TROPICAL PULMONARY EOSINOPHILIA- BEWARE OF RELAPSES

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PRESENTATION OF CASE

Tropical Pulmonary Eosinophilia (TPE) is a peculiar syndrome of wheezing, fever and eosinophilia seen predominantly in the Indian subcontinent and other tropical areas. Peripheral blood eosinophilia with levels over 3000/µL and elevated serum levels of IgE and filarial-specific IgE and IgG are the hallmark features. Treatment consists of diethylcarbamazine (DEC) for at least 3 weeks. Prognosis is good with opportune treatment. However, despite optimum treatment with DEC, about 20% of patients may relapse and require retreatment with DEC or alternative management. This concept needs to be taken cognisance of whilst contemplating further management and disease prognostication.

Tropical Pulmonary Eosinophilia (TPE) is an eosinophilic lung disease associated with a hypersensitivity response to microfilariae of the parasites, Wuchereria bancrofti and Brugia malayi.[1] It is fairly common in areas with filarial endemicity including regions of the Indian subcontinent, South East Asia, South America and Africa. It frequently occurs in the age group of 15-40 years with a male:female ratio of 4:1.[1] The criteria for diagnosis of TPE include residence in an area endemic for filariasis, symptoms of recent onset of paroxysmal nocturnal cough with or without sputum, absolute blood eosinophil count of 2,000/µL or above, absence of circulating microfilaria in blood and successful clinical and haematological remission with Diethylcarbamazine (DEC) therapy.[1] The standard treatment is DEC given in the dose of 3-5 mg/kg bodyweight for a duration of 3 weeks. However, failure rates of approximately 20-40% have been reported with DEC therapy.[2] Though usually considered an acute and treatable disease, a chronic state has also been described in TPE.[2] We herein report a patient who continued to have persistently elevated eosinophil counts despite of being adequately treated with DEC therapy and also had clinical flare up of the disease. He was managed with DEC therapy again with normal eosinophil counts on subsequent follow up.

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A 29-year-old nonsmoker car painter hailing from Uttar Pradesh, India, presented with 4 years history of episodic cough, recurrent rhinitis episodes with serial complete blood counts suggestive of high counts of eosinophils.

Date	TLC (Per mm^3)	DLC with Eosinophil Percentage	AEC (per mm^3)
20/05/2014	66,600	59%	39,294
12/06/2014	17,200	28%	4,816
17/11/2014	9,300	2%	211

The patient then was managed with DEC therapy 100 mg TDS for 21 days associated with relief of symptoms. Currently, patient again become symptomatic 3 years later on with increased cough with mucoid expectoration and fever with blood reports of serum total IgE >4000 IU/mL; TLC (20/6/2017) 39,300/mm^3 DLC with eosinophil % of 57% and AEC of 2240/mm^3. Patient received 10 days of DEC therapy 100 mg TDS and followed to us where he was admitted with provisional diagnosis of Pulmonary Infiltrate with Eosinophilia (PIE) syndrome with differential diagnosis of relapse TPE and ABPA. Subsequently, patient evaluated with chest radiograph, which was normal; TLC 6600/mm^3 with eosinophil % of 43% and AEC of 2838/mm^3. To confirm the final diagnosis, patient was further evaluated with serum antifilarial antibody against Wuchereria Bancrofti, which was positive and specific IgE against Aspergillus fumigatus, which was negative, thus ruling out the ABPA. High-Resolution Computed Tomography (HRCT) of the thorax was done to radiologically discern the diagnosis, which was suggestive of only mild bronchial prominence with mucoid impaction. Spirometry was normal study and fiberoptic bronchoscopy was not remarkable with transbronchial lung biopsy being noncontributory. So, with clinic-radiological-serological correlation, diagnosis of relapse TPE was made and DEC therapy 100 mg TDS was continued for a total duration of 21 days. The patient was also started on therapy with intranasal corticosteroid with antihistamine combination nasal spray 1 puff BD for rhinitis. After completion of DEC therapy, the patient showed improvement of his clinical symptoms, blood counts in the form of TLC of 7700/mm^3 and DLC with eosinophil % of 2% and AEC of 154/mm^3.

PATHOLOGICAL DISCUSSION

Tropical Pulmonary Eosinophilia (TPE) is a syndrome predominantly in the Indian subcontinent with the most common aetiological agents being the parasites Wuchereria bancrofti and Brugia malayi. The pathogenesis is explained

by various types of hypersensitivity reactions, mainly type I, type III and type IV reactions based on an exaggerated immune response to the filarial antigens. First described in 1940 and labelled as "pseudotuberculosis with eosinophilia"[3] the term Tropical Pulmonary Eosinophilia (TPE) was first coined by Weingarten in 1943.[4]

Pathologically it can present in- Acute stage- It can show alveolitis and eosinophilic exudates along with microabscesses and granulomas are visible sometimes chronic stage- replacement of eosinophilic exudates with mixed cell exudates with evident fibrosis with chronicity fibrosis becomes more and more prominent with formation of scarring.[5,6]

CLINICAL PRESENTATION

TPE occurs mostly in young males with a male-female ratio of 4:1 and in an age group between 15-40 years.[7] It may involve multiple body systems, but predominantly affects the lungs.[6] The hallmark symptoms include mainly cough, dyspnoea, wheezing and chest pain. Symptoms strikingly occur during night time owing to the nocturnal habitat of the culprit parasites. Sputum is generally less in amount and maybe viscous and mucoid in appearance. Sometimes, sputum eosinophilia is also seen. Constitutional symptoms in the form of fever, weight loss, fatigue and malaise are commonly encountered. Other systemic manifestations include lymphadenopathy and hepatosplenomegaly. The characteristic laboratory findings are eosinophilia >3000/µm with diurnal variability lowest during the night and may rise as high as 80,000/µm through the day. Nutman et al[8] showed strikingly elevated total IgE in the lower respiratory tract Epithelial Lining Fluid (ELF) along with high levels of filarial-specific IgG, IgM and IgE.

Radiology

The main radiological features include reticulonodular opacities more in the mid-to-lower zones. About 20 percent of patients with TPE may have a normal chest radiograph.[6] Computerised Tomography (CT) scan often reveals bronchiectasis, air trapping, lymphadenopathy, cavitation, consolidation or pleural effusions in addition to the miliary mottling and interstitial shadows. Radiologic findings show response to DEC therapy and very often regress on treatment with DEC therapy.

Pulmonary Function Test

Spirometry is variably restrictive or obstruction or a combination of both elements depending on the degree of airway and interstitial involvement. Occasionally, spirometry can be normal during initial phase of the diseases. Vijayan et al[9] also reported a low transfer factor for carbon monoxide (TLCO).

Management and Frequency of Relapses

Treatment is essentially pharmacotherapy with the drug DEC. Initially, Baker et al[10] had recommended a 7-10 days course of DEC at a dose of 5 mg/kg/day. However, Udwadia[6] found that the response to treatment was better when the drug was used for four weeks. About 4-5% of the patients may not respond to DEC and may require alternative therapies like steroids[11] and ivermectin.[12] In chronic patients with a long duration of symptoms, the drug may be ineffective even in up to 20-40% cases probably due to already established fibrosis.[6] The relapse rate was found to be almost 20% after DEC therapy.[6] As a result, monthly courses at 2-3 month intervals for 1-2 years have been suggested. In a few patients, DEC was not found to be as effective in successive relapses as it was in the original episode leading to chronic respiratory impairment and also the degree of peripheral eosinophilia decreased with successive relapses.[6]

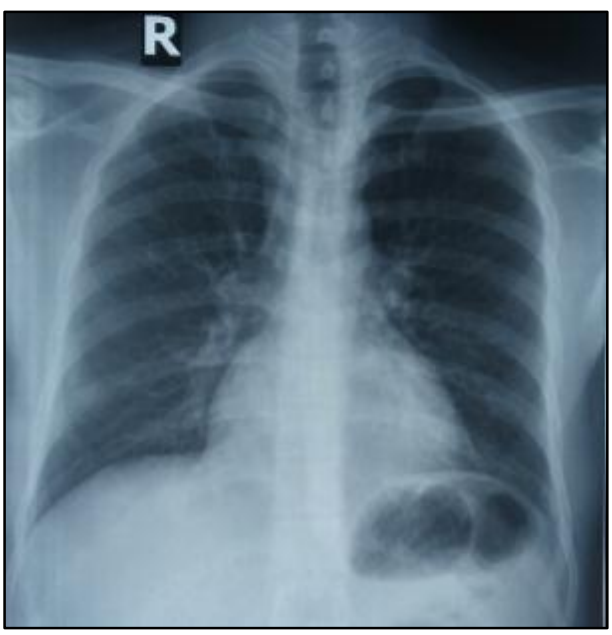

Figure 1. Chest X-Ray - Normal

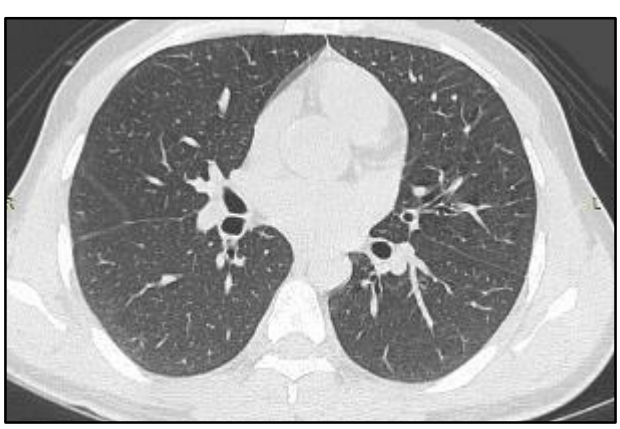

Figure 2. HRCT Thorax Suggestive of Mild Bronchial Prominence with Mucoid Impaction

FINAL DIAGNOSIS AND TAKE HOME MESSAGE

Our patient developed a relapse of the disease in spite of a satisfactory course of DEC. He was reinstituted on DEC therapy after a prompt diagnosis. Thus, it should be borne in mind that TPE is an entity, which can relapse and remit. It should not be considered merely as a benign and curable acute condition, but a condition with a potential to progress to a chronic lung disease. The failure to identify such

relapses can lead to misdiagnosis and haphazard management. Hence, our case though seemingly common intends to diligently serve the imperative purpose of reminding the clinicians of the heterogenous and unpredictable course of this disease.

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