Tropical pulmonary eosinophilia: a rare cause of cough in immigrants to Australia

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Clinical records

Patient 1

A 27-year-old man presented to an infectious diseases outpatient clinic in May 2006 with a 3-month history of nocturnal dry cough, paroxysmal dyspnoea, malaise and unintentional weight loss of 5 kg. He had previously presented to a general practitioner and was treated with two courses of antibacterial drugs without a decrease in symptoms. He had no significant past history of chronic respiratory illness or tuberculosis, was a non-smoker and had been working in Australia for 5 years. He was born in India and had recently returned there on a holiday to visit family and friends. Physical examination, including respiratory system examination, was unremarkable. Full blood examination revealed marked eosinophilia (28.8×10^9/L; reference range [RR], 0.0–0.5 $\times 10^9$/L). A chest x-ray and computed tomography (CT) showed a diffuse, bilateral fine micronodular pattern throughout both lung fields (Figures A and B).

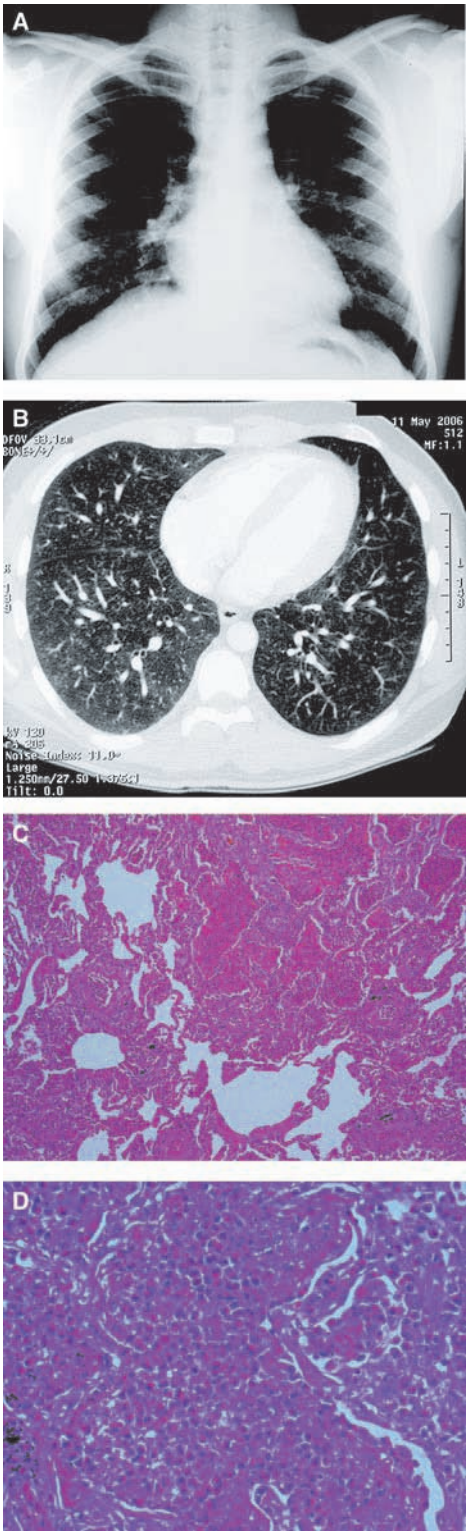
The patient had a raised serum IgE concentration of 24 020 kU/L (RR, 0–120 kU/L), and was positive for filarial IgG by enzyme immunoassay, but negative for filaria on a midnight blood smear. Strongyloides serological tests were also positive, but treatment with two doses of ivermectin did not resolve the nocturnal cough. Three stool specimens were examined for helminths, all of which were negative.

The patient was given antifilarial treatment with diethylcarbamazine (150 mg three times daily) for 14 days. Symptoms decreased rapidly, and the eosinophil count was nearly normal (2.7×10^9/L) by 4 weeks. Tropical pulmonary eosinophilia was diagnosed on the basis of the clinical syndrome, positive serological results for filaria, exclusion of other parasitic infections and successful clinical response to a trial of antifilarial treatment.

Patient 2

A 25-year-old woman from Sri Lanka presented to the Royal Melbourne Hospital emergency department in September 1994 with a 3-day history of productive cough, pleuritic chest pain and increasing exertional dyspnoea. She had arrived in Australia 6 months previously. Empirical treatment with salbutamol and doxycycline prescribed by her GP had not decreased the symptoms. Examination revealed scattered bilateral expiratory wheezes. A full blood examination revealed an eosinophil count of 21.5×10^9/L, and the initial chest x-ray showed diffuse pulmonary infiltrates, which were confirmed on CT. A bronchoscopy was performed to investigate these pulmonary lesions, which showed pus cells but no visible parasites. An open lung biopsy was then performed, before knowledge of relevant serological results, which revealed an eosinophilic infiltration of the alveolar spaces, suggestive of an eosinophilic pneumonia (Figures C and D).

Results of other investigations included three negative stool specimens, a strongly positive serological result for filaria, negative blood film for microfilariae, and a raised serum IgE concentration (28 400 kU/L). Serological tests for schistosomiasis and strongyloides were also both positive at low titres. Given the marked eosinophilia, widespread chest infiltrates and strongly positive filarial serological result, the most likely diagnosis was thought to be tropical pulmonary eosinophilia. The patient was treated with diethylcarbamazine (100 mg three times daily) for 21 days. After some initial nausea, her symptoms decreased, and the eosinophil count was resolving (0.7×10^9/L) by 8 weeks after treatment.



A: *Patient 1 — chest x-ray showed diffuse fine nodules.*
B: *Patient 1 — computed tomography showed a widespread, bilateral fine micronodular pattern.*
C, D: *Patient 2 — low and high magnification (x 200 and x 400) views of a lung biopsy specimen showed eosinophilic infiltration of alveolar spaces (haematoxylin and eosin stain).*

Clinical records *(continued)*

Patient 3

A 30-year-old man from India presented to an infectious diseases outpatient clinic via migrant screening in October 2006 with an abnormal appearance on chest x-ray, which showed fine reticulonodular opacities throughout both lung fields. The patient was born near Calcutta and had arrived in Australia 3 months previously. He was a non-smoker and reported a history of non-productive cough over several days. Physical examination was unremarkable including the respiratory system examination. A full blood examination revealed eosinophilia (13.0×10^9/L) and a positive serological result for filarial IgG. Results of other investigations included a raised serum IgE concentration (> 5000 kU/L), a positive serology result for strongyloides and negative serology results for schistosomiasis and toxocara, a negative immunochromatography result for *Wuchereria bancrofti*, and three negative stool specimens to particularly exclude strongyloides. A blood film did not show microfilariae. Pulmonary function tests showed moderate restriction (forced vital capacity, 3.0 L, or 67% of reference range) without obstruction and normal gas transfer.

The patient was initially treated for strongyloides infection with ivermectin, but the eosinophilia persisted. Diethylcarbamazine (150 mg three times daily) was given for 14 days. Within 2 weeks, the eosinophil count had dropped to 1.0×10^9/L. The patient was clinically well at follow-up 3 months later. ◆

Tropical pulmonary eosinophilia is a rare but well recognised syndrome characterised by pulmonary interstitial infiltrates and marked peripheral eosinophilia. We report three cases of this syndrome presenting with cough in immigrants to Australia, to highlight awareness of this treatable infectious disease. This condition is more widely recognised and promptly diagnosed in filariasis-endemic regions, such as the Indian subcontinent, Africa, Asia and South America. In non-endemic countries, patients are commonly thought to have bronchial asthma.[1,2] Chronic symptoms may delay the diagnosis by up to 5 years.[1] Early recognition and treatment with the antifilarial drug, diethylcarbamazine, is important, as delay before treatment may lead to progressive interstitial fibrosis and irreversible impairment.[3]

The condition of marked eosinophilia with pulmonary involvement was first termed tropical pulmonary eosinophilia in 1950.[4] The syndrome is caused by a distinct hypersensitivity immunological reaction to microfilariae of *W. bancrofti* and *Brugia malayi*.[3,5] However, only a small percentage (< 0.5%)[6] of the 130 million people globally who are infected with filariasis apparently develop this reaction. The clearance of rapidly opsonised microfilariae from the bloodstream results in a hypersensitive immunological process and abnormal recruitment of eosinophils, as reflected by extremely high IgE levels of over 1000 kU/L.[3,7] The typical patient is a young adult man from the Indian subcontinent.[5]

The diagnostic criteria for tropical pulmonary eosinophilia[7] include:

- history supportive of exposure to lymphatic filariasis;
- peripheral eosinophilia count ($> 3 \times 10^9$/L);
- elevated serum IgE levels (> 1000 kU/L);
- increased titres of antifilarial antibodies;
- peripheral blood negative for microfilariae; and
- clinical response to diethylcarbamazine.

High antifilarial IgG titres to microfilariae often result in cross reactivity with other non-filarial helminth antigens,[8,9] such as strongyloides and schistosoma antigens, as demonstrated in our reported cases. It is important to exclude other parasitic infections before tropical pulmonary eosinophilia is diagnosed, by serological tests, examination of stool specimens in a laboratory experienced in parasitic infections, or a trial of antihelminth medication. Other parasitic infections, such as the zoonotic filariae, dirofilariasis, ascariasis, strongyloides, visceral larva migrans and hookworm disease, may also be confused with tropical pulmonary eosinophilia because of overlapping clinical features, serological profile

1 Characteristic features of parasitic infections with pulmonary symptoms and eosinophilia

Condition	Parasite	Respiratory symptoms	Geographical distribution	Laboratory diagnosis	Treatment
Tropical pulmonary eosinophilia	*Wuchereria bancrofti*, *Brugia malayi*	Nocturnal cough, wheeze, dyspnoea	Tropical and subtropical areas, especially India and Sri Lanka	Serology, blood film, IgE levels	Diethyl-carbamazine
Strongyloides	*Strongyloides stercoralis*	Loeffler's-like syndrome,* hyperinfection syndrome	Tropical and subtropical, including northern Australia	Serology, stool	Ivermectin
Schistosomiasis	*Schistosoma mansoni*, *Schistosoma haematobium*, *Schistosoma japonicum*	Katayama fever, pulmonary hypertension, cor pulmonale	Asia, Africa, South America	Serology, stool and urine	Praziquantel
Ascariasis	*Ascaris lumbricoides*	Loeffler's-like syndrome*	Asia, Africa, South America	Stool	Albendazole
Visceral larva migrans	*Toxocara canis*, *Toxocara cati*	Eosinophilic pneumonia, wheeze, dyspnoea	Worldwide	Serology	Albendazole
Dirofilariasis	*Dirofilaria immitis*	Pulmonary lesion	Tropical and subtropical, including Australia	Serology	None
Hookworm disease	*Ancylostoma duodenale*	Loeffler's-like syndrome	Tropical and subtropical areas	Stool	Albendazole

* Loeffler's-like syndrome: transient pulmonary infiltrates and eosinophilia from transpulmonary passage of helminth larvae. ◆

and response to diethylcarbamazine[3,7,9,10] (Box 1). Radiological findings are non-specific, with normal appearance on chest x-ray in up to 20%.[5] Although lung biopsy was performed in Patient 2, it is not part of the routine diagnostic work-up of tropical pulmonary eosinophilia.

No universal treatment guidelines have been established for tropical pulmonary eosinophilia.[1,7] The antifilarial diethylcarbamazine (6 mg/kg/day for 21 days[6]) remains the main therapeutic agent and is generally well tolerated. Reported side effects include headache, fever, pruritis and gastrointestinal upset.[11] The eosinophil count often falls dramatically within 7–10 days of starting treatment.[3] Diethylcarbamazine is available only through the Special Access Scheme of the Therapeutic Goods Administration. Symptoms persist after treatment in up to 25% of patients.[5] The role of adjunctive therapy with corticosteroids in preventing long-term fibrosis has not been studied.

Our three cases demonstrate the variable clinical presentations and symptom duration of tropical pulmonary eosinophilia. With increased travel and migration of patients from filaria-endemic areas, physicians need to remain aware of tropical pulmonary infections presenting with cough, dyspnoea and variable systemic symptoms, as delayed recognition of this uncommon clinical entity may increase morbidity.

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Lessons from practice

- Tropical pulmonary eosinophilia should be considered in patients who have lived in filaria-endemic countries, such as the Indian subcontinent, and present with respiratory symptoms and hypereosinophilia.
- The most common misdiagnosis is asthma, with overlapping symptoms of chronic cough, paroxysmal dyspnoea and wheeze.
- Early diagnosis and treatment with diethylcarbamazine (DEC) may prevent progressive pulmonary disease. ◆

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