FEVER AND BILATERAL INFILTRATES ON CHEST RADIOGRAPHS IN PATIENTS WITH BRONCHIAL ASTHMA

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ABSTRACT
Idiopathic acute eosinophilic pneumonia is an acute febrile illness that can result in life-threatening respiratory failure. Typical symptoms on presentation are dry cough, tachypnea, dyspnea, fever, chest pains and myalgias lasting a few days. Radiographic signs consist of areas of opacity in the air space of non-segmental distribution, interlobular septal thickening, Kerley B lines and pleural effusion, therefore mimicking the imaging pattern of cardiogenic pulmonary edema. Since it may be mistaken for other diseases the diagnosis may be missed or delayed. Therapy with steroids results in complete recovery without relapse.

Keywords: idiopathic eosinophilic pneumonia, bronchial asthma

INTRODUCTION
Eosinophil leucocytes are primarily tissue cells, with bi-lobar nucleus and granules containing different pre-formed and cytotoxic mediators. Besides, these cells synthesize the substances which give protection from exogenous noxes. Under normal conditions, the number of tissue eosinophils is 200–400 times higher than number of eosinophils in blood. During the last 15 years there was significant change of knowledge about cell structure, function and pathophysiological role of eosinophil leucocytes in genesis of different disorders.

The term eosinophilia designates presence of more than 450 eosinophils per microliter of blood. The causes of disorders with eosinophilia are various, and often unknown. There is whole spectrum of clinical presentations, from benign, almost asymptomatic, infiltrative shadows on chest X-ray, accompanied with eosinophilia, to malignant, often uncurable, hypereosinophil syndrome, which is close to eosinophil leukemia. The main sign of idiopathic eosinophilic pneumonia (IEP) is excessive accumulation of eosinophils in lung alveolar space (more than 50% of alveolar cells). The role of eosinophils in pathogenesis of this disorder is not clarified yet.

CASE REPORT
The patient V. S., female, 61 years old, is suffering from bronchial asthma for 10 years, being several times already hospitalized. The „atopic“ constitution was confirmed, as well as reversible obstruction of airways. She has been admitted to the hospital due to high fever, cough productive of little sputum, significant dyspnea, vertigo with unstable gait, malaise and infiltrates on chest radiographs.

The onset of the disease was sudden, around 15 days before the admission to the hospital. Before the admission, she was treated with antibiotics, but without success; she was then referred to the hospital.

On admission she presented herself with high fever (39°C), mild dyspnea, lacking dynamics, paller of skin and mucose membranes, medium constitution and usual appearance. Auscultation of the chest revealed decreased breath sounds with lot of late expiratory cracks, on both sides from the lower parts, but somewhat more on the right. Moderate tachycardia was noted (108 beats/min), and heart sounds were normal; blood pressure was 140/80mmHg.

Physical examination of other parts of the body did not reveal other signs of a disease.

The chest radiograph shows bilateral infiltrates (Figure 1).

Figure 1. Chest radiographs at admission to hospital.
Measurement of arterial blood gas composition showed decreased partial pressure of oxygen (PaO$_2$ 7.6kPa), hemoglobin saturation 91%, hypocapnia (PaCO$_2$ 3.82kPa) and respiratory alkalosis (pH: 7.48). The electrocardiograph showed only sinus tachycardia.

The blood chemistry showed signs of inflammation: sedimentation rate 122 mm/h, fibrinogen 9.6 g/l, leukocyte count 16.0 x 10$^9$/L, mild anemia (hemoglobin 110 g/l), mild increase in aminotransferases (AST 136 μmol/l, ALT 70 μmol/l). The differential leukocyte count showed 68% of neutrophils, 24% of lymphocytes, 4% of eosinophils, and 4% of monocytes. The other blood chemistry tests were within normal reference range. The culture of sputum did not reveal patogens, and direct microscopy of sputum smears did not reveal acid-fast rods. Several blood cultures were negative, as well as tuberculin test. Pulmonary function tests showed restrictive ventilatory insufficiency of medium severity (VC 1.72-65.8%, FEV$_1$ 1.49 -66.1%, FEV$_1$/FVC 79.5%).

Based on the patient's history (sudden onset), physical examination, chest radiograph and blood chemistry, the first working diagnosis was bilateral pneumonia, and antibiotic treatment was started (combination of cephalosporin, aminoglycoside and quinolone). After initial antibiotic therapy clinical improvement was not observed: high fever was persistent, erythrocyte sedimentation rate increased, leukocytosis was also present (ESR 117mm/h, Le 11.0 x 10$^9$/L), and repeated chest radiography 7 days later showed new infiltrations (Figure 2).

The pulmonary function tests were in the reference range at discharge from the hospital (VC 2.16 - 88.2%, FEV$_1$ 1.92 -92.4%, FEV$_1$/FVC 85.74%), as well as the arterial blood gas composition (PaO$_2$ 11.2kPa, PaCO$_2$ 5.42kPa, pH 7.43). Treatment with systemic corticosteroids was administered for 40 days, and then inhaled corticosteroids were continued.

**DISCUSSION**

Disorders of lung parenchyme accompanied by eosinophilia in peripheral blood and lung tissue, were named in various ways, making confusion. Only recently the terms became more precise and agreed by majority.
After the first description of eosinophil pneumonias, there were several other attempts to describe and classify this disorder. One of the classifications was done by Liebow and Carrington (1966 and 1969), and it was based on main causes of migrating lung infiltrates accompanied with tissue and blood eosinophilia (1).

Wide spectrum of conditions accompanying eosinophilia enabled categorization of these disorders, and use of popular abbreviation CHINA:

Connective tissue diseases
Helminthic infections
Idiopathic Hypereosinophil Syndrome
Neoplasm
Allergies

During the last two decades, the role of eosinophils in pathogenesis of these diseases was clarified. Primary stimuli for growth and differentiation of eosinophils are Interleukin-5 (IL5), Interleukin-3 (IL3) and Granulocyte-macrophage colony-stimulating factor (GM-CSF). The eosinophils release toxic, pre-formed products, like main alcaline protein, eosinophil cation protein, eosinophil neurotoxin and eosinophil peroxidase. Eosinophils also produce different cytokines, including IL-2, IL-3, IL-4, IL-5, IL-7, IL-13, IL-16, growth factors (TGF-beta) and tumor necrosis factor (TNF-alfa). Accumulation of eosinophils in lungs leads to destruction of parenchyme through release of the cytotoxic substance, eosinophil cation protein (ECP), which is responsible for the eosinophil’s nickname „angry cells“ (2).

The latest classification of eosinophil pneumonias recognizes two groups:

Primary (idiopathic): which by their course could be acute and chronic,
Secondary: caused by drugs (amiodarone, nitrofurantoin, sulphonamides, gold salts) or parasites (Ascaris lumbricoides, Strongiloides stercoralis).

Acute eosinophil pneumonia comes with sudden onset, high fever, muscle pain, tachycardia, tachipnea, pleural pain with possible development of respiratory insufficiency, and basal cracks without wheezing. Chest radiograph shows bilateral, peripheral lung infiltrates (3, 6, 7). Chronic eosinophil pneumonia comes with gradual onset, low-grade fever of long duration (several weeks or months), cough, dispnea, decrease of body weight and night sweating. The majority of patients (about 60%) suffered from allergic rhinitis and bronchial asthma, and physical examination reveals wheezing during expiration. The chest radiographs shows lung infiltrates, and the picture looks like the „negative“ of lung edema (4).

Laboratory tests which suggest eosinophil pneumonia are: eosinophilia in peripheral blood and sputum, increased level of IgG immunoglobulins (in two-thirds of the patients), positive C-reactive protein and increased erythrocyte sedimentation rate (5). Finding of parasites in fecal specimens points to secondary eosinophil pneumonia.

In our patient, clinical presentation, chest radiographs and eosinophilia in peripheral blood suggested a kind of lung eosinophilia. Simultaneous existence of eosinophilia and bronchial asthma raised suspicion on allergic granulomatous angitis (Churg-Strauss). However, the absence of other signs (renal insufficiency, skin disorder, nasal polyps, sinusitis, allergic rhinitis) does not stand for sistemic vasculitis. The absence of intestinal infestation, negative skin prick test on Aspergillus fumigatus and abstinence from use of certain drugs (amiodarone, sulphonamides, gold salts) excludes parasite-induced eosinophil pneumonia, allergic broncho-pulmonary aspergilosis and drug-induced lung eosinophilia.

In the case of our patient, establishing of diagnosis was delayed, due to dominant vertigo with neurological deficit, which, together with suspicious cytological findings, raised concern for brain metastases. Considerable amount of time was spent on excluding malignant disease, which also could be accompanied with eosinophilia. Neurological deficit accompanying eosinophil pneumonia is known in medical literature, albeit as rare phenomenon. However, due to unclear pathogenetic mechanisms, they are still object of intense research.

REFERENCES