Idiopathic acute eosinophilic pneumonia

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Abstract
Idiopathic acute eosinophilic pneumonia (IAEP) is characterized by acute febrile respiratory failure associated with diffuse radiographic infiltrates and eosinophilia in bronchoalveolar lavage fluid (BAL) in the absence of infection. Patients, who are initially healthy and often young, present with severe hypoxemia (partial pressure oxygen / fractional inspiratory oxygen, PaO2/FiO2 < 200 in most cases). BAL allows diagnosis by showing eosinophilia (25-80%) without evidence of infection. IAEP may be mistaken for acute respiratory distress syndrome if BAL differential cell count is not performed. The exact prevalence of IAEP is unknown. It is a rare disorder with less than 100 cases reported so far and the largest series including 15 patients only. Steroid treatment is recommended since IAEP can lead to life-threatening respiratory failure. No relapse is observed after recovery.

Keywords
eosinophilic pneumonia, bronchoalveolar lavage, respiratory failure, ARDS

Disease name and synonyms
Idiopathic acute eosinophilic pneumonia (IAEP)
Acute eosinophilic pneumonia

Definition
Idiopathic acute eosinophilic pneumonia (IAEP) is an eosinophilic pneumonia of undetermined etiology without systemic manifestations. It is characterized by acute respiratory failure, diffuse bilateral lung infiltrates on chest X-ray, and pulmonary eosinophilia (1). IAEP has been characterized as a distinct entity in 1989 (2).

Diagnosis criteria
The criteria currently proposed for diagnosis are:
1. Acute onset: onset of any symptoms usually within 7 days before presentation;
2. Fever;
3. Bilateral infiltrates in chest films;
4. Severe hypoxemia: PaO₂ (partial pressure oxygen) on room air < 60 mm Hg, and/or oxygen saturation on room air < 90 %, and/or A-a (alveolo-arterial) gradient > 40;
5. Lung eosinophilia: bronchoalveolar lavage (BAL) differential cell count with > 25% eosinophils (or predominance of eosinophils in open lung biopsy);
6. no history of hypersensitivity to drugs, no history or laboratory evidence of infection, and no other known cause of eosinophilic lung disease (3).

Frequency
The exact prevalence of IAEP is unknown. It is a rare disorder with less than 100 cases reported so far and the largest series including 22 patients only (3, 4). In June 1999, we conducted a multicentric retrospective study of IAEP: in June 1999, 5300 specialists in intensive care and/or respiratory medicine in France, Belgium, and Switzerland received a letter asking them to report the cases of IAEP they had previously observed. Among the 34 answers, 22 cases fitted with the above-mentioned diagnosis criteria of IAEP (5).

Etiology
No well-defined cause was found in the reported cases of IAEP. However, in some patients, IAEP developed after exposure to dust (1). IAEP has also been reported in patients who started smoking less than 3 months before disease onset (6, 7). In our experience 6 out 8 smokers with IAEP were recent smokers (5). It is unlikely that smoking is the sole cause of IAEP, but exposure to smoke or other environmental agents may facilitate the onset of IAEP.

Clinical presentation
IAEP onset is acute in individuals that are initially healthy. In contrast with chronic eosinophilic pneumonia, patients are young, with an average age at presentation usually below 30 years (29±15 in our series). Males are predominantly affected (3, 5). The duration of symptoms until diagnosis of IAEP is usually less than 7 days (2 to 3 days). However, IAEP cases have been reported in patients with symptoms which lasted up to 1 month (5, 8). All the patients initially present with fever and dyspnea, and two thirds of them have cough and chest pain. Myalgia and abdominal pain may also be noted, but in less than one third of patients (3). At physical examination, all patients are tachypneic, and crackles are a predominant finding at auscultation (1, 3). Chest X-ray shows bilateral infiltrates in all the patients. Diffuse bilateral air-spaces opacities, mixed air-space and interstitial opacities are the 3 most current radiographic patterns (3, 9). Bilateral small pleural effusion is common. Computed tomography of the chest confirms that bilateral air-space opacities are the most current imaging pattern, associated with bilateral pleural effusion in most of the patients. The chest X-ray returns to normal within 1 month (3).

Diagnostic methods
BAL is the key to diagnosis of IAEP, showing eosinophilic alveolitis (37 to 54 %) and increased neutrophils and lymphocytes (3, 5). BAL fluid culture and staining for fungi or other infectious agents are negative. When performed, transbronchial or open lung biopsy shows alveolar and interstitial infiltration by eosinophils, associated with interstitial edema (3). Organizing diffuse alveolar damage may also be present (8). Lung biopsy may be considered in immunocompromised patients developing IAEP, especially when potential fungi exposure is present (3), but BAL eosinophilia obviates this procedure in most non-immunocompromised patients.

Differential diagnosis
1. Chronic eosinophilic pneumonia (CEP)
IAEP differs from CEP mainly by its acute onset within a few days (average of 19 weeks in CEP), the absence of asthma (about of half of the patients in CEP), a higher proportion of smokers, a male predominance, the onset of acute respiratory failure and no relapse after pneumonia improves (11).

2. Eosinophilic pneumonia of determined origin
IAEP can resemble fungal pneumonia (especially invasive aspergillosis or Pneumocystis carinii pneumonia in immunocompromised patients) or parasitic lung infection (Strongyloides stercoralis, filaria, and...
others). A large number of drugs can also cause eosinophilic pneumonia (1, 3).

3. **Churg-Strauss syndrome**

This systemic vasculitis associated with adult-onset asthma differs from IAEP by the presence of peripheral blood eosinophilia and the involvement of non-pulmonary organs (1).

**Treatment and outcome**

Steroid therapy has been used in most of the reported cases of IAEP. However, it may be initiated only when an infectious cause has been confidently excluded (3). The dose and duration of steroid treatment vary widely in the literature, but all treated patients received intravenous steroid first, and orally thereafter. In our experience and in the literature, some patients recovered spontaneously (5, 12). Although efficacy of steroid therapy has not been demonstrated, it is recommended in IAEP patients with life-threatening hypoxemia. When mechanical ventilation is required, the patient’s condition improves rapidly and weaning is possible within 1 week (3, 5). In our experience non-invasive ventilation has also been successfully used with favourable outcome within a few days (5). Except one reported case of hypoxemia-related death, patients usually recover rapidly. This constant favorable outcome is another clinical feature that distinguishes IAEP from ALI/ARDS. After recovery, no eosinophilia is found at BAL (1). In contrast with CEP, no relapse occurs after stopping steroid treatment.

**References**