

CASE REPORT

PHOTOGRAPHIC NEGATIVE OF PULMONARY EDEMA. DIFFERENTIATING CHRONIC EOSINOPHILIC PNEUMONIA FROM CHRONIC HYPERSENSITIVITY PNEUMONITIS.

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ABSTRACT:

A 60 years old diabetic and hypertensive lady presented with exertional dyspnea and dry cough of one year duration. Respiratory evaluation revealed bilateral coarse crackles, SpO₂ was 96% and her spirometry had restrictive abnormality. High resolution computerised tomography (HRCT) chest was consistent with patchy ground glass and dense opacities predominantly involving peripheral and lower lung zones (photographic negative of pulmonary edema) and her BAL eosinophilia (41%) in the presence of clinical and radiological abnormalities was diagnostic of chronic eosinophilic pneumonia. She showed good response to oral prednisolone treatment.

Key words: Bronchoalveolar lavage, chronic eosinophilic pneumonia, peripheral alveolar infiltrates, pulmonary edema, transbronchial biopsy.

INTRODUCTION:

Chronic eosinophilic pneumonia (CEP) is an idiopathic disorder characterized by an abnormal accumulation of eosinophils in the lung parenchyma and often presents as a subacute illness¹. The typical chest radiographic findings are of bilateral peripheral or pleural-based infiltrates with lung tissue showing eosinophilia on lavage or biopsy². The mainstay of management remains corticosteroids¹.

CASE REPORT

A 60 years old lady resident of Lahore presented in pulmonary clinic with history of gradually progressive exertional dyspnea of grade II (NYHA) and dry cough of one year duration. She was suffering from diabetes mellitus and hypertension with good control and was taking her medications (Lantus insulin, losartan potassium and acetyl salicylic acid) regularly. In the past, she was never hospitalized for any medical or surgical ailment. She was married, with four healthy children and was a never smoker, who also denied any addiction and narrated the presence of many types of avian in the backdoor neighbors. However, she had no direct contact with any domestic pets, organic or inorganic dusts or aerosols. She belonged to a middle social class and her family & gynecological histories were insignificant. On examination she was an average built lady, well oriented and cooperative with following vitals: pulse 74/min, regular, BP 110/70 mmHg, respiratory rate 20 breaths per minute, temperature of 98 °F and SpO₂ was 96% (on room air). Chest examination was consistent with bilateral coarse crackles and slightly increased vocal resonance in middle to lower parts of chest bilaterally both anteriorly and posteriorly. Remaining general and systemic examination was normal. Chest radiographic findings included preserved lung volumes with patchy peripheral subpleural linear opacities; more concentrated on left middle and lower zones (figure 1).

Her office spirometry showed severe restriction (FEV₁ 1.00 L {56 % pred}, FVC 1.02 L {48 % pred}, FEV₁/VC ratio 126%. Her arterial blood gas analysis revealed pH 7.39, PO₂ 85 mmHg, PCO₂ 34 mmHg and HCO₃ 22 mmol/L. Based on the history of questionable exposure to neighbour's birds, clinical examination of crackles on chest auscultation, lower lung field infiltration and restrictive spirogram, a provisional diagnosis of chronic hypersensitivity pneumonitis was constructed with a plan of further investigations.

Laboratory evaluation showed a hemoglobin of 14.3 g/dL, WBC count 12000/cmm (neutrophils 37.3%, lymphocytes, 47.4%, monocytes 10.8%, **eosinophils 3.8%** and basophils 0.7%) platelets 300000/cmm and ESR of 20 mm/1st hour. Her serum biochemical analysis included blood urea nitrogen 16 mg/dL, creatinine 1.0 mg/dL, albumin 3.5 mg/dL while other liver function tests and serum electrolytes were within the normal range. Serum avians precipitins test was not available and total serum IgE level was 50.8 IU/mL. RA factor and ANA were negative, urine routine analysis was normal and stool examination showed no ova or parasites. Echocardiography showed no significant abnormality except mild left ventricular hypertrophy with ejection fraction of 70%. HRCT of the chest (figure III, IV and V) was consistent with patchy ground glass and dense opacities predominantly involving peripheral and lower lung zones (photographic negative of pulmonary edema). Analysis of grossly clear BAL cells revealed WBC 390/ul, RBC 02/ul, neutrophils 19%, monocytes 40% and eosinophils 41%, while BAL cytology revealed alveolar macrophages, few scattered benign columnar and squamous epithelial cells with inflammatory cells comprising eosinophils, lymphocytes and occasional multinucleated giant cells in background, all features highly suggestive of chronic eosinophilic pneumonia while absence of plasma cells and mast cells was against the diagnosis of chronic hypersensitivity pneumonitis. BAL malignant cytology was negative and Gram staining, ZN staining, fungal smear and pyogenic bacterial culture were also negative. Transbronchial biopsy showed normal lung parenchyma without any granuloma or malignant change.

On the basis of her HRCT chest findings (patchy ground glass and dense opacities predominantly involving peripheral and lower lung zones) and BAL eosinophilia (41%), she was finally diagnosed as having chronic eosinophilic pneumonia and was started with prednisolone 30 mg daily. She came for follow up after one month and revealed much improvement in her symptoms, her office spirometry showed values of FEV₁ & FVC almost double from the previous values and there was slight improvement in the radiological shadowing on chest radiograph. She was advised to continue prednisolone in the same dosage and was advised regular monthly follow ups.



Figure I: CXR-PA: Patchy peripheral subpleural opacities; more concentrated on left side.

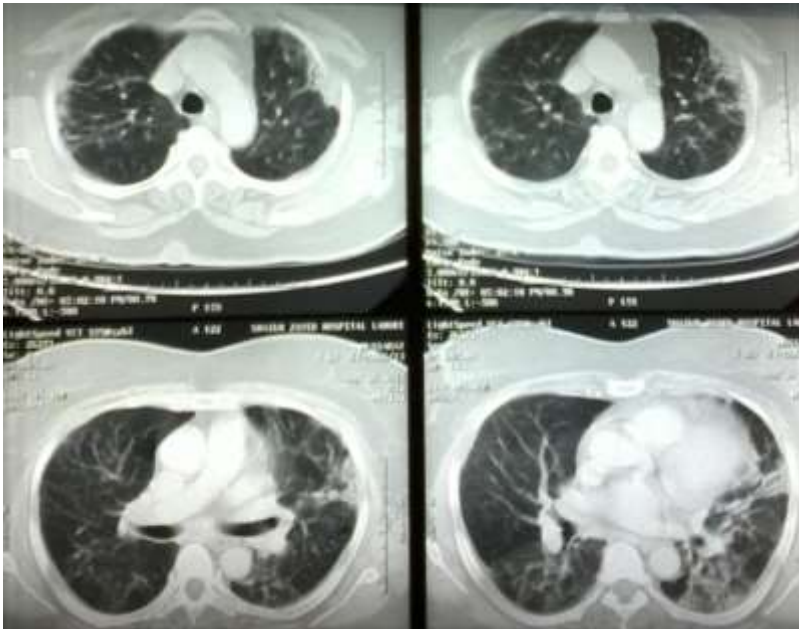


Figure II: HRCT Chest: Patchy ground glass opacities predominantly involving peripheral and lower lung zones, more concentrated on the left side.



Figure III: HRCT Chest: Patchy ground glass opacities predominantly involving peripheral and lower lung zones.



Figure IV: CXR-PA: Follow up at 6 weeks after treatment with corticosteroids showing slight improvement in bilateral opacities (ignore line artifact on left side).

DISCUSSION:

The eosinophils mature in the bone marrow and circulates in the blood for about one day before being attracted into tissues, where they undergo apoptosis unless survival factors are present.³ Activation results in degranulation with release of major basic protein (MBP), eosinophil cationic protein (ECP), eosinophil-derived neurotoxin (EDN), & eosinophil peroxidase (EPO); all of these can result in tissue inflammation and damage.³ Eosinophilic lung diseases are characterized by abnormally increased numbers of eosinophils within the pulmonary parenchyma². The defining characteristics needed for the diagnosis of pulmonary eosinophilia include either, peripheral blood eosinophilia with radiographically identified pulmonary abnormalities, lung tissue eosinophilia demonstrated in Transbronchial or open lung biopsies or increased eosinophils in bronchoalveolar lavage (BAL) fluid³. Peripheral blood eosinophilia is, by no means, uniformly increased in many types of eosinophilic lung diseases, and routine chest radiographs may fail to detect infiltrates in some cases⁴. The classification of peripheral blood eosinophilia include mild (500 to 1500 cells/microL), moderate (1500 to 5000 cells/microL), severe (>5000cells/microL) and hypereosinophilia with counts >1500/microL />1.5 x 10⁹/L on two examinations separated in time by at least one month and/or tissue hypereosinophilia⁵. Primary eosinophilia usually occurs in the context of hematologic malignancies, such as acute leukemias or chronic myeloid disorders; secondary eosinophilia causes include tissue invasive parasites, allergic disorders, medications, toxins, autoimmune diseases, & endocrine disorders e.g Addison's disease while idiopathic eosinophilia is documented after ruling out either a primary or secondary cause of eosinophilia⁵.

Chronic eosinophilic pneumonia (CEP) is an idiopathic disorder characterized by an abnormal accumulation of eosinophils in the lung and presents clinically as a subacute illness with a constellation of symptoms including cough, fever, progressive breathlessness, weight loss, wheezing, and night sweats of weeks to several months duration². CEP can often present as a fulminant illness with a constellation of symptoms including cough, fever, progressive breathlessness, weight loss, wheezing, and night

sweat¹. Asthma accompanies or precedes the illness in 50 percent of cases and peripheral eosinophilia is common, but may be absent in 10 to 20 percent of patients⁶. CEP occurs predominantly in women and non-smokers and cases have been reported following radiation therapy for breast cancer⁷. Peripheral blood eosinophilia (>6 percent), a very high sedimentation rate, C-reactive protein, iron deficiency anemia, and thrombocytosis are all common laboratory abnormalities in patients with CEP⁸. On chest radiograph or HRCT, bilateral peripheral or pleural-based infiltrates (photographic negative of pulmonary edema) is virtually pathognomonic for the disease but found in less than one third of cases⁹. These radiological findings can also be found in chronic hypersensitivity pneumonitis (CHP) and cryptogenic organizing pneumonia (COP) and the differentiation can be made with bronchoalveolar lavage and lung biopsy findings¹⁰. BAL eosinophilia of greater than 25 % is consistent with acute eosinophilic pneumonia (AEP) and greater than 40% is suggestive of CEP, while CHP and COP are characterized by BAL lymphocytosis^{2,10}. Histopathologic findings in CEP are characterized by interstitial and alveolar eosinophils and histiocytes, including multinucleated giant cells in contrast to CHP where plasma cells and mast cells predominate with evidence of non caseating granulomas^{1,2,10}. Rarely there may be tracheobronchial nodular lesions in patients with CEP¹¹.

The management of CEP including relapses are treated with corticosteroids (prednisolone) for 6-9 months and occasionally patients require lifelong treatment¹. A favorable response to corticosteroid therapy is typically defined by resolution of presenting symptoms, especially dyspnea, cough, and fever, decline in peripheral eosinophilia, marked reduction or clearing (in most cases) of roentgenographic abnormalities and physiologic improvement as measured by FVC, TLC, DLCO, and resting and exercise gas exchange¹. Fewer than 10% of patients with CEP spontaneously recover or improve and the overall prognosis is excellent¹². Relapse does not appear to indicate treatment failure, a worse prognosis, or greater morbidity as patients with CEP continue to be steroid-responsive and to respond to corticosteroid doses at levels similar to those prior to the relapse¹². In addition, CEP occasionally leads to physiologically important, irreversible fibrosis or mild persistent airflow obstruction¹³.

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