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Idiopathic Hypereosinophilic Syndrome with Stroke in Young: A Case Report

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Abstract

Idiopathic hypereosinophilic syndrome (IHES) is a rare disorder with prolonged eosinophilia of unknown cause with an organic dysfunction. It is associated with eosinophil induced neurological deficit, pulmonary fibrosis and gastrointestinal abnormality. A case of 30-year-old man with IHES who developed cerebral infarction with organic dysfunction is reported. Treatment with prednisolone resulted in reduction of peripheral eosinophil count and marked improvement in his CNS dysfunction. The pathophysiology of the disorder is also discussed.

Introduction

Eosinophilia is associated with various organ dysfunctions due to many underlying causes. The common causes for eosinophilia are parasitic infestations, allergic diseases, neoplasias and vasculitis syndromes[1]. Patients in whom no known underlying cause of eosinophilia can be proved and who continue to be have absolute eosinophil count of more than 1500/cumm for more than six months with a organic dysfunction can be labeled as idiopathic hypereosinophilic syndrome (IHES). Patients who suffer from IHES develop many neurological abnormalities, the common are recurrent stroke, encephalopathy, peripheral neuropathy and seizures. Due to the rarity of the cases we would like to report a case of IHES who developed stroke with seizures and the effective treatment given after long follow up.

History

A 30-year-old male was referred to PMR OPD from neurology with history of sudden onset of weakness in the right half of the body with inability to speak for three months. There was no history of trauma at the time of onset, no history of seizures, and no history suggestive of raised intracranial tension. There was no history of difficulty in breathing, cough, skin rash, nasal allergy or any other history suggestive of worm infestation. He was admitted to the local hospital in the acute phase and CT scan of brain was done, which revealed infarction in the left middle cerebral artery territory. He was discharged along with advice to take aspirin and enalapril. He started with gradual recovery of function in right upper limb initially, later in right lower limb. There was a marked recovery in his motor functions after 3 months, he was able to stand and walk independently but was unable to speak. He was brought to OPD of Neurology in the month of June 2001 for his speech problem and weakness in right half of the body. Again the routine investigations, carotid doppler and echocardiography was done which were normal. He was diagnosed as stroke in young with unknown cause and referred to PMR OPD for further management.

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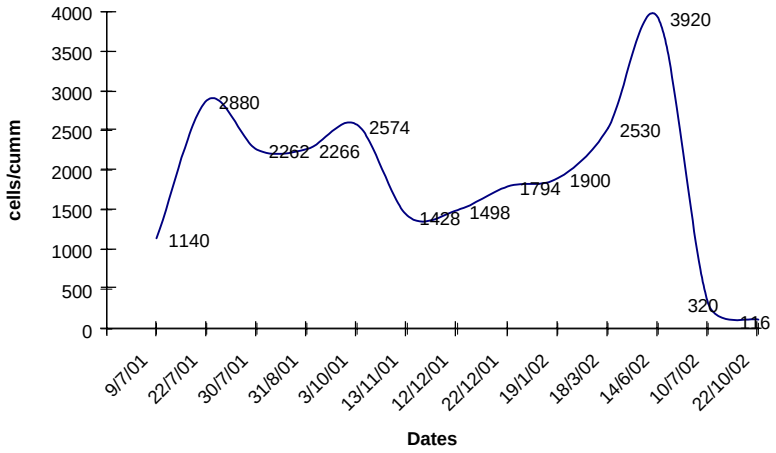
At the time of initial evaluation in PMR OPD general physical examination was normal with blood pressure 130/90. He was conscious, co-operative and well oriented. He had right seventh nerve upper motor neuron palsy with motor aphasia. Right upper limb and lower limb had spasticity of grade-II. Motor power of 3/5 was noted in right upper and lower limbs with weak right hand grip. Deep tendon reflexes were brisk with positive Babinski sign and gait was hemiplegic. Examination for the cardiovascular system, respiratory system and per abdomen was normal.

Initial investigations revealed Hb: 14gm%, TLC: 11400/cumm (N-70%, L-20%, E-10%) ESR: 27mm/1st hour, SGOT: 111 IU, SGPT: 157 IU other liver functions tests were normal. Repeated absolute eosinophil count was 2680/cumm. Patient was admitted in the PMR ward to find out the cause for raised absolute eosinophil count and stroke in young. Again the repeated AEC was 2266/cumm, and investigations for parasitic infections (mid night sample for filariasis, stool examination) came negative, chest-x ray and urine examination were normal. Investigations for connective tissue disorders (RA Factor, ANA, Anti-DS DNA) and anti phospholipid syndrome (Acl: 5 GPL units/ml, Anti thrombin-III: 80μl, (protein C: 100% and Protein S: 78%) were negative. Bone marrow biopsy revealed no results. Due to the raised AEC his antihypertensive medication (Enalapril) was changed to tab: amlodepine and other medications were continued. There was a short drop in AEC (Fig: 1) after ingestion of diethylcarbamazepine and change of enalapril.

He was discharged and followed up in OPD of PMR regularly. Patient developed seizures in the month of October 2001, Jan & Feb 2002, for which he was started with phenytoin sodium 100mg BD. The seizures got controlled but his AEC count was persistently elevated. In the mean time he was given range of motion exercises, hand strengthening exercises, gait training with ankle foot orthosis, facial muscles exercises and speech training. His speech improved to an extent and his handgrip was also showed improvement.

In the month of June 2002 again the bone marrow aspiration and biopsy was repeated. Bone marrow touch preparation revealed 27% eosinophils along with haematopoietic cells of series and normal blast cells. Biopsy showed normocellular hematopoetic elements of all three series with myeloid preponderance with eosinophilic precursors were prominent. Due to the persistent raise of AEC (more than 1500 cells/cumm) for more than ten months with involvement

Chart 1: Absulute Eosinophil Count



of the liver he was finally diagnosed as a case of Idiopathic hypereosinophilic syndrome with stroke in young. He was started with prednisolone 50mg OD and the older medications were continued along with exercises and ADL advice. Just after one month of therapy his absolute eosinophil counts reduced dramatically to 2%. Prednisolone was continued in the same dose for 3 months and later tapered. Now patient is on 10mg of prednisolone daily along with ranitidine and calcium carbonate, other medications (amlodepine and aspirin) were continued.

Discussion

This patient initially had normal hematological and liver function tests. Because of no abnormality was found in laboratory findings he was treated just like any other cases of stroke in young. He developed the laboratory abnormality and raised eosinophil count only after three months of onset of stroke. There was no evidence of any worm infestation. Once the worm infestation was ruled out we stopped the enalapril and started with amlodepine. Barnes JN[2] reported a case of chronic renal failure, which was on enalapril therapy and developed eosinophila. Inspite of this change in therapy AEC count was markedly elevated. Repeated bone marrow biopsy also ruled out the eosinophilc leukemia and confirmed the IHES. We started treatment with oral prednisolone as reported by Weaver et al[3] and observed dramatic response just after one month of therapy with an almost normal eosinophil count.

Eosinophils exert non-specific toxic effects that induce tissue damage to host tissues. The central and peripheral nervous system are frequent recipients of this misplaced toxicity; the resulting phenomenon is called eosinophil induced neurotoxicity (EIN). The mechanisms of eosinophil induced neurotoxicity are (1) direct neural tissue infiltration; (2) damage related to eosinophil function either by direct cytotoxicity or by antibody dependent cellular cytotoxicity; (3) damage related to eosinophil products secretion; (4) embolic cerebral infarction related either to thrombi or generalized hypercoagulable state and (5) nervous system damage secondary to eosinophil-mediated damage in remote organ systems[3]. Wassom et al reported that eosinophilc major basic protein causes endothelial damage and by this the tissue damage. In this case vasculitis or antiphospholipid syndrome as a cause for stroke is unlikely as all laboratory findings for these disorders was normal. It's likely that the neurological deficit in this case is due the damage caused by products derived from eosinophilia. An eosinophilic cationic protein has been reported to have a profound effect on coagulation system and this protein has also been shown to be responsible for thromboembolic phenomena[4]. There are several reports on the best therapy for IHES[5], alpha interferon, hydroxyurea and prednisolone are commonly used. But till now the most effective single treatment is with prednisolone. This case also responded well for prednisolone therapy.

In conclusion this is a unique case that had elevated eosinophil count after the development of neurological deficit. Long term follow-up and high index of suspicion is required to establish and treat a rare disorder.

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