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Tropical Pulmonary Eosinophilia

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INTRODUCTION

Tropical pulmonary eosinophilia is a distinct syndrome of wheezing, fever, nocturnal cough, and eosinophilia seen predominantly in the Indian subcontinent and other tropical areas like Brazil, Guyana. It results from an immunological hyper responsiveness to filarial parasites in some infected individuals. Its etiological link with Wuchereria bancrofti and Brugia malayi has been well established. It affects males and females in a ratio of 4:1 and often during the third decade of life.

EPIDEMIOLOGY

TPE is endemic in the tropical and subtropical regions of the Indian subcontinent, South East Asia, South America, South Pacific islands and Africa. In India, it is mostly found around the coastal regions from Maharashtra to Kerala and West Bengal to Tamil Nadu. The prevalence of TPE in various settings in India has varied from 0.5 per cent among children in Tamil Nadu to 9.9 per cent among jail inmates in Patna. TPE is seen in only less than 1% of 120 million persons infected with filarial infections worldwide. Due to a tremendous increase in the number of individuals travelling from filarial endemic areas to other parts of the world, TPE has been increasingly reported from countries that are not endemic to filarial infection.

PATHOLOGY

Open lung biopsy studies have demonstrated that three types of histopathological reactions can be seen in TPE:

i. interstitial, peribronchial and perivascular exudates consisting of histiocytes,

ii. acute eosinophilic infiltrations of interstitial, peribronchial and perivascular tissues and

iii. a mixed cell type of infiltration consisting of histiocytes, eosinophils and lymphocytes with well-marked interstitial fibrosis. A predominant histiocytic response develops 2 years after the onset of the disease, and ultimately progresses to fibrosis with marked scarring. In some cases, if untreated, a picture resembling fibrosing alveolitis with honeycombing develops in the end stage. Lung biopsies after 1 month of treatment with DEC demonstrate incomplete histological regression, although symptoms subside within 7 days of therapy, and peripheral eosinophilia returns to normal.

PATHOGENESIS

Adult filarial worms, living in the lymphatics, release the microfilariae which are trapped in the pulmonary circulation; the degenerating microfilariae in the pulmonary circulation then release their antigenic constituents, triggering a local inflammatory process. Though the lung bears the major brunt of the disease as a result of the trapped microfilariae in the pulmonary circulation, the antigenic material released from the microfilariae can reach the systemic circulation and cause extra pulmonary manifestations. BAL studies have demonstrated an intense eosinophilic inflammatory process in the lower respiratory tract. Eosinophil degranulation products, eosinophil derived neurotoxin (EDN), eosinophilic cationic protein (ECP) and major basic proteins (MBP) have been found to be critical to some of the pathology seen in TPE.

The Bm23-25, an IgE inducing antigen of the infective L3 stage larvae of B. malayi has been detected in patients with TPE. There is molecular mimicry between this antigen and the human gamma-glutaryl transpeptidase present on the surface of the pulmonary epithelium. In BAL studies IgE against Bm23-25 has been detected. This may hence play an important role in the pathogenesis of TPE.

CLINICAL FEATURES

The disease occurs predominantly in males, with a male to- female ratio of 4: 1, and is mainly seen in older children and young adults from 15–40 years of age. The systemic symptoms include fever, weight loss and fatigue. Respiratory symptoms are paroxysmal cough, breathlessness, wheezing and chest pain. Symptoms occur predominantly at night probably related to the nocturnal periodicity of microfilariae. Sputum is usually scanty, viscous and mucoid, often shows clumps of eosinophils, and Charcot-Leyden crystals are rarely observed. Severe cough can lead to fracture of the ribs. Bilateral scattered rhonchi and rales may be heard on auscultation. The hallmark of TPE is leucocytosis with an absolute increase in eosinophils (> 3000 eosinophils/μL) in the peripheral blood. Extra pulmonary manifestations include lymphadenopathy, hepatosplenomegaly, pericarditis, pericardial effusion and cor-pulmonale. Gastrointestinal, musculoskeletal and central nervous system manifestations are also reported in TPE.

CHEST IMAGING CHANGES

The chest radiological features of TPE include

reticulonodular shadows, predominantly seen in mid and lower zones, and miliary mottling of 1–3mm diameter – often indistinguishable from miliary tuberculosis. Normal chest radiographs are observed in 20% of patients. In patients with a long-standing history, a few have honeycomb lungs. Computerized 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 very often regress on treatment with DEC but many patients may show residual changes.

PULMONARY FUNCTION CHANGES

Lung function tests primarily reveal a restrictive ventilation defect with superimposed airways obstruction. The main pulmonary function abnormality in untreated TPE is a reduction in single breath transfer factor for carbon monoxide (TLCO), which has been found to be reduced in 88% of untreated patients.

DIFFERENTIAL DIAGNOSIS

Infestations with helminths are the commonest causes of pulmonary eosinophilia in tropical countries. Non-infectious causes of pulmonary eosinophilia include bronchial asthma, acute eosinophilic pneumonia, chronic eosinophilic pneumonia, idiopathic hyper eosinophilic syndrome, cryptogenic pulmonary fibrosis, Wegener's granulomatosis, lymphomatoid granulomatosis and eosinophilic granuloma of the lung, Churg-Strauss syndrome, and drug hypersensitivity reactions.

Differentiating TPE from eosinophilic pneumonia due to Strongyloides stercoralis is especially important, as corticosteroids which are useful in the treatment of TPE can cause life threatening disseminated strongyloidiasis, particularly in immunocompromised individuals.

Until a diagnostic test is available to differentiate filarial TPE from other TPE-like syndromes, the following diagnostic criteria can be used for the diagnosis of TPE:

1. Appropriate exposure history (e.g. mosquito bite) in an endemic area of filariasis.
2. History of paroxysmal nocturnal cough and breathlessness.
3. Chest radiographic evidence of pulmonary infiltrations.
4. Leucocytosis in blood.
5. Peripheral blood eosinophils more than 3000 cells/mm3.
6. Elevated serum IgE levels.
7. Elevated serum antifilarial antibodies (IgG and/or IgE).
8. Clinical response to DEC.

MANAGEMENT

The standard treatment recommended by the WHO for treatment of TPE is oral Diethylcarbamazine (6 mg/kg per day) in three divided doses for 3 weeks. Most patients show marked symptomatic and radiographic improvement one month after the start of treatment, and significant improvement in almost all aspects of lung function. A mild alveolitis persists despite treatment. Treatment with prednisolone significantly reduces lower respiratory tract inflammation and release of oxidants. Relapses occur in 20% of patients followed-up for 5 years. The persistent mild interstitial lung disease and the high relapse rates in TPE have suggested that repeated monthly courses of DEC at 2–3 monthly intervals for a period of 1–2 years may be useful. TPE can be controlled if the mosquito-borne lymphatic filariasis is eliminated. The World Health Assembly has resolved to eliminate lymphatic filariasis as a public health problem by the year 2020. The strategy proposed by the WHO to eliminate filariasis is to prevent transmission of parasites through mosquitoes from the blood of infected individuals. The aim is to treat the entire population at risk for lymphatic filariasis through yearly, single-dose treatment with a combination of two drugs (DEC and albendazole) and to continue to cover the reproductive lifespan of adult-stage parasites for 4–6 years. The combination regimen can be given in a dosage of 6 mg/kg DEC and 400mg albendazole. A community-based study from Egypt has reported success in such a programme.

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