Eosinophilia–Myalgia Syndrome not Associated with the Ingestion of Nutritional Supplements

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Eosinophilia–myalgia syndrome (EMS) is a systemic illness that occurred as an epidemic by ingestion of over-the-counter L-tryptophan preparation in the United States in October 1989.

We report a Korean case of EMS not associated with the ingestion of either L-tryptophan or other nutritional supplements such as lysine and niacin.


Key Words: Eosinophilia–myalgia syndrome

CASE REPORT

A 74-year-old man was referred for evaluation of a 3-month history of recurrent episodes of severe disabling myalgia, flu-like symptoms such as recurrent episode of fever, chill, cough, weakness, and dyspnea, abdominal discomfort and weight loss of unknown cause. He had no history of the use of any other drugs and nutritional supplements such as recombinant L-tryptophan, lysine and niacin, and had no personal history of atopy and known medication allergies.

On the 5th hospital day, physical examination revealed morphea-like features involving both forearms which were indurated and had a glistering, ivory-colored surface (Fig. 1). Laboratory evaluation revealed a peripheral eosinophilia (902/mm3), and the erythrocyte sedimentation rate was moderately elevated (50 mm/hr). Eosinophilic cationic protein (ECP) level was markedly elevated (≥ 200 μg/l). Creatine phosphokinase level was within normal limit. Anti nuclear antibodies, anti d-s DNA antibodies and ELISA for parasite infections were negative.

Chest X-ray showed linear and reticular density of both lower lung fields and high resolution computed tomography and abdominal ultrasound as well as gastrofiberscopy and colonoscopy were not contributory. Electromyogram (EMG) was not contributory, but Nerve conduction velocity study showed diffuse sensorimotor polyneuropathy.

Biopsy specimen taken from the skin of the forearm on the 5th hospital day showed perivascular and dermal inflammatory cells’ infiltrates consisting of lymphocytes and eosinophils (Fig. 2A), and from the muscle on the 20th hospital day showed perimysial and perivascular inflammation with mononuclear cells and eosinophils (Fig. 2B). During the 20-day hospitalization, eosinophil counts continued to increase (Fig. 3).

A diagnosis of eosinophilia–myalgia syndrome was made. We treated him with prednisone 20 mg daily. Within 48 hours, the patient experienced a dramatic resolution of symptoms, and eosinophil counts dramatically declined (Fig. 3).

DISCUSSION

Eosinophilia–myalgia syndrome (EMS) is a multisystem disease with a distinct acute phase, characteristic histopathologic findings, and diverse late phase.1,2 During acute phase, EMS is characterized by flu-like constitutional symptoms, intense muscle pain, and an increase in
blood eosinophil counts. Later, the syndrome is often characterized by skin rash and fascitis, which may resemble scleroderma or eosinophilic fascitis. Other chronic features include neuromuscular disease, cardiac disease, and pulmonary disease. Although more than 1,500 cases were reported in the United States between November 1989 and July 1990, the incidence of EMS in the general population is low. The diagnostic criteria for EMS was initially proposed by the Centers for Disease Control and Prevention in November 1989. Hertzman\(^5\) proposed new sets of criteria for the definition of the eosinophilia-myalgia syndrome. In determining which combination of clinical and laboratory manifestations should be included in criteria for EMS, he proposed that the following elements should be considered: (1) The presence of an acute episode with characteristic symptoms, signs, and laboratory abnormalities. (2) The presence of characteristic histopathologic abnormalities. (3) The presence of objective evidence for involvement of the most commonly affected major organs: the skin, muscle, nerve, and lung. (4) The absence of preexisting or comorbid conditions that could explain the components of illnesses on which the diagnosis is based. For classifying adult patients in clinical trials and epidemiologic studies, a person shall be said to have EMS if any of the following 3 patterns are shown. In pattern 1, there is evidence of a distinct acute episode with additional major objective clinical and histopathologic findings consistent with EMS. Pattern 2 shows evidence of a distinct acute episode highly indicative of EMS without additional major objective clinical and histopathologic findings. Pattern 3 shows evidence of major objective clinical and histopathologic findings consistent with EMS.

Fig. 1. Shiny, erythematous indurated patches on both forearms.

Fig. 2. A, Hematoxylin and eosin-stained section demonstrating perivascular and dermal inflammatory cells infiltrates including lymphocytes and eosinophils. B, Hematoxylin and eosin-stained section demonstrating perimysial and perivascular inflammation with mononuclear cells with eosinophils.

Fig. 3. Clinical and hematologic features during hospitalization.
without evidence of a distinct acute flu-like episode. Our case showed evidence of a distinct acute episode with additional major objective clinical and histopathologic findings consistent with EMS, which may be belong to Hertzman pattern 1. The use of L-tryptophan has not been included in these criteria because the precise cause of EMS has not yet been determined. The attack rate of EMS even among L-tryptophan users is low, and sporadic cases of an EMS-like syndrome not related to known L-tryptophan exposure continue to occur. In reporting the Centers for Disease Control surveillance data regarding EMS, 3% of these patients with EMS had no known exposure to L-tryptophan, and many had the onset of symptoms before the 1989 epidemic. Duffy et al. noted that 6 of 104 EMS patients had not consumed L-tryptophan: 2 had taken niacin and the others had consumed multiple nutritional supplements, or none at all. Patmas et al. reported a case of EMS associated with the ingestion of lysine, and allude to other such cases of hydroxytryptophan, which have been associated with an EMS-like disease. Our case also suggests that substances other than L-tryptophan and other nutritional supplements are capable of producing an illness with clinical, laboratory, and histopathologic features consistent with EMS. Non-L-tryptophan EMS cases were more likely to be younger and to have a pre-epidemic illness onset of EMS, but otherwise were similar to L-tryptophan associated EMS cases. Although cellular mechanisms leading to a microangiopathy and release of cytokines seem to play an important role during the acute phase of the illness, better characterization of pathophysiological events leading to the chronic phase is needed.

We report a case of EMS not associated with the ingestion of either L-tryptophan or other nutritional supplements, previously undescribed in Korea.

REFERENCES