Gallium Uptake in Tryptophan-Related Pulmonary Disease

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We describe a patient who developed fever, fatigue, muscle weakness, dyspnea, skin rash, and eosinophilia after taking "high doses" of tryptophan for insomnia for two years. A gallium-67 scan revealed diffuse increased uptake in the lung and no abnormal uptake in the muscular distribution. Bronchoscopy and biopsy confirmed inflammatory reactions with infiltration by eosinophils, mast cells, and lymphocytes. CT scan showed an interstitial alveolar pattern without fibrosis. EMG demonstrated diffuse myopathy. Muscle biopsy from the right thigh showed an inflammatory myositis with eosinophilic and lymphocytic infiltrations.

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Tryptophan-induced eosinophilia myalgia syndrome (EMS) is a newly recognized disease entity (*1,2*). L-tryptophan (LT) is an essential amino acid and recently LT ingested as a dietary supplement or used as medication for disorders such as insomnia, premenstrual syndrome, and obsessive-compulsive disorder has been known to cause EMS (*1,2*). LT-induced EMS is commonly associated with myalgia, arthralgia, fever, shortness of breath, skin rash and edema in the extremities in conjunction with eosinophilia (*1,2*).

We describe a gallium-67 (^{67}Ga) scan appearance of the lung on a patient who developed EMS after taking LT for insomnia for 2 yr.

CASE REPORT

A 57-yr-old white female was admitted to our institution for progressive myalgia. For the past 2 yr, she had been on a high dose of LT for insomnia. A year later, she experienced fatigue and was unable to rise from a sitting position or to climb stairs. When she was seen by her family doctor, she had severe lower extremity weakness, muscle tenderness, swelling, dyspnea, and rash over the thorax. Her blood counts showed elevated eosinophils. Muscle biopsy showed findings consistent with myositis. She was treated with prednisone. She showed some improvement initially but developed further muscle weakness and weight loss. She was transferred to this institution for further evaluation. The physical examination was unremarkable except for mild muscle tenderness and evidence of proximal muscle weakness. Laboratory findings showed hepatitis A, hepatitis B surface antigen positive, and negative mononuclear test. She had leukocytosis with 2% eosinophils, 7% lymphocytes, 79% segmented, and 7% monocytes. Antinuclear antibodies were negative. Creatine phosphokinase and erythrocyte sediment rates were normal. Aldolase was mildly elevated. Although she had a positive antigen test (ELISA) for trichinella, muscle biopsy showed no evidence of parasites and only inflammatory reaction of muscle with eosinophilic and lymphocytic infiltrations. Electromyogram (EMG) was consistent with diffuse myopathic disease.

During the hospital course, she developed marked shortness of breath and fever. Pulmonary function test showed a restrictive pulmonary disease. A whole-body gallium scan was performed and demonstrated diffuse increased bilateral pulmonary uptake consistent with inflammatory process (Fig. 1). Computed tomography (CT) of the chest showed interstitial alveolar pattern without fibrosis. Transbronchial biopsy was performed and revealed inflammatory changes with increased eosinophils, mast cells, and lymphocytes. There was no bacteria. Following the diagnosis of LT-induced EMS the patient was treated with a high dose of steroids (prednisone 80 mg/day). The patient was discharged and followed as an outpatient.

DISCUSSION

In recent years, patients with eosinophilia associated with severe myalgia, pulmonary symptoms, and neuromuscular symptoms have been increasingly recognized (*1–3*). This symptom complex is known as EMS, which is associated with L-tryptophan ingestion (*1,2*). EMS is often associated with various conditions such as peripheral neuropathy, thromboembolic changes, scleroderma-like skin changes, joint contracture, and pulmonary symptoms. Frank vasculitis and Guillain-Barre-like syndrome have been reported as well (*1,2*).

The exact mechanism of underlying pathologic changes in EMS is not known. It has been suggested that tryptophan-associated syndrome could be caused by infectious agents in the contaminated tryptophan

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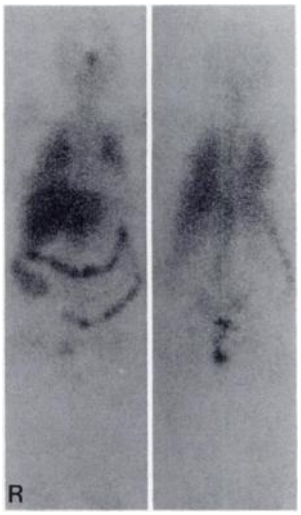

FIGURE 1
Whole-body ^{67}Ga (5 mci ^{67}Ga-citrate) imaging was performed 72 hr postinjection. Anterior/posterior scan showed diffuse increased pulmonary uptake bilaterally. There was no abnormal uptake in the arms (not shown) or legs (R = right).

preparation, but the source could not be found (*1,2*). The findings of eosinophilia, rash, and pulmonary disease seen in these patients suggested a type I IgE-mediated hypersensitivity reaction, but IgE levels were sometimes normal (*4*). Abnormality in the tryptophan metabolism also was suggested (*4*). The Centers for Disease Control (CDC) suggested the diagnosis of EMS under the following conditions:

1. Eosinophil counts of >1000 cells per mm^3.
2. Generalized myalgia.
3. Absence of any infection or neoplasm that could account for items 1 and 2 (*2*).

In 1971, Lavender et al. reported that ^{67}Ga accumulates in areas of inflammation (*3*). Since that time, ^{67}Ga has been widely used in the detection of inflammatory lesions. The mechanism of ^{67}Ga uptake in the inflammatory lesion is different than in tumors (*5*).

Gallium-67 scintigraphy is more sensitive in the detection of early inflammatory or infectious disease than the chest-radiograph (*6,7*) Diffuse pulmonary uptake has been reported in *pneumocystitis carinii* pneumonia, metastasis, pneumoconiosis, radiation therapy, uremia, following contrast lymphangiography, intravenous talc, miliary tuberculosis, sarcoidosis, and drug-induced pulmonary toxicity such as bleomycin and nitrofarantoin (*6–10*).

Inflammatory changes with eosinophils and lymphocytes were reported in LT-induced EMS as vasculitis, myositis, pneumonitis, fasciatis (*11–14*). Our case illustrates that identification of such disease processes and monitoring of treatment response in EMS can be obtained with ^{67}Ga scintigraphy. It is interesting to note that absence of ^{67}Ga uptake in muscular distribution in this case may be related to prior steroid treatment. We have seen another patient with LT-related pulmonary disease fail to take up ^{67}Ga while the patient was on high-dose steroid therapy.

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