CASE REPORT

Tropical Pulmonary Eosinophilia*

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CLINICAL and roentgenographic features of tropical pulmonary eosinophilia (TPE) were originally described by Weingarten[1] in 1943. Whereas cases of TPE were initially recorded in India, the disease is now known to occur throughout the world. Presentation can be varied, and diagnosis is difficult or frequently missed, particularly in areas where the disease is not prevalent. With increasing international air travel, TPE must be considered in patients who have compatible respiratory symptoms after traveling from endemic areas.

The diagnosis of tropical pulmonary eosinophilia was made in a Samoan woman who appeared to have lymphangitic carcinomatosis. In this case report we describe the clinical course, and the laboratory and pulmonary function data before and after the patient's spontaneous remission. We also review the recent literature on TPE.

CASE REPORT

A 53-year-old Samoan woman was referred to the Pulmonary Service at the Tripler Army Medical Center in Honolulu for evaluation of a two-month history of persistent nonproductive cough, pleuritic chest pain, wheezing, and shortness of breath. The paroxysms of coughing were more frequent and severe at night, with marked respiratory distress after each episode. The patient had had a left breast lumpectomy and left axillary node dissection for infiltrating ductal carcinoma of the breast at the onset of symptoms two months before referral. The axillary nodes were negative for metastatic disease, and the patient received a two-week course of radiation therapy (2,000 rad) to the left side of the chest. She denied any history of travel outside American Samoa before her referral to Tripler. She was a nonsmoker and denied a history of tuberculosis, asthma, helminthic disease, or atopic disease. Medications included only chronic thyroid replacement after resection of a cold nodule.

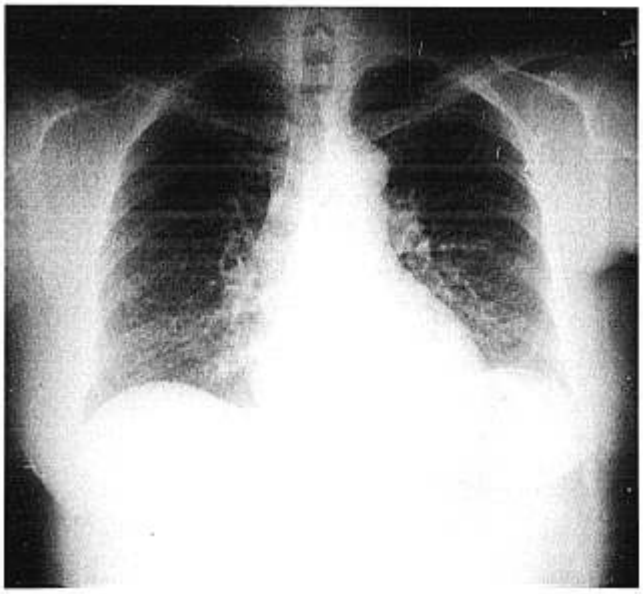

FIGURE 1. Chest film shows bilateral, diffuse reticulonodular infiltrate.

Physical examination revealed an obese Samoan woman in mild respiratory distress. Auscultation of the chest revealed bilateral rhonchi with expiratory wheezing. Cardiac examination was unremarkable. There was no lymphandenopathy or peripheral edema. A posteroanterior chest roentgenogram revealed a bilateral, diffuse reticulonodular infiltrate (Fig 1).

With the patient breathing room air, arterial blood gas values were PaO_2 73 mm Hg, $PaCO_2$ 35 mm Hg, and pH 7.43. The white blood count was 16,600/cu mm with a differential count of 21% segmented neutrophils, 7% band forms, 16% lymphocytes, 3% monocytes, and 53% eosinophils. The total eosinophil count was 8,798/dl. Pulmonary function testing revealed vital capacity of 49% of predicted, FEV_1 of 54% of predicted, peak expiratory flow rate of 71% of predicted, total lung capacity of 67% of predicted, and midmaximal expiratory flow (MMEF) of 61% of predicted. The decreased total capacity was consistent with a restrictive ventilatory defect, whereas the decreased MMEF was consistent with small airway obstruction. The single breath diffusing capacity for carbon dioxide was 74% of predicted.

Determination of calcium, uric acid, blood urea nitrogen, total bilirubin, total protein, albumin, and serum electrolytes yielded normal values. Mycobacterial and fungal cultures of the sputum were negative. Studies of stool specimen for ova and parasites showed moderate numbers of *Blastocystis hominis.*

The chest roentgenogram and the clinical picture were

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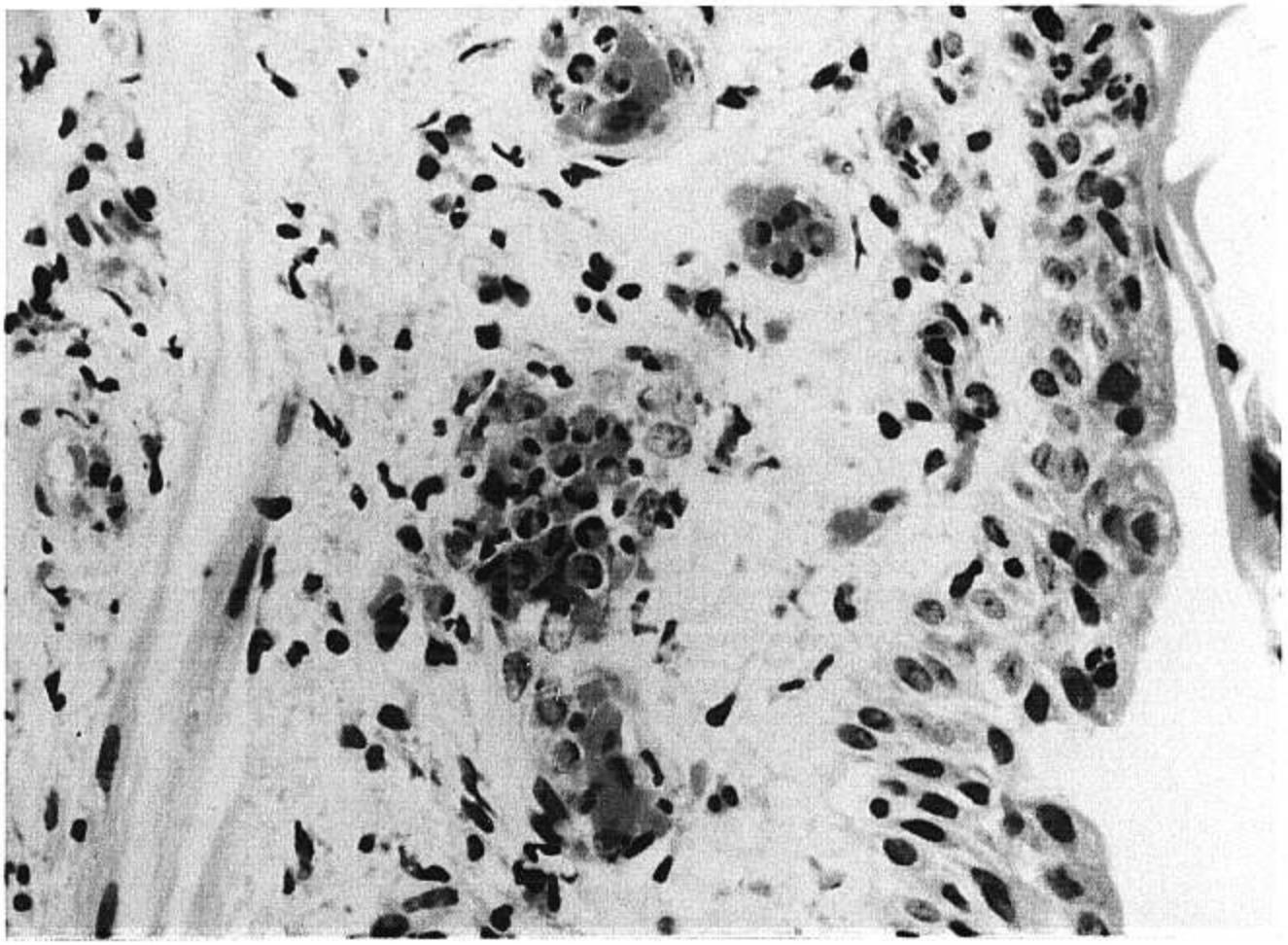

FIGURE 2. Transbronchial biopsy shows filling of alveolar spaces with eosinophils, Charcot-Leyden crystals, fibrin, and occasional chronic inflammatory cells.

highly suggestive of lymphangitic spread of carcinoma of the breast, and the patient had fiberoptic bronchoscopy with transbronchial biopsy. The bronchial washings yielded numerous eosinophils without evidence of malignant cells. Histology of the biopsy specimen revealed filling of the alveolar spaces with eosinophils, Charcot-Leyden crystals, fibrin, and occasional chronic inflammatory cells (Fig 2). There was ingrowth of fibroblasts into the alveolar spaces with alveolar septa thickened by edema and focally infiltrated with eosinophils, consistent with eosinophilic pneumonia.

Subsequent laboratory reevaluation revealed an IgG level of 2,000 mg/dl (normal 639 to 1,349 mg/dl). The serum IgE level was markedly elevated at 1,684.7 μg/ml (normal 0 to 180 μg/ml). Serum *Aspergillus* titers were negative, but filarial titers were positive by ELISA with a titer of more than 1:1,024. Examination of the peripheral smear was negative for microfilaria.

The patient was treated symptomatically with oral theophylline and inhaled beta-agonists, with marked improvement of bronchospasm. A seven-day course of metronidazole led to clearing of the *Blastocystis hominis* infection found on stool examination. Within a month of initial evaluation, the chest roentgenogram was normal, the peripheral eosinophilia resolved, and the pulmonary function returned to normal. No specific antifilarial chemotherapy was given. The patient completed a six-week course of radiation therapy and returned to Samoa without recurrence of the bronchospastic symptoms. Subsequent follow-up at four months revealed no recurrence of symptoms.

DISCUSSION

Tropical pulmonary eosinophilia (TPE) is a condition characterized by respiratory and systemic symptoms and extreme peripheral eosinophilia due to occult filariasis. TPE is endemic in the filarial zones, most commonly in India, Indonesia, Africa, and South America.[2] There are occasional reports of the disease among immigrants to the United States[3,4] and Great Britain.[5] With increased international air travel, TPE is a "tropical" disease that may be encountered throughout the world.

The illness usually begins with respiratory symptoms, chronic cough being most common and typically more severe at night. Dyspnea is frequently so severe and prolonged that the syndrome may resemble bronchial asthma or even status asthmaticus.[6] Current diagnostic criteria include peripheral eosinophilia (>3,000/ml), absence of microfilaria in the blood, high titers of antifilarial antibody, markedly increased IgE, and a favorable response to diethylcarbamazine (DEC).[7,8]

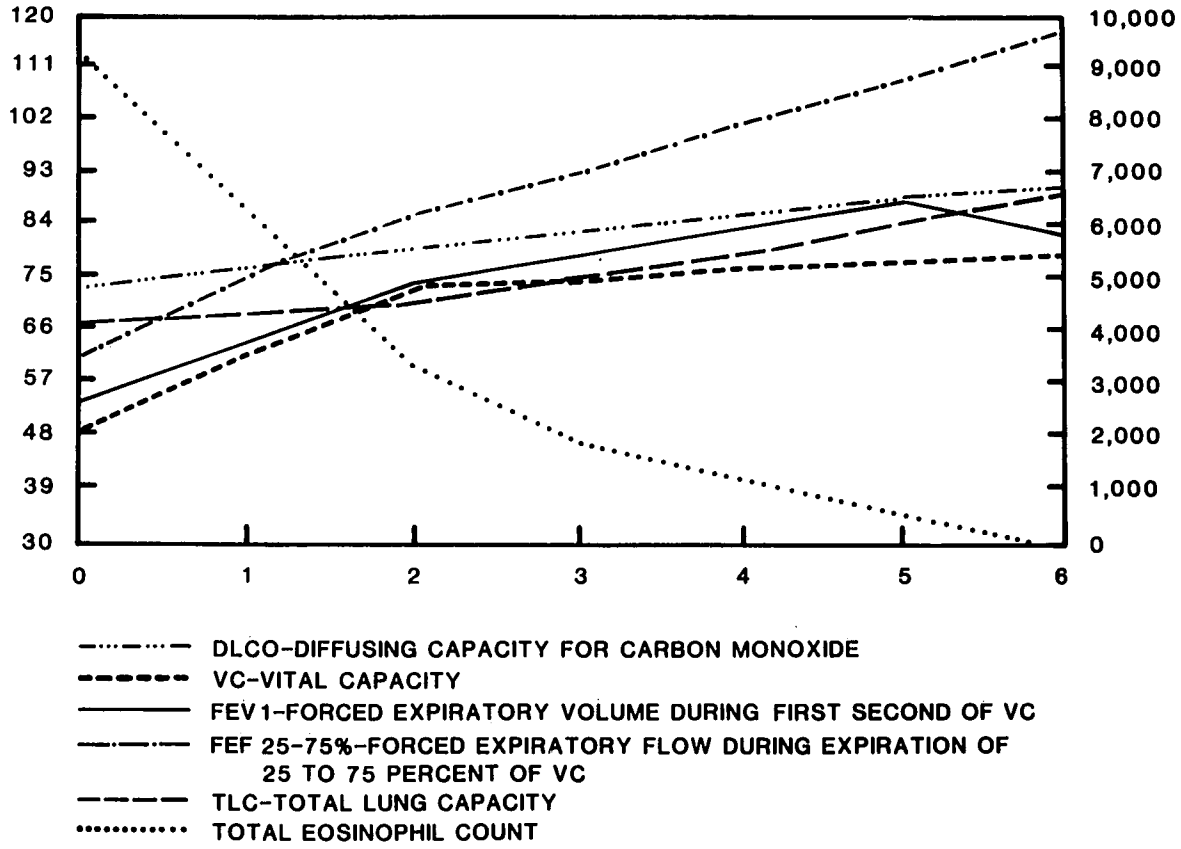

FIGURE 3. Relationship of various pulmonary function parameters to degree of peripheral eosinophilia over time.

Our patient fulfilled all criteria for the diagnosis of tropical pulmonary eosinophilia except for the response to DEC, a trial of which was not warranted in view of her spontaneous clinical resolution. This is still consistent with TPE, as spontaneous remissions and recurrences may be observed.[7,9]

The patient did present significant eosinophilia, which appeared to resolve in parallel with her improving pulmonary function (Fig 3). The level of peripheral blood eosinophilia has been previously reported not to correlate with ventilatory function.[10]

The patient also had a markedly elevated antifilarial antibody titer, without microfilaria in the peripheral blood. This is consistent with the proposed pathogenesis of an immune hypersensitivity reaction.[11] Microfilaria reaching the lung are destroyed by an intense tissue reaction, which accounts for the pulmonary symptoms, the roentgenographic appearance, and the negative circulating microfilaria.[11] Patients with TPE have been found to be more highly sensitized to microfilarial antigens than patients with non-TPE filariasis.[12] Thus patients with TPE develop a host hypersensitivity to the microfilarial stage of the parasite not present in other individuals with the more common lymphatic manifestations of filarial disease.

The remarkable elevation of IgE is commonly seen in TPE, with relatively insignificant changes in levels of IgG, IgM, and IgA.[12] The patient's eosinophilia is consistent with the direct relationship between IgE levels and the degree of peripheral blood eosinophilia previously reported.[13]

The pulmonary function abnormalities revealed a combined restrictive and obstructive ventilatory defect. Previous pulmonary function studies in TPE have documented mild to moderate obstructive disease, which is typically present from the onset of symptoms and progresses if untreated.[14] In patients with long-standing disease (two years or more), a common feature is a predominantly restrictive defect.[15]

The differential diagnosis of pulmonary eosinophilic syndromes is extensive and includes Löffler's syndrome, chronic pulmonary eosinophilia, allergic aspergillosis, vasculitic syndromes, drug allergies, and other helminthic infections as well as TPE.[7] In addition to a history of exposure in an endemic area, the best distinguishing features of tropical pulmonary eosinophilia are the presence of filarial antibodies and the therapeutic response to

diethylcarbamazine.[7]

In nonendemic areas, TPE may be mistaken for pulmonary tuberculosis, bronchial asthma, bronchiectasis, or atypical pneumonia.[6] Our patient was clinically thought to have lymphangitic carcinomatosis. TPE was considered only after the bronchial washings and transbronchial biopsies revealed eosinophilic pneumonia.

We report this case for three reasons. In our review of the literature, we found no previous case report of TPE masquerading as interstitial infiltrates and lymphangitic carcinomatosis. Secondly, increased international air travel makes TPE a "tropical" disease that may be encountered in the United States in patients with a history of travel from an endemic area. Finally, TPE must be considered in any patient from an endemic area who develops symptoms of bronchospasm, with or without a previous history of asthma.

SUMMARY

Tropical pulmonary eosinophilia is an unusual pulmonary disorder caused by occult filariasis. Presentation can be varied and can mimic asthma, pulmonary tuberculosis, or atypical pneumonia. We have reported a case of tropical pulmonary eosinophilia mimicking lymphangitic carcinomatosis.

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