Pulmonary eosinophilia in identical twins

N BARNES, BJ GRAY, R HEATON, JF COSTELLO

From the Chest Unit, King's College Hospital Medical School, London

Familial cryptogenic pulmonary eosinophilia has not previously been described. We report cryptogenic pulmonary eosinophilia occurring at different times in identical twins.

Case reports

Case 1

A 25-year-old nurse presented in September 1977 with a four-week history of sustained pyrexia, rigors, anorexia, weight loss, non-productive cough, and pleuritic chest pain. Since the age of 16 she had noticed transient mild wheeziness, associated with hay fever during the summer months. Wheezing had become episodic and more severe during her present illness, and she was taking salbutamol 400 µg by metered-dose inhaler as required (on average about twice daily) to control her wheeziness. She had no history of eczema or drug reactions, and there was no history of ingestion of any drugs likely to be associated with pulmonary eosinophilia. She had never travelled outside Europe.

Examination showed a temperature of 37.5°C and tachycardia of 96 beats/min. There was a pleural rub heard widely over the right lower chest anteriorly and in the right axilla. Widespread bilateral inspiratory crackles were also audible. Her chest radiograph (fig 1) showed bilateral but predominantly right-sided confluent infiltrates with a mainly peripheral distribution. The white blood cell count (WBC) was $16 \times 10^9/l$, with an eosinophil count of $4.5 \times 10^9/l$ and an erythrocyte sedimentation rate (ESR) of 100 mm in the first hour. Microscopic examination of the sputum showed numerous eosinophils, but no hyphae were seen. Skin prick tests showed weak reactions (<2 mm) to grass pollen, tree pollen, and house dust mite, but no reaction to six other common allergens, including *Aspergillus fumigatus*. Precipitins to *A. fumigatus* were not demonstrable in the serum. The total immunoglobulin E (IgE) concentration was 132 IU/l (upper limit of normal 100 IU/l). No ova, cysts, or adult worms were found in the stool examination. Repeated Gram stain and culture of the sputum showed no pathogens. *Mycobacterium tuberculosis* was not demonstrable either by direct sputum staining or subsequently by culture. Pulmonary function tests showed a restrictive defect associated with a reduced carbon monoxide transfer factor (TLCO). The forced expiratory volume in the first second (FEV₁) was 1.6 l (predicted 3.1 l) and the vital capacity 1.8 l (predicted 3.5 l). TLCO was $11.9 \text{ ml min}^{-1} \text{ mm Hg}^{-1}$ ($4.0 \text{ mmol min}^{-1} \text{ kPa}^{-1}$), the predicted value being $27.3 \text{ ml min}^{-1} \text{ mm Hg}^{-1}$ ($9.1 \text{ mmol min}^{-1} \text{ kPa}^{-1}$).

Address for correspondence (no reprints): Dr N Barnes, Chest Unit, King's College Hospital Medical School, London SE5 8RX.

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The diagnosis was cryptogenic pulmonary eosinophilia, and treatment was started with prednisolone 30 mg orally each day. Within two weeks the chest radiograph, blood eosinophil count, and results of pulmonary function tests had returned to normal. The patient remained well and symptom free on decreasing doses of prednisolone, which was stopped in April 1978. A relapse occurred after 14 months without steroids, in June 1979. She had gradually worsening asthma and a severe systemic illness similar to the one when she first presented. Her chest radiograph, which had been normal since September 1977, again showed bilateral confluent peripheral pulmonary infiltrates, and again there was blood eosinophilia ($2.9 \times 10^9/l$ eosinophils). The ESR was 107 mm in the first hour. Prednisolone was restarted orally, 30 mg per day, and she rapidly improved.

It has been possible to reduce the dose of prednisolone progressively to the present dose of 10 mg on alternate days. The current chest radiograph, results of pulmonary function tests, and eosinophil count are normal.

Case 2

The identical twin sister of the first patient (zygosity confirmed by HLA typing) presented at the age of 29 in July 1981. She had a four-month history of weight loss and increasing breathlessness, with nocturnal wheeze and

Fig 1 Case 1: chest radiograph at presentation, September 1977.

Fig 2 Case 2: chest radiograph four days after presentation, July 1981.

cough, which were not controlled by increasing doses of inhaled salbutamol and beclomethasone. She had had mild asthma since the age of 14, and this had been controlled on small doses of inhaled β -adrenergic agonists and latterly by inhaled beclomethasone. She had not experienced rigors or pleuritic chest pain, and there was no history of travel outside Europe or recent drug ingestion. Examination of the chest showed widespread wheeze, but no crepitations or pleural rub.

The initial chest radiograph (fig 2) showed irregular peripheral infiltrates, with some perihilar infiltrates. In subsequent radiographs the distribution of these infiltrates evolved into a predominately peripheral and apical pattern. The blood eosinophil count was $2.5 \times 10^9/l$, the ESR was 110 mm in the first hour, and the serum IgE level was 210 IU/l. Sputum microscopy and culture showed no pathogens and no hyphae were seen. Skin prick showed mild positive reactions (<2 mm) to dog fur, grass and tree pollen, and house dust mite, but no reaction to *Aspergillus fumigatus*. Precipitins to *Aspergillus fumigatus* were not demonstrable in the serum, and stool examination showed no evidence of ova, cysts, or parasites.

As in case 1, the pulmonary function tests showed a restrictive defect associated with a reduced TLCO. The FEV₁ was 2.1 l (predicted 2.9 l) and the VC was 2.4 l (predicted 3.4 l). The TLCO was $17.7 \text{ ml min}^{-1} \text{ mm Hg}^{-1}$ ($5.9 \text{ mmol min}^{-1} \text{ kPa}^{-1}$), the predicted value being $26.6 \text{ ml min}^{-1} \text{ mm Hg}^{-1}$ ($8.8 \text{ mmol min}^{-1} \text{ kPa}^{-1}$).

Cryptogenic pulmonary eosinophilia was diagnosed, and oral prednisolone 20 mg/day was started. Within two weeks her chest radiograph, eosinophil count, and results of pulmonary function tests had returned to normal. Her dose of prednisolone has been gradually reduced to 10 mg on alternate days, and no relapses have occurred.

Two relatives of the twins (an elder sister and a nephew) are atopic and have mild asthma. Neither relative has had a recorded eosinophil count above $0.5 \times 10^9/l$, and neither has evidence of allergic bronchopulmonary aspergillosis.

Case 1 was a staff midwife at a London hospital at the time of her initial illness. Her sister (case 2) was a secretary in the Midlands at the time of her illness, and had lived in Germany for some years previously. The twins had not lived together since the age of 18. Neither had visited each other or their parental home for several weeks before their initial episodes of pulmonary eosinophilia. We have been unable to identify any common environmental factor to explain their pulmonary eosinophilia.

Discussion

The classification of pulmonary eosinophilia has undergone continuous refinement since Crofton *et al*¹ first introduced a coherent clinical scheme. The term cryptogenic pulmonary eosinophilia was used by McCarthy and Pepys² in 1973 to describe a group of 27 patients in whom the cause of chronic pulmonary eosinophilia could not be established. The recognised features of the cryptogenic group have been elaborated in subsequent reviews³ and include a systemic illness of varying severity with fever, weight loss, rigors and sweating, and a raised ESR with anaemia, an absolute polymorphonuclear leucocytosis, and a raised blood eosinophil count (usually greater than $2.5 \times 10^9/l$). In atopic patients, although the blood eosinophil count tends to be high, there is usually only a marginal elevation of the serum IgE concentration. Corticosteroids characteristically produce a rapid response and complete resolution. The chest radiograph (as in case 1—fig 1) typically has a peripheral and apical distribution of confluent infiltrates resembling the "photographic negative of pulmonary oedema."⁴

In the United States terminology has varied and possibly some of the patients described as having pulmonary infiltrates with eosinophilia or chronic eosinophilic pneumonia had allergic bronchopulmonary aspergillosis.⁴

Deteriorating asthma was a component in the presenting illness of both twins but especially in case 2, whereas a severe systemic illness was the predominant feature in the presentation in case 1. This difference in presentation has been commented on previously; it does not seem to affect prognosis.³ The pleuritic component of the illness in case 1 is not a common feature of pulmonary eosinophilia, although it has been described.⁵

References

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