Case Report

Acute eosinophilic pneumonia simulating severe community acquired pneumonia

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ABSTRACT

Idiopathic acute eosinophilic pneumonia is a recently described cause of acute respiratory failure. It usually affects young healthy individuals. Usually non-pulmonary organs are not involved. Bronchoalveolar lavage eosinophilia is required for diagnosis. This disease responds uniformly to a short course of corticosteroids and does not recur. We report a young man who presented with a 2-day history of acute respiratory failure simulating severe community acquired pneumonia and necessitating mechanical ventilation. The diagnosis was made based on the classical clinical presentation and bronchoalveolar lavage and peripheral blood eosinophilia. Acute eosinophilic pneumonia in our patient was associated with acute hepatitis and erythema multiforme. To our knowledge, this is the first time to report such an association. The case is reported with review of the literature.

Keywords: Acute eosinophilic pneumonia, eosinophilic lung diseases, hepatitis, erythema multiforme.

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Idiopathic acute eosinophilic pneumonia (AEP) has been described recently as a rare cause of acute respiratory failure in previously healthy individuals. While in adults the first 2 reports appeared in 1989,[1,2] in pediatrics, the first report appeared in 1992.[3] The largest case series included 15 cases.[4] We report here a young patient with AEP who presented with acute respiratory failure and bilateral lung infiltrate simulating severe community acquired pneumonia. Our patient developed hepatitis and erythema multiforme. To our knowledge these associations have not been reported before.

Case Report. Our patient is an 18-year-old non-smoker Saudi male who is new to our institute. He is known to have mild intermittent bronchial asthma on salbutamol inhaler. He presented initially to a local dispensary with a 2-day history of high fever, dry cough, progressive shortness of breath, myalgias and generalized skin rash where salbutamol nebulizer was prescribed as a possible exacerbation of bronchial asthma. As the patient's condition continued to deteriorate, the family brought the patient to King Khalid University Hospital (KKUH) a few hours after his initial presentation for further management. There was no history of wheeze, chest pain, hemoptysis, recent travel, contact with animals, recent use of medications or illicit drug use.

On presentation, the patient was in severe respiratory distress. Respiratory rate was 49/minute, heart rate 138/minute, blood pressure 140/70 and temperature 37.4°C. He was cyanosed. There was no clubbing, palpable lymph nodes or pallor and jugular venous pressure was not raised. Breath sounds were diminished bilaterally, with prolonged expiration and coarse basal inspiratory crackles and scattered ronchi. Apart from tachycardia, cardiac examination was normal. The patient had mild tenderness in the right upper quadrant but no palpable organomegaly. He had target like skin lesions involving palms, soles and trunk (diagnosed by the dermatologist as erythema multiforme). The

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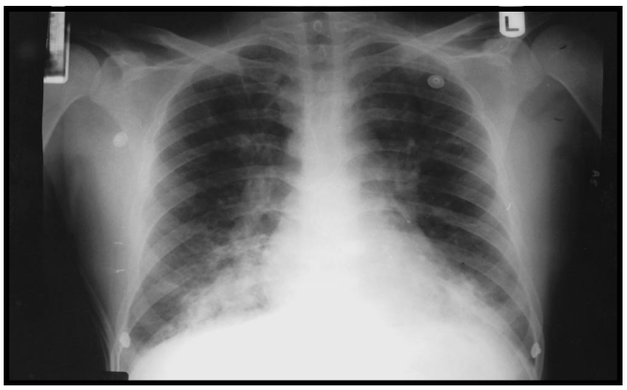

Figure 1 - Confluent areas of mixed alveolar and interstitial infiltrates at both bases extending to the perihilar areas with Kerley B lines.

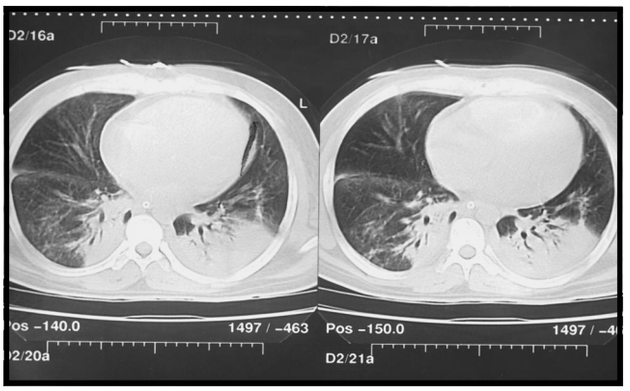

Figure 3 - Computed tomography scan of the chest showed basal areas of consolidation and ground glass appearance.

rest of the examination was normal. Chest radiograph (CXR) showed confluent areas of mixed alveolar and interstitial infiltrates at both bases extending to the perihilar areas with Kerley B lines (**Figure 1**). Electrocardiogram showed sinus tachycardia. Room air arterial blood gases showed: pH 7.36, partial pressure of oxygen oxygen (PO_2) 53 mmHg, partial pressure of carbon dioxide (PCO_2) 36 mmHg, serum bicarbonate (HCO_3) 20 mmol/L. Complete blood count showed white blood cell (WBC) of 28,000 with 85% neutrophils and 3% eosinophils. Erythrocyte sedimentation rate (ESR) was 5 mm/hour. Liver function test showed mild elevation in transaminases (double normal). Other blood tests were normal.

The patient was admitted to the medical intensive care unit. Due to respiratory failure, the patient was intubated and mechanically ventilated within a few hours of his admission. Chest radiography after intubation showed significant increase in the alveolar infiltrates and bilateral pleural effusion (**Figure 2**). After septic work up, he was started on broad-spectrum antibiotics as a case of severe community acquired pneumonia.

Transthoracic echocardiogram revealed normal left ventricular dimensions and function and absence of pericardial effusion. Fibro-optic bronchoscopy showed edema and erythema of the bronchial mucosa. Broncho-alveolar lavage (BAL) showed no bacteria, mycobacteria, pneumocyctis carinii nor fungi. Antinuclear antibody was negative as well as legionella and mycoplasma antibodies and viral antigens and culture. He required FiO_2 of 80% in addition to sedation and muscle relaxants. His peak airway pressure was 43 cmH_2O and plateau of 37 cmH_2O with a tidal volume of 500 ml. Computed tomography scan of the chest showed basal areas of consolidation and ground glass appearance (**Figure 3**). Two days after admission, eosinophils percentage increased to 13% and 2 days later to 40% and ESR increased to 105 mm/hour. Liver enzymes (transaminases) were increasing gradually where they reached 6 times normal (alanine transaminase ALT 252 U/L {range13-40 U/L}, aspartate

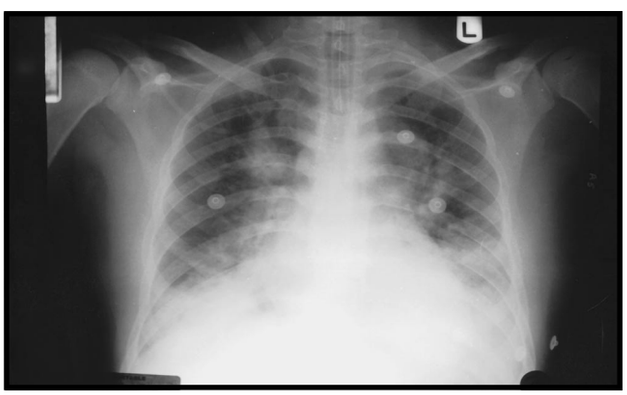

Figure 2 - Chest radiograph after intubation showed significant increase in the alveolar infiltrates and bilateral pleural effusion.

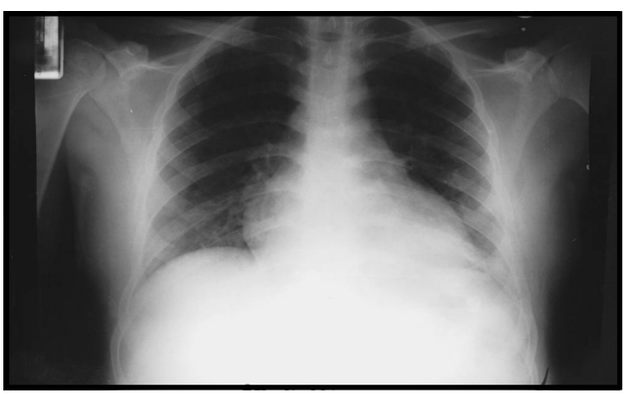

Figure 4 - Chest radiograph 10 days after starting steroids showing significant resolution of infiltrates.

transaminase AST 166 U/L {range12-37 U/L}). Repeat BAL showed 45% eosinophils. A presumptive diagnosis of idiopathic AEP was made and the patient was started on methylprednisolone 80 mg intravenously every 6 hours. Twelve hours after starting steroids, BAL showed no eosinophils and eosinophil percentage in the blood went down to 0.3%. Liver enzymes returned to normal and skin lesions disappeared within a few days. The patient was extubated 3 days after starting steroids and discharged home 11 days later in good condition with room air PaO_2 of 70 mmHg. Chest radiograph 10 days after starting steroids showed significant resolution of infiltrates (**Figure 4**). Stool analysis for ova and parasites was negative. A repeat analysis after 4 weeks was negative as well. Skin test for Aspergillus species was negative. Serum immunoglobulin E (IgE) level was 3408 IU/ml (normal range: 2-489 IU/ml). Prednisolone was continued in a tapering dose for 6 weeks. Two months later, pulmonary function test returned to normal including spirometry, diffusion capacity and lung volumes. The patient is being followed for 3 years with no recurrence of his symptoms.

Discussion. Although AEP can affect any age, it appears to occur typically in young healthy individuals. Most patients are between 20-40 years of age.[4] Males are affected more than females in a ratio of 2:1.[4,5] Usual complaints on presentation include acute febrile illness of short duration (usually less than 7 days), progressive dyspnea, dry cough, malaise, myalgias and occasionally pleuritic chest pain. Hypoxemic respiratory failure is frequent at presentation. Hyperdynamic shock has been reported but is unusual.[6] Physical examination is usually remarkable for dyspnea, fever and tachycardia. Basilar inspiratory crackles and occasional expiratory ronchi are the most common respiratory findings. No skin manifestations have been reported before in patients with AEP. Our patient developed erythema multiforme, which could not be explained by any particular exposure. To our knowledge, this is the first time to report this manifestation in patients with AEP. Routine laboratory studies are nonspecific. As in our case, most patients present initially with neutrophilic leukocytosis, although the eosinophil fraction in some patients becomes markedly elevated during the subsequent course of AEP.[5,7] Our patient developed a laboratory picture of hepatitis with elevation in liver transaminases. Screening for viral hepatitis was negative and the patient did not receive any medications that can cause hepatitis. Liver function returned to normal with treatment. To our knowledge, hepatitis picture was not reported before in patients with AEP. The liver function derangement responded nicely to treatment with corticosteroids and normalized within a few days. Erythrocyte sedimentation rate and IgE levels are elevated in most patients. Chest radiography generally shows infiltrates of non-segmental distribution, which may begin in an interstitial pattern and progress later to alveolar or mixed infiltrate with Kerley B lines.[4,8,9] The pattern is different from that seen in chronic eosinopilic pneumonia, in which the infiltrate is localized to the periphery. Small pleural effusion had been reported to occur in about two-thirds of the patients.[4,8,9] Eosinophil count is often elevated in the pleural fluid. Bilateral random patchy ground glass or reticular opacities often characterize high resolution CT scan of the chest. Some patients show airspace opacity.[4,8,9]

As we may predict from the above discussion, it is often difficult to differentiate AEP from infectious causes of community-acquired pneumonia based on history, physical examination, basic laboratory tests and radiological findings. Bronchoalveolar lavage is the key test for AEP diagnosis yielding very high percentage (greater than 25%) and number of eosinophils without evidence of infection.[4-5] Therefore, early BAL with cell count should be considered for patients with unexplained acute respiratory failure accompanied by fever and pulmonary infiltrate. In addition to AEP, several respiratory disorders are characterized by the presence of eosinophils in the BAL. **Table 1** provides a brief differentiation between AEP and some of the known causes of BAL eosinophilia. Transient pulmonary eosinophilia has been reported in asthmatic patients.[10] However, the clinical picture in our patient does not support that diagnosis.

In the reported cases in literature, few patients have undergone lung biopsy (open and transbronchial). In those, acute and organizing diffuse alveolar damage was common with increased interstitial and alveolar eosinophils.[7] Therefore, AEP is a diagnosis of exclusion that mandates the presence of BAL eosinophilia in addition to the presence of the characteristic clinical features.

The specific etiology of AEP remains unknown. Several mechanisms have been proposed including hypersensitivity reaction,[1,4,11] and exposure to some environmental factors.[12] Acute eosinophilic pneumonia has been reported to occur in association with several drugs and chemicals including minocycline,[13] trazodone,[14] GM-CSF,[15] cigarettes,[16,17] heroin,[18] cocaine,[19] pentamidine[20] and diclofenac.[21]

Although spontaneous remission has been reported in some cases,[11,22] most reported cases progressed to acute respiratory failure. In one report of 15 cases,[4] 53% of patients required mechanical ventilation. For this reason, early BAL with cell count should be considered when a previously healthy person presents with acute respiratory failure of unknown etiology. Despite the fact that AEP can lead to life-threatening respiratory failure, patients with AEP

Table 1 - A brief differentiation between AEP and some of the known causes of BAL eosinophilia.

Causes of BAL eosinophilia	Presentation	Peripheral Eosinophilia	BAL Eosinophilia	Organs involved	IgE	Chest radiography
AEP	Acute (days) febrile illness with dyspnea and cough, often progresses to respiratory failure	Eosinophilia may become markedly elevated during the subsequent course of AEP	Elevated	Lungs	Elevated in most patients	Diffuse interstitial and alveolar infiltrates
CEP	Subacute presentation (weeks to months), rarely progresses to respiratory failure	Common	Elevated	Lungs	Normal or mildly elevated	Photographic negative of pulmonary edema
ABPA	Generally presents in patients with steroids dependent asthma	Common	Elevated	Lungs	Significantly elevated	Most patients have central bronchiectasis by the time the diagnosis is made
Loffler's syndrome	Minimal symptoms	Mild peripheral eosinophilia	Elevated	Lungs	Could be elevated	Migratory bilateral infiltrates
CSS	Allergic rhinitis and asthma with involvement of other organs especially skin	Prominent peripheral eosinophilia	Elevated	Multi-organ	Could be elevated	Fleeting patchy densities. Hilar lymphadenopathy and pleural effusion may occur
IHES	Multi-organ involvement. Cough is a prominent feature	Marked peripheral eosinophilia	Elevated	Multi-organ	A subgroup of patients have elevated IgE	Pulmonary consolidation and effusion

AEP - Acute eosinophilic pneumonia; CEP - chronic eosinophilic pneumonia; ABPA - Allergic broncho-pulmonary aspergillosis; CSS - Churg Straus syndrome; IHES - Idiopathic hyper-eosinophilic syndrome; BAL - Broncho-alveolar lavage.

respond promptly and uniformly to corticosteroids. The response is quick and dramatic with apparent clinical response within 1-2 days. Our patient was extubated 3 days after starting corticosteroids. Moreover, his peripheral blood and BAL eosinophils returned to normal within 12 hours of starting treatment. To our knowledge, this is the first report to document normalization of BAL eosinophils within hours of starting treatment. In the literature, there is no standardized protocol or dose for corticosteroid administration. Based on the reported cases, intravenous methylprednisolone in a dose of one mg/kg every 6 hours can be started in patients with acute respiratory failure. If respiratory failure is not present oral prednisolone in a dose of 40-60 mg daily can be started. The high dose should be continued until respiratory failure resolves. Oral prednisolone should be continued in a tapering dose for 2-4 weeks after the disappearance of symptoms and normalization of the chest radiograph. There are no reports on other modalities of treatment. Recurrence has not been reported in any case before. Our patient has been followed for 3 years with no recurrence. His pulmonary function and radiological tests have returned to normal.

We conclude that AEP is an acute febrile illness that may result in acute life-threatening respiratory failure. It usually affects young healthy individuals and simulates severe community acquired pneumonia. Due to the differing treatments, it is important to distinguish AEP from infectious pneumonia. Therefore, early BAL with cell count should be considered when a previously healthy person presents with acute respiratory failure of unknown etiology. Other causes of pulmonary eosinophilia should be excluded always. Treatment with corticosteroids can be life-saving as AEP responds easily and uniformly to corticosteroids. Acute eosinophilic pneumonia has not been reported to recur in any patient. Based on our report, AEP can be associated with erythema multiforme and acute hepatitis.

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