CASE REPORT

Chronic eosinophilic pneumonia: a paediatric case

Davide Tassinari, Chiara Di Silverio Carulli, Francesca Visciotti, Roberta Petrucci

Department of Paediatric
Emergency, S Orsola-Malpighi
Hospital, University of Bologna,
Bologna, Italy

Correspondence to

Dr Davide Tassinari,
davide.tassinari@aosp.bo.it

SUMMARY

Chronic eosinophilic pneumonia (CEP) is a rare disorder in children, characterised by respiratory and systemic symptoms, with a generally good prognosis. A 11-year-old asthmatic girl was admitted to our clinic with a 3-month history of progressive cough, dyspnoea, weight loss and asthenia. Peripheral blood eosinophilia, multiple bilateral pulmonary infiltrates to the x-ray, multiple nodules with a surrounding ground-glass halo and peripheral predominance to the chest CT suggested the diagnosis of eosinophilic lung disease (ELD). Further investigations ruled out other ELD and supported diagnosis of CEP. The response to oral corticosteroids was dramatic, no relapses were reported in 2-year follow-up while the patient was under inhaled corticosteroids for pre-existing asthma.

BACKGROUND

Chronic eosinophilic pneumonia (CEP) is an extremely rare condition in children characterised by respiratory and general symptoms, associated with alveolar or blood eosinophilia and pulmonary infiltrates on chest imaging. The insidiousness of the clinical presentation and its rarity make the diagnosis difficult in children. Its management has not been standardised yet and further information are necessary to establish the proper treatment.

CASE PRESENTATION

A 11-year-old girl was admitted to the paediatric emergency unit for cough, dyspnoea, weight loss and asthenia progressively increasing in the previous 3 months; she had a history of asthma, cat hair allergy and was treated with inhaled fluticasone propionate/salmeterol and montelukast during the previous 3 years.

INVESTIGATIONS

The blood tests showed $4.300/\text{mm}^3$ eosinophils, thrombocytosis ($827\,000/\mu\text{l}$), increased IgE level (4476 UI/ml) and high erythrocyte sedimentation rate (ESR: 112 mm/h). The child was dyspnoeic with 98% O_2 -saturation in room air, breath sounds were reduced. The pulmonary function tests (PFT) showed a mixed obstructive/restrictive pattern: forced vital capacity (FVC) was 44% and forced expiratory volume in one second (FEV_1) 41% of predicted value, with a slight decrease in FEV_1/FVC (79%). The chest x-ray revealed multiple bilateral pulmonary infiltrates with discrete hilar involvement, without pleural effusion (figure 1). Chest CT demonstrated the presence of a mixed pattern of ground-glass areas and parenchymal nodules, with predominantly peripheral distribution, associated with thickening of interlobular

Figure 1 Chest x-ray at onset of symptoms: multiple bilateral pulmonary infiltrates with discrete hilar involvement.

septa, mainly in the apical zones (figure 2). Bronchoscopy was performed but the collection of bronchoalveolar lavage (BAL) was hampered by the presence of jelly secretion plugs in the main bronchial tree.

DIFFERENTIAL DIAGNOSIS

There was no evidence of bacterial, fungal or mycobacterial infection in BAL, bronchial and

Figure 2 Chest CT at onset of symptoms: mixed pattern of ground-glass areas and parenchymal nodules, with predominantly peripheral distribution, mainly in the upper lung zones; thickening of interlobular septa, mainly in the apical zones, and enlarged mediastinal lymph nodes (maximum diameter 25 mm).

To cite: Tassinari D, Di Silverio Carulli C, Visciotti F, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-008888

pharyngeal aspirate. Tuberculin skin test and Quantiferon-TB Gold-in-Tube were negative. Serological tests were negative for *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, *Adenovirus*, *Legionella*, *Aspergillus*, *Cladosporium* and *Candida*. Serological tests and stool exams were negative for parasites. The negativity of antinuclear antibody, antinuclear double-stranded DNA, antimitochondria, anti-LKM antibodies, c-ANCA and p-ANCA ruled out autoimmune diseases.

There are various known causes of ELD, including allergic bronchopulmonary aspergillosis, drug reactions, parasitic infections and eosinophilic vasculitis (Churg-Strauss syndrome). Allergic bronchopulmonary aspergillosis, parasitic infections, drug-induced eosinophilic pneumonia (EP) were excluded; absence of cutaneous vasculitis and other multiorgan involvement ruled out Churg-Strauss syndrome.

Along with CEP, acute eosinophilic pneumonia (AEP), simple pulmonary eosinophilia (SPE) and idiopathic hypereosinophilic syndrome (IHS) belong to the group of ELD of unknown origin. Diagnostic criteria of AEP include acute febrile illness of less than 5 days, SPE is characterised by spontaneous resolution within 1 month, IHS includes multiorgan system dysfunction, particularly against heart and nervous system.

After excluding other possible known causes of eosinophilic lung diseases, the diagnosis of CEP was suspected mainly on the basis of blood hypereosinophilia, CT evidences, persistence of symptoms for about 3 months and absence of multiorgan involvement. In our patient the increased number of eosinophils in blood, the finding of multiple bilateral pulmonary infiltrates on chest x-ray and the characteristic ground-glass pattern with peripheral distribution on chest CT were suggestive of CEP; other findings consistent with the diagnosis, although not specific, were high IgE level, increased ESR and thrombocytosis.

TREATMENT

Treatment with intravenous dexamethasone (0.3 mg/kg/die) was commenced.

OUTCOME AND FOLLOW-UP

After 6 days of treatment clinical conditions improved dramatically, eosinophils declined to $20/\text{mm}^3$, total IgE count was 2898 UI/ml, ESR was 2 mm/h. The chest x-ray showed an important reduction of infiltrates and peripheral ground-glass areas (figure 3); PFT showed an increase in FVC (78%), FEV₁ (87%) and FEV₁/FVC (96% of predicted value). A second BAL was performed after 1 week: the cytology examination showed 850 000 cell/ml with a differential count of 85% macrophages, 1% lymphocytes, 7% neutrophils, 5% eosinophils and 3% monocytes.

The patient was discharged with 50 mg/die oral prednisone and in the following weeks there was an almost complete normalisation of respiratory dynamics and PFT, the blood eosinophil count returned to normal and the radiological findings receded. Oral corticosteroids were progressively reduced over 6 months and when suspended, she took-on her originally antiasthmatic therapy.

After 4 months of therapy a chest CT showed a regression of the mixed pattern of ground-glass areas and parenchymal nodules.

In two-year follow-up there were no relapses. Two episodes of acute asthma occurred during transient respiratory infections and CEP was excluded because of normal chest x-ray and eosinophilic peripheral count.

Figure 3 Chest x-ray after 1 week of treatment: important reduction of the infiltrates.

DISCUSSION

CEP, first described by Carrington *et al* in 1969,¹ is a rare disorder in children,^{2–5} but the true incidence and prevalence is unknown.⁶ In the adult population, women are more frequently affected than men^{7–9} but this ratio is not confirmed in children. The onset is insidious with non-specific general symptoms including cough, fever, dyspnoea, weight loss, night sweats, wheezing and sputum production.^{6 7 9 10} These symptoms might easily be misdiagnosed as an infectious illness contributing to a delay in the diagnosis and treatment.

Diagnostic criteria were described by Marchand *et al*.¹¹ They are usually based on the association of respiratory symptoms lasting more than 2 weeks, alveolar and/or blood eosinophilia (more than $1000/\text{mm}^3$), pulmonary infiltrates with peripheral predominance at the imaging and exclusion of other known causes of eosinophilic lung disease. There are not specific findings to confirm the diagnosis, and then other causes of eosinophilia with pulmonary infiltrates need to be ruled out. Differential diagnosis includes a heterogeneous group of pulmonary disorders characterised by an increase of eosinophils in peripheral blood, in BAL and/or in the pulmonary interstitial space, generally defined as eosinophilic lung diseases (ELD).^{6 8 12 13} Although in our patient it was not possible to confirm the BAL eosinophilia at the time of diagnosis, the second BAL showed an elevated eosinophilic cell percentage (5%) even after 6 days of corticosteroid treatment; however, although the increase of eosinophils in BAL fluid is useful, its absence does not contradict the diagnostic criteria for CEP.^{11–16}

Many studies on adult showed a closed correlation between onset of CEP and previous, contemporary or future diagnosis of asthma.^{6 17} A history of asthma is reported in one-third to one-half of the patients with CEP,¹¹ was relatively severe and got worse after the diagnosis of CEP.¹⁷ Including our patient, CEP in children was till now described only in five case-reports,^{2–5} while another one was described in a review on pulmonary infiltrates with eosinophilia syndromes in children¹⁴; three of these patients had a previous history of asthma. Patients with no asthma seem to be at higher risk of relapses,¹¹ possibly because of a higher frequency of long-term inhaled corticosteroids use in asthmatics.¹⁷ There are few data to support the use of inhaled corticosteroids in preventing relapses of CEP.⁷

A study conducted by Minauchi *et al*¹⁸ on a small number of asthmatic and non-asthmatic adults with CEP concluded that inhaled corticosteroids in monotherapy are not sufficient in treatment and prophylaxis of CEP but may be useful in reducing the dose of oral corticosteroids; it is likely that the benefit of inhaled corticosteroids in asthmatic patients with CEP is due to the action on asthma rather than on CEP, with an action on the airway but not on alveolar disease.¹⁹ In adults and children therapeutic approach is not standardised⁷ but there is general agreement that treatment of CEP is based on oral corticosteroids: also our patient showed a dramatic good response to this approach. Clinical conditions and findings improved after 6 days and disappeared in few weeks of treatment.

We replaced systemic treatment with inhaled antiasthmatic steroids for her previous history of asthma. In two-year follow-up we did not observe any relapse.

In adults relapses are reported to be quite common in patients with CEP when systemic steroids are tapered or withdrawn, but inhaled-steroids appear to reduce both relapses and maintenance dose of systemic steroids^{9–11}. Recently omalizumab was successfully used in an asthmatic 36-year-old woman with continuous relapses and systemic side effects due to prolonged and elevated doses of oral corticosteroids.²⁰ It was suggested that this anti-IgE treatment could be an alternative choice in order to reduce oral steroids when their systemic side effects are present.

Learning points

- ▶ Although rare in children, chronic eosinophilic pneumonia (CEP) should be suspected in patients with recent onset of general symptoms, acute severe asthma episode not completely responding to appropriate treatment associated with characteristic chest x-ray findings and alveolar and/or blood eosinophilia.
- ▶ Bronchoalveolar lavage may support the diagnosis if eosinophilia is present, it may contribute to rule out other diagnosis, but a negative result does not rule out CEP.
- ▶ Oral corticosteroids dramatically improve the clinical course of CEP. The proper regimen and duration of treatment is not standardised.
- ▶ The use of inhaled steroids for pre-existing asthma has been suggested as a possible factor to reduce risk of relapses in adults; whether this approach should be recommended for CEP is still unknown and further studies are needed, especially in children.

Contributors DT conceptualized the case report, drafted the initial manuscript and approved the final manuscript as submitted. CDSC performed the literature review on eosinophilic lung disease and approved the final manuscript as submitted. FV performed the literature review on eosinophilic disease in children and approved the final manuscript as submitted. RP revised and reviewed the manuscript, provided support on data presentation and approved the final manuscript as submitted.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Carrington CB, Addington WW, Goff AM, *et al*. Chronic eosinophilic pneumonia. *N Engl J Med* 1969;280:787–98.
- 2 Nathan N, Guillemot N, Aubertin G, *et al*. Chronic eosinophilic pneumonia in a 13-year-old child. *Eur J Pediatr* 2008;167:1203–7.
- 3 Cakir E, Aksoy F, Cakir FB, *et al*. Chronic eosinophilic pneumonia with mucous plugs in a child. *Pediatr Pulmonol* 2010;45:1040–2.
- 4 Tanir G, Piskin IE, Aydemir C, *et al*. Idiopathic chronic eosinophilic pneumonia: a case report. *Tuberk Toraks* 2005;53:167–71.
- 5 Rao M, Steiner P, Rose JS, *et al*. Chronic eosinophilic pneumonia in a one-year-old child. *Chest* 1975;68:118–20.
- 6 Ribeiro JD, Fischer GB. Eosinophilic lung diseases. *Paediatr Respir Rev* 2002;3:278–84.
- 7 Marchand E, Reynaud-Gaubert M, Lauque D, *et al*. Idiopathic chronic eosinophilic pneumonia. A clinical and follow-up study of 62 cases. The Groupe d'Etudes et de Recherche sur les maladies 'Orphelines' pulmonaires (GERM'O'P). *Medicine (Baltimore)* 1998;77:299–312.
- 8 Jeong YJ, Kim KI, Seo IJ, *et al*. Eosinophilic lung diseases: a clinical, radiologic, and pathologic overview. *Radiographics* 2007;27:617–37.
- 9 Alam M, Burki NK. Chronic eosinophilic pneumonia: a review. *South Med J* 2007;100:49–53.
- 10 Naughton M, Fahy J, FitzGerald MX. Chronic eosinophilic pneumonia. A long-term follow-up of 12 patients. *Chest* 1993;103:162–5.
- 11 Marchand E, Cordier JF. Idiopathic chronic eosinophilic pneumonia. *Orphanet J Rare Dis* 2006;6:1–11.
- 12 Allen JN, Davis WB. Eosinophilic lung diseases. *Am J Respir Crit Care Med* 1994;150:1423–38.
- 13 D'Amours P, Leblanc P, Boulet LP. Chronic eosinophilic pneumonia associated with thrombocytosis and pleural effusion. *CMAJ* 1990;142:837–9.
- 14 Oermann CM, Panesar KS, Langston C, *et al*. Pulmonary infiltrates with eosinophilia syndromes in children. *J Pediatr* 2000;136:351–8.
- 15 Allen JN, Davis WB, Pacht ER. Diagnostic significance of increased bronchoalveolar lavage fluid eosinophils. *Am Rev Respir Dis* 1990;142:642–7.
- 16 Marcq M, de Muret A, Letourmy JM, *et al*. Carrington's disease without eosinophils in the bronchial lavage. *Rev Mal Respir* 2007;24:896–9.
- 17 Marchand E, Etienne-Mastroianni B, Chanez P, *et al*. Groupe d'Etudes et de Recherche sur les Maladies Orphelines Pulmonaires. Idiopathic chronic eosinophilic pneumonia and asthma: how do they influence each other?. *Eur Respir J* 2003;22:8–13.
- 18 Minakuchi M, Niimi A, Matsumoto H, *et al*. Chronic eosinophilic pneumonia: treatment with inhaled corticosteroids. *Respiration* 2003;70:362–6.
- 19 Durieu J, Wallaert B, Tonnel AB. Long-term follow-up of pulmonary function in chronic eosinophilic pneumonia. Groupe d'Etude en Pathologie Interstitielle de la Société de Pathologie Thoracique du Nord. *Eur Respir J* 1997;10:286–91.
- 20 Kaya H, Gumus S, Ucar E, *et al*. Omalizumab as a steroid-sparing agent in chronic eosinophilic pneumonia. *Chest* 2012;142:513–16.

Copyright 2013 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow