L-tryptophan and scleroderma: Significance of nutritional supplements containing L-tryptophan

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Pregnancy supplements containing amino-acid components like L-tryptophan have been banned in some countries, but continue to be available in India. We report a case of scleroderma-like syndrome possibly linked to L-tryptophan containing pregnancy supplements.

A 28-year-old female patient, housewife, presented to our outpatient department with a history of gradually increasing thickening and tightness of skin mainly over the extremities and face of three months duration. The patient had her first delivery five months earlier. There was no history of any significant co-morbidities or associated symptoms. Patient did not give a history of dysphagia, exertional dyspnea or Raynaud's phenomena. The patient gave a history of taking a particular nutritional supplement for about a month following her delivery. This particular supplement had amongst its constituent's L-tryptophan and l-phenylalanine (she was getting approximately 15 mg per day of each L-tryptophan and l-phenylalanine).

A clinical examination showed diffuse sclerosis in an acral distribution [Figures 1 and 2]. There was no evidence of digital pitted scars or significant lung findings. Clinically a possibility of scleroderma was considered and the patient was investigated for the same. Blood investigations showed an elevated erythrocyte sedimentation rate (ESR) and a weakly positive anti-nuclear antibody screen. A subsequent antinuclear antibody profile was negative including anti-SCL-70 and anti-centromere antibodies. Chest radiology and high-resolution computerized tomography did not show any suggestion of interstitial lung pathology. Esophageal manometry and barium studies were also normal. A skin biopsy and immuno-fluorescence study was done. The skin biopsy showed a normal epidermis with prominent collagenization of the dermis and a minimal lymphocytic infiltrate which was consistent with scleroderma. The immunofluorescence studies were negative.

Based on the clinical and investigation findings we considered a possibility of a scleroderma-like illness possibly induced by l-tryptophan. Based on the Naranjo monogram for adverse drug reactions we obtained a score of 4 (possible adverse drug reaction) as far as the causal role was concerned.

There have been many reports of scleroderma-like syndromes following the prolonged intake of L-tryptophan in various
forms. Tryptophan-containing medications and dietary supplements had been banned by the US FDA (Food and Drug Administration) in 1989, following reports of a large number of cases of eosinophilia-myalgia syndrome (EMS). However, nutritional supplements containing L-tryptophan are still available in India. In our case, the patient had a history of taking such a preparation for a period of more than one month as a nutritional supplement (a daily dose of around 15 mg L-tryptophan). Considering the relatively rapid development of her symptoms in relation to the period of tryptophan intake, predominant acral involvement and absence of evident systemic involvement, we thought of associating the development of scleroderma-like features to the consumption of L-tryptophan. However, our case does not fit in with accepted criteria for EMS. Centers for Disease Control (CDC) defined EMS, in 1989, as an illness characterized by 1) eosinophil count of greater than or equal to 1000 cells per mm³, 2) generalized myalgia (at some point during the course of illness) of severity sufficient to affect a patient’s ability to pursue his or her usual daily activities, and 3) absence of any infection or neoplasm that could account for 1 or 2 above. Hertzman et al.,[1] used modified criteria in studies of EMS wherein the following four specifications were mentioned: eosinophil count of 1000 cells/mm³ or greater; presence of fasciitis, peripheral neuropathy, polyradiculopathy, interstitial pulmonary disease, pulmonary hypertension, or myocardial involvement; history of L-tryptophan consumption; and absence of other conditions that could account for these findings. Moreover, the presence of features like Raynaud’s phenomenon and digital scars are not common in L-tryptophan-induced scleroderma-like illness. However, it has been well documented that peripheral eosinophilia need not be a necessary feature of L-tryptophan-induced scleroderma-like illness.[2] At the same time some studies have tried to illustrate that while L-tryptophan can induce a scleroderma-like illness it does not induce classical progressive systemic sclerosis per se.[3,4] The exact mechanism of sclerosis induced by L-tryptophan is still not definite. Of the many hypotheses suggested one is that ‘peak E’ (1,1-ethylidenebis[L-tryptophan]), a dimer of L-tryptophan, is a potent stimulus for human dermal fibroblast DNA and collagen synthesis.[5]

Our hypothesis though conjectural, (especially considering that there could have been other causal factors for scleroderma in our patient) mainly aims to highlight the possibility that a drug known to cause a particular illness is available as part of an over-the-counter nutritional supplement. Considering the fact that L-tryptophan-containing dietary supplements are freely available in India, larger studies are probably warranted to assess any causal relationship between the intake of these supplements and scleroderma-like disease.

References

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