

Pulmonary Hypereosinophilia

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Abstract

Introduction: Eosinophilic lung diseases are a diverse group of pulmonary disorders linked by the common finding of increased eosinophilia in blood and/or tissue. They usually present to the clinician as pulmonary infiltrates with eosinophilia for which the differential diagnoses is fairly broad. **Clinical Picture:** Three patients presented with subacute cough, pulmonary infiltrates and a markedly elevated eosinophil count $>1.5 \times 10^9/L$. Each case exemplifies its clinical peculiarities and pearls and illustrates the diversity in this group of disorders. **Treatment:** A common theme in the approach to its management is excluding infection before proceeding with therapy, often with steroids. **Outcome:** There is often a dramatic response to steroid therapy with resolution of symptoms and chest radiographic findings. **Conclusion:** The arbitrary label of “pulmonary hypereosinophilia” enables the differential diagnoses to be narrowed to the 4 main categories of infections with parasites or fungus, the Churg-Strauss syndrome, chronic eosinophilic pneumonia and the idiopathic hypereosinophilic syndrome.

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Introduction

Eosinophilic lung diseases encompass a heterogeneous spectrum of lung disorders defined by increased eosinophils in blood and/or tissue.¹ In 1952, Crofton et al² proposed the term “pulmonary eosinophilia” for disorders characterised by chest radiographic infiltrates and peripheral eosinophilia. We report 3 such cases with a striking peripheral eosinophilia $>1.5 \times 10^9/L$. We arbitrarily defined this as hypereosinophilia with the level used in the hypereosinophilic syndrome and coined the term “pulmonary hypereosinophilia”. All the cases presented with the very common pulmonary symptom of subacute cough and each case demonstrates its own clinical pearls.

Case Reports

Case 1

A 23-year-old non-smoking man presented with cough associated with intermittent fever of 3 weeks' duration, a pruritic rash on his hands and feet for a week, and weight loss. He was treated for acute sinusitis 2 weeks prior to admission. He was diagnosed with asthma 4 months earlier at another hospital when he presented with shortness of breath and wheezing. Then, his metacholine challenge test

was positive and his symptoms had improved with inhaled corticosteroid and beta-agonist therapy.

On examination, he was febrile at 38°C with a papular rash on both hands and feet. Both heart sounds were normal and an ejection systolic murmur was heard. His lungs were clear on auscultation. Blood investigations revealed a haemoglobin of 12.3 g/dL and white cell count of $14.62 \times 10^9/L$ (eosinophils, 6.67×10^9). Chest radiograph showed mild cardiomegaly, right upper lobe infiltrates with blunting of both costophrenic angles and computed tomography (CT) of the thorax (Fig. 1) showed consolidation in the right upper lobe with bilateral pleural effusions and a pericardial effusion. Sputum for acid-fast bacilli smear and culture were negative. Skin biopsy of his right palm rash showed superficial perivascular dermatitis (eosinophilic) compatible with Churg-Strauss syndrome. He was treated with a course of prednisolone at 0.5 mg/kg/day and reviewed in the outpatient clinic a month later. By then his symptoms, rash and peripheral hypereosinophilia had resolved and a repeat chest radiograph was normal. His prednisolone was then gradually tapered off over the next 4 months when he was noted to be well before he subsequently defaulted follow-up. This patient's presentation had evolved from asthma to

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acute sinusitis to a pneumonia with atypical features of weight loss, rash and peripheral hypereosinophilia. He had never been treated with a leukotriene receptor antagonist.

Case 2

A 45-year-old non-smoking woman presented with cough and episodic wheezing of 8 weeks' duration. Prior to presentation 4 weeks later, her chest radiograph showed only small areas of scarring in the apical segments of both upper lobes. Clinical examination revealed bilateral expiratory rhonchi and spirometry showed reversible airflow obstruction. She was treated for asthma with a corticosteroid and long-acting beta-agonist combination inhaler. Her symptoms improved within a month. Two months later, her cough returned despite a course of antibiotics, this time associated with loss of appetite and weight loss of 4 kg. Her lungs were clear on auscultation then and blood investigations revealed a haemoglobin of 10.1 g/dL and white cell count of $14.28 \times 10^9/L$ (eosinophils, $3.30 \times 10^9/L$). Chest radiograph (Fig. 2) showed patchy alveolar infiltrates in the right lung and bilateral apical fibrosis. High-resolution CT thorax showed bilateral apical fibrosis and patchy consolidation in the right lung periphery. Bronchoscopy was normal and bronchoalveolar lavage showed bronchial epithelial cells, lymphocytes, macrophages and multi-nucleated cells. Stains and cultures for acid-fast bacilli were negative. Transbronchial lung biopsy showed an inflammatory cell infiltrate consisting of lymphocytes, plasma cells, a prominent increase in the number of eosinophils and an occasional giant cell and this confirmed the diagnosis of chronic eosinophilic pneumonia. Pulmonary tuberculosis was ruled out and she was treated with prednisolone at 0.75 mg/kg/day. There was a dramatic response to treatment with resolution of her symptoms and

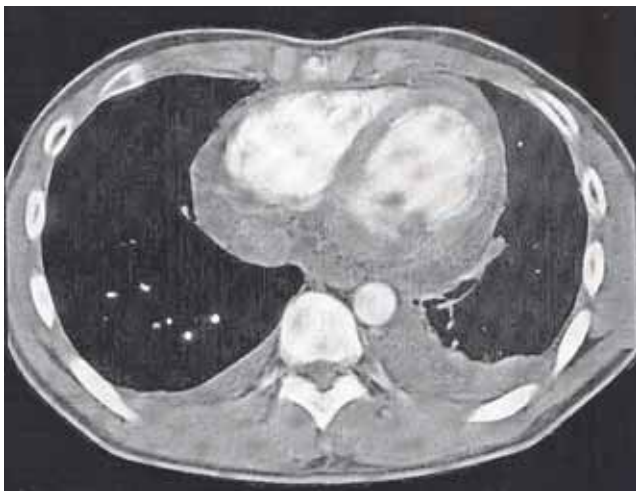


Fig. 1. Computed tomograph of the thorax shows bilateral pleural effusions and a pericardial effusion.

peripheral hypereosinophilia on review 7 weeks later. A repeat chest radiograph then showed only bilateral apical scarring that was present on her first chest radiograph. Her oral steroids were gradually tapered off and she was subsequently maintained on inhaled corticosteroids until her follow-up 3 months later when she remained well and her chest radiograph remained stable.

Case 3

A 31-year-old man presented with cough of 3 weeks' duration that partially improved with post-nasal drip syndrome treatment. Clinical examination was unremarkable and blood investigations revealed haemoglobin of 14.5 g/dL and a white cell count of $32.56 \times 10^9/L$ (eosinophils, $25.4 \times 10^9/L$). Chest radiograph showed bilateral diffuse nodular infiltrates. Stools for ova and parasites were negative, but his anti-filarial antibody was positive (1/64), suggesting the diagnosis of tropical pulmonary eosinophilia. He was treated with a course a diethyl carbazepine (DEC) and his eosinophil count dropped to $0.84 \times 10^9/L$ a month later. The peripheral hypereosinophilia prompted the serological study that led to the diagnosis, which was confirmed after the dramatic and favourable response to DEC.³

Discussion

Churg-Strauss syndrome is a multi-system disorder characterised by asthma, vasculitis, eosinophilic tissue



Fig. 2. Chest radiograph shows patchy infiltrates in the right lung and upper lobe scarring.

inflammation, fever and a peripheral hypereosinophilia. It is rarely seen not only in steroid-dependent asthmatics, where oral steroid withdrawal was facilitated by a leukotriene receptor antagonist,⁴ but also where a leukotriene receptor antagonist had been substituted for inhaled steroids.⁵ Asthma is one of the most common manifestations at presentation.⁶ Other frequent clinical findings include mononeuropathy multiplex (78%), weight loss (71%), sinusitis (61%), myalgias (54%) and skin manifestations (50%). Chest radiographs commonly show fleeting infiltrates that change over time but, as in case 1, may often look like a pneumonia with an accompanying parapneumonic effusion.⁷ Treatment is with corticosteroids and most patients respond favourably.

Chronic eosinophilic pneumonia is usually subacute in onset with a constellation of symptoms, such as cough, progressive breathlessness, wheezing, fever, night sweats and significant loss of weight.⁸ As in case 2, asthma accompanies or precedes 50% of cases. The classical chest radiographic finding is diffuse peripheral infiltrates described as “photographic negative” of pulmonary oedema.⁹ There is coexistence of blood eosinophilia and pulmonary eosinophilic infiltration without an obvious cause. Treatment is with daily oral corticosteroids and patients are uniformly responsive.

Tropical pulmonary eosinophilia used to be a disease of the tropics, but with the mobility of today’s population, it is increasingly seen elsewhere. Symptoms include nocturnal cough, breathlessness and wheezing, thus resembling asthma, but the chest radiograph is usually abnormal, characteristically showing an ill-defined reticulo-nodular infiltrate with a mottled appearance (usually in the mid and lower lung zones). The eosinophilia can be quite striking, with a count of $>3 \times 10^9/L$ taken as the cut-off for diagnosis.¹⁰ High anti-filarial antibody titres are helpful and histopathological confirmation is usually not practical or necessary. Stool examinations aid in the search for parasites. As in case 3, there is a favourable clinical and haematological response to diethylcarbamazine.¹¹

We have revisited Crofton’s description of pulmonary eosinophilia and taken a step further by arbitrarily defining “pulmonary hypereosinophilia” as disorders with chest radiographic infiltrates and peripheral hypereosinophilia $>1.5 \times 10^9/L$. An absolute eosinophil count $>1.5 \times 10^9/L$ is one of the criteria used to define the hypereosinophilic

syndrome, an idiopathic condition associated with marked peripheral eosinophilia with involvement of multiple organs, such as the heart, gastrointestinal tract, lungs, brain and kidneys.¹² Besides this condition, the other 3 main differential diagnoses for “pulmonary hypereosinophilia” are infections with parasites or fungus (allergic bronchopulmonary aspergillosis), the Churg-Strauss syndrome and chronic eosinophilic pneumonia.

This case series illustrates the diverse spectrum of “pulmonary hypereosinophilia” and stresses that though many of these diseases are treated with steroids, it is important to exclude infection before commencing these drugs.

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