

A Case of Eosinophilia Myalgia Syndrome: Imaging Features of a Unique and Rare Entity

Dear Editor,

We would like to describe a case of EMS presenting with a clinical picture of skin rashes, pneumonitis, myalgias, and cognitive impairment with plaque-like T2 frontal white matter hyperintensities on magnetic resonance imaging of brain to better acquaint clinicians and radiologists with this rare entity.

The eosinophilia-myalgia syndrome (EMS) is a multisystem disorder falling on the spectrum of eosinophil-mediated ailments. First identified in 1989, approximately 1500 cases have been reported so far worldwide and almost twice that number failed to meet the CDC diagnostic criteria.^[1] Previously associated with ingestion of therapeutic L-tryptophan, EMS has now been identified in the absence of such history. An increase in eosinophil count, which forms the key component of the host immune system can result in cytotoxic tissue

damage associated with release of granulocytes which can present as a variety of clinical manifestations ranging from skin abnormalities (Rashes, fasciitis, sclerosis, thickening of deep fascia), pulmonary disorders (Pneumonitis, vasculitis), hepatic dysfunction to systemic manifestations like fatigue, arthralgias, edema and sensory/motor abnormalities and cognitive impairment.

A 65-year-old woman presented to us with complaints of fatigue with skin rashes, undocumented intermittent fever, forgetfulness, and gradually progressive shortness of breath since 3 months. A complete hemogram, liver, and kidney function tests, and CECT (Contrast Enhanced computed tomography) chest were performed. Hemogram revealed normocytic normochromic anemia with total leukocyte count (~8400) with differential leukocyte count showing elevated lymphocytes and severe eosinophilia ~47% with

an absolute eosinophil count ~ 3950 cells/mm³. Liver and kidney function tests were within normal range. CECT chest showed presence of B/L pleural effusion with fluid tracking along the fissures with minimal pericardial effusion as shown in [Figure 1a]. Analysis of the pleural fluid revealed benign eosinophilic effusion with DLC: N (20%), M (6%), E (68%), L (6%). Pleural fluid ADA was within normal range. Pleural fluid cytology showed absence of atypical/malignant cells. Echocardiography revealed normal ejection fraction (60%) and no vegetations/clots. Electrocardiography showed normal sinus rhythm. Dermatological consultation showed chronic urticaria. Inflammatory markers including ESR (110 mm/h) and s. ferritin (425) were raised. Serological tests for trichinosis, scrub typhus, brucellosis and leptospirosis came back negative. The patient also complained of generalized body weakness with myalgias. Nerve conduction study revealed mixed neuropathy (axonal > demyelination) B/L median, ulnar, common peroneal, tibial nerves. Bone marrow imprint smear revealed severe eosinophilia with DLC showing 70% eosinophils, however, no immature/dysplastic forms of eosinophils were seen in the smear. Other tests including Anti-nuclear, anti-double-stranded DNA, anti-neutrophil/cytoplasmic, and anti-CCP antibodies were negative or normal. The patient was a known hypertensive for which she was on

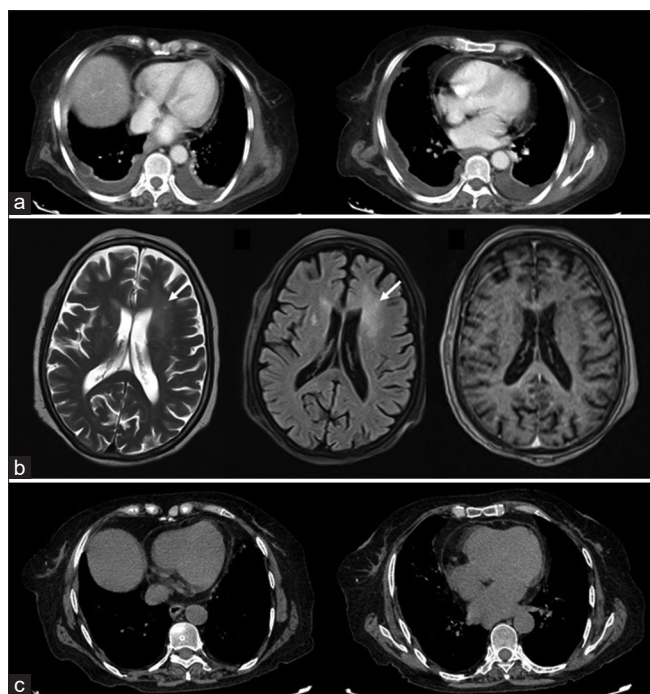


Figure 1: (a) Contrast enhanced computed tomography images of the chest shows presence of B/L pleural effusion with fluid tracking along the fissures, with pericardial thickening and minimal pericardial effusion. (b) T2 Weighted image, fluid attenuation inversion recovery (FLAIR) and T1 weighted image of brain acquired on 1.5 T magnetic resonance imaging shows presence of T2/FLAIR hyperintensities (arrows) involving the periventricular/deep white matter of the B/L frontal lobes (left (arrow) > right). (c) Follow-up noncontrast CT chest obtained 1 month later showing resolution of B/L pleural Effusion and pericardial effusion

medication. Other than that, the patient denied a history of any drug intake, ayurvedic or alternative medication. Our patient denied a history of consumption of L-tryptophan-containing dietary supplements. Neurological and psychiatric consultation revealed impaired working and semantic memory and impaired sustained attention for which MRI brain was performed which revealed the presence of plaque-like T2 FLAIR hyperintensities in B/L frontal (Left > Right) periventricular/deep white matter as shown in [Figure 1b].

The diagnostic criteria for Eosinophilia myalgia syndrome (EMS) described by Philip A. Hertzman *et al.*^[2] includes fulfillment of either pattern 1 or pattern 2 and absence of exclusions as follows:

Pattern 1: Presence of documented illness of relatively discrete or abrupt onset of all three manifestations including eosinophilia, myalgia, and at least one rash, edema, pulmonary involvement or neuropathy within 6 months in absence of exclusions.

Pattern 2: Presence of illness with/without documented early episode accompanied by one of the following within 24 months of illness onset: 1. Fasciitis, neuropathy, myalgia or muscle cramps; or 2. Any 3 or more of fasciitis, myopathy, neuropathy or eosinophilia (within 6 months of onset).

Exclusions: EMS is not to be diagnosed in presence of trichinosis, vasculitis or any other documented infectious, allergic, neoplastic, connective tissue, or other diseases that could adequately explain the clinical manifestations.

Neurological imaging in EMS shows evidence of white matter injury in the form of T2 FLAIR (Fluid attenuated inversion recovery) hyperintensities predominantly involving the frontal lobe periventricular/deep white matter showing no diffusion restriction, susceptibility changes, mass effect or post-contrast enhancement^[3] similar to our patient [Figure 1b]. Studies conducted by Armstrong *et al.*^[3] revealed white matter hyperintensities on MRI in the frontal lobe in EMS patients with no other neurological diseases such as hypertension or diabetes which could account for these lesions like in our case.

Based on the above findings provisional diagnosis of EMS was kept and the patient was started on oral corticosteroids at 1 mg/kg body weight. After 4 weeks response assessment showed a dramatic response in the form of fall in peripheral eosinophilia (3.7% DLC), fall in ESR (32 mm/h), and complete resolution of pleural and pericardial effusion on follow up chest CT as shown in [Figure 1c]. The patient showed improvement in cognition with improved working memory.

Other than eosinophil-derived toxicity, autoimmune responses including cellular and humoral immunity have been shown to play a role in the pathogenesis of this rare multisystem disease. Although our patient tested negative for the presence of anti-nuclear antibodies (ANA) which are found in up to 50% of patients of EMS,^[4-6] elevated lymphocytes as a result of cellular immune response was seen in our patient.

The presence of peripheral eosinophilia with neurological symptoms should raise the suspicion of Eosinophilic meningitis, eosinophilia-myalgia syndrome, and hypereosinophilic syndrome in that order. Eosinophilic meningitis may be idiopathic or may occur as a reaction to helminthic infestation elsewhere in the body. Eosinophilia myalgia syndrome will present as extensive body ache and multiorgan system involvement. Hypereosinophilic syndrome rarely results in CNS involvement. Imaging may help differentiate these entities and arrive at the correct diagnosis. Eosinophilic meningitis will show leptomeningeal enhancement with edema in the underlying brain parenchyma. EMS shows confluent frontal white matter hyperintensities as seen in our case. Hypereosinophilic syndrome shows enhancing open ring active demyelination with white matter hyperintensities.

Emotional distress including depression was found to be significantly higher in patients with EMS. Our patient showed improvement in working memory and attention span with treatment.

Studies have shown that 100% of the patients of EMS showed fatigue and myalgias as a symptom.^[6] Our patient complained of generalized body weakness that was severe enough to impair her day-to-day functions with myalgias. Myalgias showed a significant response to treatment enabling the patient to carry out daily activities. Perimyositis appears to be the histopathological process behind myalgias in EMS with infiltrating inflammatory cells seen at perivascular, perimysial, and fascial locations.^[7,8]

Even though the clinical, pathological, and radiological findings in patients of EMS have been well demonstrated, the etiopathogenesis of this disease is yet unknown. Acquainting treating clinicians and radiologists with this disease can help in preventing delayed diagnosis, improve our understanding of the disease, and possibly aid in understanding the cure.

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Conflicts of interest

There are no conflicts of interest.

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