induced by minocycline, confirmed by TBLB and re-challenge test. Re-challenge test suggested that Arthus-type reaction was pathognomonic, and prominent Kerley B lines represented a local hypersensitivity reaction in this patient.

Key words: Drug-induced pneumia, Tetracyline, Kerley line

Eosinophilic pneumonia is a rather confusing clinico-pathological concept and has a variety of etiologies. This type of pneumonia is known to be induced by some drugs. Here we report a case of minocycline-induced acute eosinophilic pneumonia. So far six such cases have been described (1-6) but this case is quite unique because the chest roentgenogram taken after re-challenging showed a particular shadow characterized by prominent Kerley B lines. This case indicates that Kerley B lines may appear as a result of local allergic reaction to drugs.

CASE REPORT

A 30-year-old woman was admitted because of dry cough, fever up to 39°C and bilateral reticulonodular opacities on the chest roentgenogram (Fig. 1).

She had been treated for acute pneumonia of the right middle lobe with 100 mg minocycline twice a day for 7 days starting 14 days before admission. Her body temperature had returned to normal range and the abnormal shadow disappeared 7 days before admission, though slight dry cough persisted. On the day prior to admission, she took 100 mg of minocycline twice because she felt that she was getting sick again.

Physical examination revealed a body temperature of 38.5°C. No skin rash was noted but she had had physical dermographism for several years. Auscultation of the chest revealed no rales. The white blood cell count (WBC) was 18,400/cu mm, with 75% segmented forms, 17% band forms, 5% lymphocytes, 3% monocytes and no eosinophils. The serum level of C-reactive protein was 7.2 mg/dl.

A bronchoscopic examination was performed on the day of admission including bronco-alveolar lavage (BAL) and transbronchial lung biopsy (TBLB). The differential counts of BAL fluid were 86% macrophages, 5.6% neutrophils, 4.4% lymphocytes and 4% of eosinophils. The TBLB specimen (Fig. 2) showed mild edema of the alveolar walls with infiltration predominantly by small round cells and eosinophils. These findings were consistent with acute eosinophilic pneumonia (7).

On the third day of hospitalization, the patient became afebrile. On the fourth day the chest roentgenogram and the WBC were within normal limits whereas the total eosinophil count increased to 1,087/cu mm. Dry cough persisted until the 10th day.
Fig. 1. Chest X-ray film taken on the day of admission, showing reticulo-nodular shadows on both lungs except right middle and lower lung.

The possibility of a hypersensitivity reaction to minocycline was considered, though intradermal skin test with this drug alone (1 mg/ml) and the patient's serum (preincubated at 1:1, final 1 mg/ml) were negative. The lymphocyte stimulation test (LST) was also negative. Then a provocation test was carried out with informed consent on the 13th day after admission. About 10 hours after oral administration of 50 mg of minocycline, she experienced frequent non-productive cough. Her body temperature elevated to 39°C at 13 hours after re-challenging. The chest roentgenogram taken the following day showed a faint reticular shadow in the left middle lung field accompanied by prominent multiple Kerley B lines in both lungs (Fig. 3). The WBC was up to 10,000/cumm, with 55% neutrophils and 23% eosinophils. The level of CRP rose from 0.5 mg/dl (4 days before re-challenging) to 6.8 mg/dl. Her symptoms and abnormal shadows cleared up three days later without medication.

**DISCUSSION**

The patient presented here had eosinophilic pneumonia, which was self-limited and resolved spontaneously and rapidly. In this case, drug-induced etiology was considered and confirmed by a re-challenge test. There are four case reports of suspected minocycline-induced pneumonia in Japan (1-4) and two cases are described in English literature (5, 6).

Hypersensitivity reactions are usually categorized into four types according to Gell and Coombs. Among the 4 reported cases, one (4) was considered to be by type III (Arthus-type), one (2) type IV (delayed-type) and two (1, 3) a combination of type I (immediate-type) and type III mediated mechanisms. In this patient, the reaction might have been due to a type III mechanism because the latent time was too long to be type I and too short to be type IV. The negative result of LST supports this notion. Because minocycline may act as a full antigen after binding some serum proteins, we per-
formed intradermal skin test with this drug alone and after preincubation with serum of the patient. No positive sign was noted during 48 hours of observation. If the dose was enough to elicit the reaction, the antigen may have been a metabolite of minocycline.

The pathogenesis of Kerley B lines in this patient may be interlobular edema and cell infiltration.
secondary to Arthus-type reaction but not to pulmonary venous hypertension which is the most common cause. The patient had no signs of cardiac failure, suggesting that gravity did not influence the distribution of the lines. Although these lines also appear in interstitial lung diseases, they are usually not a predominant feature of the abnormalities seen on chest roentgenograms. This case suggests that clinicians, again, should be alert to the possibility of eosinophilic pneumonia when prescribing minocycline, and that prominent Kerley B lines may represent local hypersensitivity reaction to the drug.

REFERENCES


