be definitive in the diagnosis of intrathoracic extramedullary hematopoiesis. In difficult cases, however, tissue biopsy or aspiration is confirmatory.

REFERENCES

Broncholitis Obliterans Organizing Pneumonia Associated With Massive L-Tryptophan Ingestion*

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A 51-year-old woman developed acute febrile illness with respiratory failure following intake of L-tryptophan. An open lung biopsy specimen established the histopathologic nature of the lung lesion as broncholitis obliterans organizing pneumonia (BOOP). There was no evidence of other known causes usually associated with BOOP. Her condition improved with corticosteroid therapy. The entity of BOOP now should be added to the growing list of illnesses associated with the use of L-tryptophan.

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L-tryptophan has recently been implicated in a variety of clinical syndromes as a consequence of its popularity among health enthusiasts for use in sleep and pain disorders. The majority of reported cases have been associated with the eosinophilic-myalgia syndrome (EMS) and eosinophilic fasciitis. Some also had respiratory symptoms and chest radiographic findings suggestive of L-tryptophan-related pulmonary disease.

We describe a patient who presented with an acute respiratory illness complicated by respiratory failure following ingestion of L-tryptophan prior to the onset of her clinical syndrome.

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BOOP = broncholitis obliterans organizing pneumonia
respiratory illness. Subsequent investigations, including an open lung biopsy, established the histopathologic nature of the lung disease as bronchiolitis obliterans with organizing pneumonia (BOOP).

**CASE REPORT**

A 51-year-old woman was admitted to the hospital because of difficulty in breathing for 2 days associated with a cough productive of yellowish sputum, fever, chills, nausea, and weakness. Her respiratory symptoms worsened despite treatment with erythromycin and she was admitted for further evaluation.

Medical history was unremarkable, except for a previous hospitalization for depression in 1982. She denied any allergies. She took L-tryptophan at a daily dose of 2,068 mg for 2½ months prior to hospital admission. She had smoked 1 pack of cigarettes per day for 30 years. She denied any exposure to toxic materials.

Pertinent findings from physical examination revealed mild respiratory distress with elevated temperature of 37.2°C, pulse rate of 106 per minute, respiration rate of 22/min, and BP of 110/50 mm Hg. She had no cyanosis. Chest auscultation revealed bilateral basilar crackles. Results of the remainder of the physical examination were unremarkable.

Significant laboratory data at the time of hospital admission showed a hemoglobin of 14.8 g/dl, hematocrit of 44.9 percent, and a WBC count of 16,600/mm³ with a normal differential cell count. Arterial blood gas showed a pH of 7.47, Pco₂ of 26.8 mm Hg, Po₂ of 44.9 mm Hg, with oxygen saturation of 85 percent on 2.5 L/min by nasal cannula. A 12-factor automated blood chemistry analysis showed an elevated lactate dehydrogenase level of 733 IU/L (normal, 250 IU/L). Blood, sputum, and urine cultures showed no pathogens. Initial chest radiograph revealed bilateral diffuse bronchopneumonic infiltrates (Fig 1).

She was treated with multiple antibiotics. Her respiratory status deteriorated and on the third hospital day, she developed respiratory failure requiring intubation with mechanical ventilatory support. Antinuclear antibody, rheumatoid factor, C3 and C4 complement, total complement (CH50), and quantitative immunoglobulins were unremarkable. Various serologic tests, including titers for influenza A and B, adenovirus, Mycoplasma pneumoniae, and Legionella showed no evidence of recent infection.

Her respiratory status improved but she still had shortness of breath with hypoxemia and showed no resolution of the bilateral pulmonary infiltrates on subsequent chest radiographs. Her follow-up blood cell count showed an increasing eosinophil count of 8,554/µm³ with a WBC count of 17,000/mm³. The eosinophilia persisted even after all antibiotic therapy was discontinued.

Pulmonary function tests showed a FVC of 1.90 L (59 percent predicted), FEV₁ of 1.89 L (69 percent predicted), FEF25-75 percent of 2.77 L/s (94 percent predicted), vital capacity of 1.9 L (59 percent predicted), and diffusing capacity for carbon monoxide (Dco) of 4.2 ml/min/mm Hg (18 percent predicted) indicating a moderate restrictive lung disease with a decreased diffusing capacity.

The patient underwent a thoracotomy with open lung biopsy. Microscopically, the bronchioles, alveolar ducts, and adjacent alveoli contained organized granulation tissue. Scattered lymphocytes, plasma cells, and eosinophils were present in the interstitium. No vasculitis or granulomatous process was seen. The lesions were patchy in distribution. The histopathologic features were consistent with BOOP (Fig 2). She was treated with intravenous steroids methylprednisolone sodium succinate [Solu-Medrol], 60 mg every 6 h with prompt resolution of her symptoms, and a repeated chest radiograph showed significant clearing of the infiltrates.

**DISCUSSION**

L-tryptophan use has been attributed to several clinical
entities, in particular the eosinophilia-myalgia and fasciitis syndromes. Other reported manifestations include dermatologic manifestations, fever, peripheral neuropathy, encephalopathy, and abdominal visceral diseases. Tazelaar and colleagues described five patients with respiratory illness who had a history of ingestion of L-tryptophan; four had radiologic evidence of bilateral interstitial lung disease. Biopsy specimens of lung tissue in those patients demonstrated chronic interstitial pneumonia, eosinophilia, and evidence of vasculitis.

Our patient presented with clinical, radiologic, and histopathologic features of BOOP, a distinct subset of diffuse infiltrative lung diseases. Patients with BOOP usually present with nonspecific respiratory symptoms and signs and occasionally with no abnormal auscultatory finding. Chest radiographs usually reveal bilateral patchy infiltrates, although segmental consolidations have also been reported. Diminished diffusion and vital capacity are the commonly abnormal pulmonary function tests. Histopathologic examination usually reveals plugging of the bronchioles and alveolar ducts with young granulation tissue in a patchy distribution. The alveoli show acute inflammatory and fibrinous exudates that may undergo organization with interstitial infiltrates of lymphocytes, plasma cells, and eosinophils. Pulmonary parenchyma is relatively preserved. A favorable prognosis with rapid response to corticosteroid therapy has also been described as a distinct feature of BOOP.

This entity has been reported in association with respiratory illness with influenza A and B, parainfluenza virus, respiratory syncytial virus, and Mycoplasma infection. It has also been reported following inhalation of noxious fumes, postheart-lung transplants, and connective tissue diseases. To our knowledge, BOOP has not been previously reported following the use of L-tryptophan. In our patient, investigations failed to reveal the usual infectious or noxious agents (described in the literature) or any connective tissue disorders.

Several hypotheses to explain tissue injury with L-tryptophan have been proposed. A contaminant in the L-tryptophan preparation has been thought to be the offending agent causing tissue changes. Eosinophil has been implicated in the pathogenesis of tissue injury in eosinophilic-myalgia syndrome. Several in vitro studies suggest that tryptophan and its metabolites are probably responsible for the pathologic changes in scleroderma-like illness associated with tryptophan ingestion. L-tryptophan may lead to increased production of serotonin and onithronic acid leading to an autoimmune response in sensitive subjects, especially in women with HLA-DR3 tissue typing or a history of autoimmune disease. The mechanism of lung injury with the use of L-tryptophan, however, is still unknown and remains to be studied.

In summary, we suggest that BOOP may be added to the expanding spectrum of L-tryptophan-related pulmonary illnesses. In patients with an acute respiratory illness compatible with "idiopathic" interstitial lung disease, a careful history of L-tryptophan use should be obtained. This specific entity of pulmonary disorder associated with L-tryptophan usage may respond favorably to corticosteroid therapy.

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