Hypersensitivity Pneumonitis and Pulmonary Vasculitis with Eosinophilia in a Patient Taking an L-Tryptophan Preparation

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Dietary intake of L-tryptophan tablets has recently been found to be associated with a potentially fatal...
A 70-year-old woman presented with a 1- to 2-week history of fatigue and weakness, cough with brown sputum, and several days of progressive dyspnea associated with bifrontal headache. An outpatient chest radiograph, 2 days before admission, showed bilateral perihilar and lower-lobe alveolar infiltrates, bilateral pleural effusions, and cardiomegaly. Arterial blood gas tests (room air) showed a \( \text{PO}_2 \) of 30 mm Hg and a \( \text{PCO}_2 \) of 37 mm Hg with a pH of 7.44. Hemoglobin was 147 g/L and the leukocyte count was 10.7 \( \times \) 10⁹/L with 5% eosinophils. Oral antibiotics had been started empirically 2 days before admission.

Her temperature was 37 °C, respiratory rate, 28/min, and blood pressure, 110/70 mm Hg. Bilateral crackles and rales were heard on pulmonary auscultation and percussion revealed dullness at the bases. She had an S₃ gallop. Her cardiogenic pulmonary edema and acute bronchitis were treated with furosemide along with empiric antibiotics. The pulmonary infiltrates and pleural effusions partially cleared after several days of intensive diuresis but she remained dyspneic and hypoxemic with a \( \text{PO}_2 \) of 65 mm Hg, a \( \text{PCO}_2 \) of 43 mm Hg, and a pH of 7.44 on a 100% oxygen mask supplemented by a 6 L/min nasal cannula. Her eosinophil count rose as high as 39% with a total leukocyte count of 10.9 \( \times \) 10⁹/L. A few eosinophils were seen in a sputum sample. Serum rheumatoid factor and antinuclear antibody tests were negative. A serum IgE level was 700 \( \mu \)g/L (normal < 430 \( \mu \)g/L).

Pulmonary function tests showed a mild restrictive defect and a moderate decrease in diffusion capacity. A gallium scan showed extensive bilateral uptake of the isotope in the lung fields. Owing to lack of improvement, an open lung biopsy was done. The lung biopsy showed moderate interstitial infiltration by lymphocytes with lymphoid aggregates, a few plasma cells, and scattered, focally prominent eosinophils (Figure 1, top). The interstitial infiltrate was prominent around bronchioles and blood vessels, with focal vasculitis (Figure 1, bottom).

After surgery the patient was started on methylprednisolone, 60 mg administered intravenously every 6 hours, with dramatic improvement. Subsequently the patient admitted to having taken three 500-mg tablets of L-tryptophan daily for 3 months for insomnia. She was also taking vitamin B complex tablets, but no other medications other than propranolol for hypertension and conjugated estrogens.

Discussion

A peripheral eosinophilia with pneumonitis is a common pattern of drug-induced pulmonary disease (3, 4). The lung biopsy in this case showed typical histologic features of hypersensitivity pneumonitis associated with drugs (5). Pulmonary vasculitis is an unusual feature, but can occur in drug reactions (3-6). The clinical and pathologic findings suggest that ingestion of the L-tryptophan preparation caused this patient's pulmonary disease.

The pathogenesis of this syndrome resembles a drug-induced hypersensitivity reaction. The inciting agent might be a contaminant in the tablets rather than the L-tryptophan itself. Interestingly, L-tryptophan, a constituent of lush pasture grasses, is thought to be the primary toxin in a common form of toxic bovine atypical interstitial pneumonia (7). Rumen microflora metabolically convert L-tryptophan to 3-methylindole, which in goats has been shown to cause diffuse alveolar damage and impaired surfactant production (8, 9). Although the clinical and pathologic features in our patient were not those of the adult respiratory distress syndrome, it is not known whether 3-methylindole plays a role in the pathogenesis of the pulmonary toxicity associated with L-tryptophan ingestion.

The incidence of this syndrome will probably de-
crease because L-tryptophan preparations have been taken off the market by the Food and Drug Administration. Until the public becomes aware of these toxic effects, more cases may be encountered. L-Tryptophan preparations should be added to the list of drugs associated with pulmonary infiltrates and eosinophilia. The combination of peripheral eosinophilia with a histologic picture of hypersensitivity pneumonitis and vasculitis is unusual and a drug reaction should be considered, particularly from L-tryptophan preparations.

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References