LEADING ARTICLE

TROPICAL PULMONARY EOSINOPHILIA

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Tropical pulmonary eosinophilia (TPE) is a disease caused by the filarial worm and occurs in countries where the parasite is endemic such as the Indian subcontinent and South East Asia. Indians are more frequently affected than other ethnic groups even in countries where they constitute a minority of the population. The patients are mainly in the younger age group (20-40 years) and there is a male predominance. In Singapore, the disease has become less prevalent over the years because of a decline in the population of Indian immigrants.

The disease is characterized by the following features:

* Systemic symptoms
  fever, fatigue and weight loss
* Respiratory symptoms
  paroxysmal cough, often nocturnal, wheezing, dyspnoea
* High peripheral eosinophil count > 2000 c mm
* Chest x-ray abnormality showing interstitial lung pattern
* Increased serum IgE levels
* Presence of antifilarial antibodies
* Response to antifilarial drug - diethylcarbamazine (DEC)

The filarial worm is introduced into the body by the bite of a mosquito. Infection is mainly due to 2 species of worms, Wuchereria bancrofti and Brugia malayi, which are of human origin, but filaria of animal origin have also been implicated. After entering the blood stream, the infective third stage larvae make their way to the lymphatics and lymph nodes where they mature into adults and release microfilariae into the blood stream. The microfilariae pass to the lungs where they are trapped and destroyed giving rise to a severe granulomatous reaction which accounts for the pulmonary manifestations. Microfilariae have never been demonstrated in the peripheral blood in spite of repeated examinations. The term "occult filariasis" has therefore been applied to this condition. However, microfilariae have been detected in the lymph nodes, liver and the lung, albeit in a degenerated state[1,2].

The clinical syndrome of TPE is due to a hypersensitivity reaction to microfilariae in the lungs. The immunological response may have a genetic basis as Indians are most susceptible to the disease. It is also influenced by factors such as the intensity, frequency and duration of exposure to the infective larvae.

The destroyed or dead microfilariae in the lungs release antigens which stimulate the production of IgE as well IgG and IgM antibodies. The IgE antibodies are involved in the asthmatic response, while the IgG or IgM antibodies are involved in clearing microfilariae from the circulation[3].

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Histopathological examination shows that in the early stage, there is infiltration of histiocytes into the interstitial tissue and alveolar space. This is followed by infiltration with eosinophils progressing to a mixed cellular pattern of eosinophils, histiocytes and lymphocytes associated with fibrosis. If the disease is left untreated, the end result is a marked histiocytic infiltration with severe fibrosis giving rise to the picture of a chronic interstitial pulmonary fibrosis[4].

Bronchoalveolar lavage has confirmed that there is an intense eosinophil alveolitis in TPE. The concentration of eosinophils in the lung is much greater than that in the blood. This suggests that the accumulation of eosinophils in the lung is due to an active process and not to a spill over of eosinophils from the blood[5]. A paper in this issue of the journal has reported that eosinophils cause an impairment of gas transfer, while the combined action of macrophages and lymphocytes leads to a reduction in lung volumes[6]. It has been suggested that the inflammatory cells may have different actions on lung function depending on the cell type.

The mechanism leading to the presence of eosinophils in the lung is not clear. The chemotactic factors for eosinophils arise from various sources eg. the microfilariae themselves, the products of inflammatory or immune effector cells and components of complement. Eosinophils play an important role in the pathogenesis of lung damage. When eosinophils are activated, marked degranulaton occurs, resulting in loss of the core and peripheral portions of the granules. The release of oxidant radicals, major basic proteins from eosinophil granule core, eosinophil cationic protein, peroxidase and collagenase produce injury to the lungs. The asthmatic response is most likely due to the release of leukotrienes. As the disease advances, a cell mediated immune response may also be involved in producing fibrosis of the lungs.

Lung function studies show a restrictive pattern in most of the patients[4,7]. However, 25-30% of patients have an obstructive defect as well. There is also a reduction in diffusing capacity particularly when the patient has untreated disease for a long time[8].

The chest x-ray shows a varied pattern, ranging from a normal appearance to a picture of increased lung markings and a diffuse reticulonodular pattern. The diffuse micronodular shadows may be confused with miliary tuberculosis[9].

A characteristic feature of TPE is its response to diethylcarbamazine (DEC) which is a specific antifilarial drug. The drug is given in a dosage varying from 6-12 mg/Kg and administered in 3 divided doses for 7-21 days. Clinical improvement occurs within 1 to 3 weeks associated with a fall in the eosinophil count, level of filarial antibody and reversal of lung function abnormality. The mode of action of DEC is unclear. It is not effective against the microfilariae in vitro but it is thought to enhance the activity of eosinophils against the microfilariae.

Response to DEC may be absent or inadequate in patients who have untreated TPE for a long duration, especially those who have symptoms for more than 3 months[4].

Although most patients with acute TPE respond very well to a course of DEC, it is known that lung function abnormalities,

especially a decreased diffusing capacity, may persist for up to 2 years after a course of treatment[10]. Inflammation of the lower respiratory tract can persist as shown by the presence of eosinophilic alveolitis, peripheral eosinophilia and raised levels of serum IgE and antifilarial antibodies in patients treated with a 3-week course of DEC (6 mg/Kg) and followed up for an average duration of 12 months[11]. Also, harmful oxidants such as superoxide anions and hydrogen peroxide have been found in the lungs. This has led to the suggestion that supplementary treatment with steroids or a new drug, ivermectin, should be given to achieve better results and prevent the development of chronic interstitial lung disease.

TPE should be considered in any person from an endemic area who has chronic cough, wheezing, and chest x-ray evidence of interstitial lung disease. Cases of TPE have sometimes been wrongly diagnosed as bronchial asthma and miliary tuberculosis. While a high eosinophil count is an important feature of TPE, it should be differentiated from other causes of pulmonary eosinophilia basing diagnosis on additional diagnostic criteria such as the presence of filarial antibodies and the response to DEC[8].

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