

4. Jederlinic PJ, Sicilian L, Gaensler EA. Chronic eosinophilic pneumonia: a report of 19 cases and a review of the literature. *Medicine (Baltimore)* 1988; 67:154–162.
5. King MA, Pope-Harman AL, Allen JN, et al. Acute eosinophilic pneumonia: radiologic and clinical features. *Radiology* 1997; 203:715–719.
6. Knutsen AP, Amin RS, Temprano J, Wilmott RW. Hypersensitivity pneumonitis and eosinophilic pulmonary diseases. In: Chernick V, Boat TF, Wilmott RW, Bush A, eds. *Kendig's Disorders of the Respiratory Tract in Children*. Philadelphia, PA: Saunders Elsevier, 2006, p. 696.
7. Tefferi A, Patnaik MM, Pardanani A. Eosinophilia: secondary, clonal and idiopathic. *Br J Haematol* 2006; 133:468–492.
8. Pardanani A, Brockman SR, Paternoster SF, et al. FIP1L1-PDGFR fusion: prevalence and clinicopathologic correlates in 89 consecutive patients with moderate to severe eosinophilia. *Blood* 2004; 104:3038–3045.
9. Cools J, Stover EH, Wlodarska I, et al. The FIP1L1-PDGFR alpha kinase in hypereosinophilic syndrome and chronic eosinophilic leukemia. *Curr Opin Hematol* 2004; 11:51–57.
10. Pope-Harman AL, Davis WB, Allen ED, et al. Acute eosinophilic pneumonia: a summary of 15 cases and review of the literature. *Medicine (Baltimore)* 1996; 75:334–342.

Address correspondence to:

Jean Bergounioux, MD, PhD

Pediatric Intensive Care

Hôpital Universitaire Necker Enfants Malades

AP-HP

149 rue de Sévres

Paris 75015

France

E-mail: jean.bergounioux@nck.aphp.fr

Received for publication November 16, 2012; accepted after revision December 18, 2012.

DOI: 10.1089/ped.2013.2316

COMMENTARY

Idiopathic Acute Eosinophilic Pneumonia—A Commentary

Yuval Tal, MD, PhD,¹ and Neville Berkman, MBCh²

Idiopathic acute eosinophilic pneumonia (IAEP) in the pediatric population is a relatively rare disease. It is one entity among a group of diseases that manifest with diffuse eosinophil infiltration of lung parenchyma and alveoli. Alveolar eosinophilia is generally defined as an eosinophil count greater than 25% in broncho-alveolar lavage (BAL; preferably more than 40%). In this case report, the authors describe a case of a 14-year-old male with acute onset of eosinophilic pneumonia, which presented with the classical clinical syndrome. In light of the differential diagnosis, the authors conducted a complete clinical and laboratory evaluation.

IAEP is a rapidly evolving condition. Disease progression can be very dramatic, hence the discrimination of acute (<1 month) versus chronic (>1 month) eosinophilic lung disease. Perhaps its dramatic evolution is the key feature that differentiates IAEP from most of the other eosinophilic lung diseases.

When diagnosed early, IAEP generally has a good prognosis, and recurrence is rare. As in the case presented here, a male predominance is noted, with a mean age of 30. The patient's medical history contains no other relevant disorders such as asthma. Smoking seems to be the most significant

risk factor, especially among patients with a recent onset of smoking, change in smoking habits, or renewal following cessation of smoking. That effect might suggest an immune facilitating agent within the tobacco smoke. IAEP may be triggered by various inhaled contaminants. However, the patient had no such exposure. Interestingly, smokers seem to have high serum IgE levels, even without overt illness. The above remark does not apply to the patient described here, as his IgE levels were well within the normal range. No drugs were used prior to the onset of disease and as such this etiology could be ruled out.

In light of its acute onset, IAEP is usually misdiagnosed at its early stages as bacterial pneumonia (community acquired pneumonia—CAP). As such, antibiotic therapy is invariably initiated. As the disease progresses, patients develop dyspnea and moderately elevated fever, generally accompanied with a cough. Most patients will suffer from pleuritic chest pain, and some will complain of myalgia and abdominal cramps. Abdominal manifestations may be a function of eosinophil activation and a TH₂ allergic inflammation, which tends to secrete IL-13 into the circulation. Indeed, most of these clinical features were noted in this case, suggesting the possibility of IAEP.

¹Allergy and Clinical Immunology Unit, Medicine Department, Hadassah University Hospital, Jerusalem, Israel.

²Pulmonology Institute; Medicine Department, Hadassah University Hospital, Jerusalem, Israel.

An important point needs to be highlighted regarding the absence of peripheral blood eosinophilia in IAEP. Most patients with IAEP have normal peripheral blood eosinophil counts initially in contrast to idiopathic chronic eosinophilic pneumonia (ICEP). As described in this case, the eosinophil titers rise quickly, within days of the onset of disease. The key to diagnosis is, of course, the BAL. As seen in the case presented, BAL is positive for IAEP when eosinophils constitute more than 25% of the lavage cell count. Other biomarkers such as elevated IL-5 and IL-18 could further point to the possibility of IAEP, but are neither specific and sensitive nor practical to perform.

The patient described here presents classical and almost complete criteria for IAEP, as adequately described in the manuscript. As the authors elaborate, the alternative, primarily infectious, diagnoses need to be excluded in order to establish the diagnosis of IAEP. Intestinal parasitism and allergy are, of course, the most prevalent causes of blood eosinophilia, and must be ruled out. However, these conditions rarely present with such a degree of eosinophilia. Consequently, the additional clinical manifestations demonstrated cannot be explained by these well-known diagnoses. One must remember that not all intestinal parasites induce elevated blood eosinophilia. While helminths ascribe for parasitic infections with eosinophilia, gastrointestinal parasitic infections such as giardiasis and *Entamoeba histolytica* usually do not elicit blood eosinophilia. In order for a parasitic infection to induce pulmonary eosinophilia, it must multiply within the human host and cause the pulmonary eosinophilia during larval migration through the lungs. As mentioned by the authors, the most common infections in the Western world are caused by *Strongyloides stercoralis*, *Ascaris lumbricoides*, *Toxocara canis*, and *Ancylostoma* species.

Two additional groups of diseases that must be ruled out are autoimmune and primary eosinophil disorders. Autoimmune diseases that sometimes involve the lungs, such as systemic lupus erythematosus, rheumatoid arthritis, and other connective tissue diseases, present with eosinophil counts that are usually significantly lower and a disease course that is often not as acute. These diseases are generally more prevalent in adults and mainly affect women. Among the autoimmune group of diseases, allergic granulomatous angiitis (formerly Churg–Strauss syndrome) should be considered. This disorder is defined as an extremely rare small vessel vasculitis with lung granuloma formation. As in ICEP, it is more common in asthmatics. Approximately half of patients have positive anti-neutrophil cytoplasmic anti-

bodies (ANCA), mainly of the perinuclear type. In the present case scenario, the acute presentation, absence of asthma, and negative ANCA antibodies refute this diagnosis. Allergic bronchopulmonary aspergillosis is yet another disease related to asthmatics and a Cystic Fibrosis background. This disease is also chronic in nature and is characterized by elevated IgE levels, a positive skin test for *Aspergillus fumigatus*, and serum specific anti-*Aspergillus* IgE or IgG antibodies.

Hypereosinophilic syndrome is a group of disorders characterized by sustained overproduction of eosinophils. Recent definition requires only the presence of more than 1,500 eosinophiles/microliter, signs of eosinophil mediated end organ damage, and lack of other apparent etiology. As seen in the case report, this group of diseases was well considered. The evaluation yielded negative bone marrow findings, no tyrosine kinase chimeric PDGFRA/FIP1L1 protein, and normal T-cell receptor complex, as could be seen in the absence of CD3–/CD4+ T cells (typical of the lymphocyte hypereosinophilic syndrome variant).

In conclusion, IAEP is a rare disorder, especially in pediatric patient, with acute onset of fever accompanied by hypoxemia, bilateral lung infiltrates, and a BAL eosinophil count greater than 25%. Peripheral blood eosinophil levels are usually not elevated at presentation. Recent onset of tobacco smoking or exposure to inhaled dust is the only apparent risk factors in otherwise healthy patients. Treatment, as was very well summarized in the case report, is based primarily on steroids. If diagnosed and treated on time, the disease has a very good prognosis overall, and does not tend to recur. The key to managing patients with IAEP is high index of suspicion in patients with “acute severe pneumonia” invariably without peripheral blood eosinophilia. Timely performance of BAL is mandatory in such patients.

Address correspondence to:
Yuval Tal, MD, PhD
Allergy and Clinical Immunology Unit
Department of Medicine
Hadassah Hebrew University
Medical Center Ein-Kerem
POB 12000 Jerusalem
Israel 91120

E-mail: yovalt@hadassah.org.il