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Case Report

A Case of Pulmonary Alveolar Proteinosis Misdiagnosed as Idiopathic Pulmonary Fibrosis from Syria

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Abstract

Ground glass opacities on chest computed tomography has many differential diagnoses which represent a diagnostic challenge to physicians. It can be the initial radio graphical appearance to many diseases. Misdiagnosed diseases lead to worst prognosis as well as bad outcomes.

Pulmonary alveolar Proteinosis is a rare lung disease with wide spectrum of symptoms (Ranged from asymptomatic patients to respiratory failure and death.

The most important radiological appearance is called 'CARZY PAVING PATTERN'.

Open lung biopsy and Bronchoalveolar Lavage (BAL) can make the diagnosis definitive.

Whole lung lavage and GM-CSF inhalation therapy are the most important therapies available.

The prognosis dependent on the type of the disease, age, early diagnosis and treatment.

Keywords: Pulmonary alveolar protenosis; GM-CSF; Crazy paving

Introduction

Many diseases did not represent their full picture of the disease like, symptoms and radiological appearances in the early stages of the disease. That fact leads to misdiagnosed cases. Most diseases that diagnosed in late stages have poor prognosis as well as bad outcomes. Our case is one of those cases.

Pulmonary alveolar Proteinosis is a rare respiratory disease characterized by progressive accumulation of proteins (Surfactant) in the alveoli leading to hypoxia ranged from mild to severe and may end up with respiratory failure [1].

Patients who have these disorders are more vulnerable to infections especially opportunistic ones [2]. There is three types of the disease are congenital, secondary and acquired [2]. The most common presentations are progressive dyspnea and cough [2]. The most effective treatment known is whole lung lavage [3].

Case Presentation

Our patient is 43 years old, Syrian, male with no travelling history.

He is active smoker (35 packet/year) with no history of alcohol consumption. He has no remarkable medical, surgical or drug history. His complains started about 4 months- before he referred to our center- with progressive dyspnea on exertion (grade 4 mMRC), fever (40 Celsius), dry cough, weight loss (15 kg/2months), and fatigue.

He has been suffering from severe hypoxia (Spo2 70% at without supplemental oxygen) and central cyanosis. On auscultation his lungs was full of fine and coarse crackles. Laboratories showed elevated White Blood cells (40 000), elevated CRP (100 mg/l) and LDH (1200 U/I).

Cxr showed bilateral patchy interstitial and alveolar infiltrates and CT scan showed diffuse ground glass opacities.

His primary diagnosis was community acquired pneumonia then his pulmonogist prescribed him antibiotics. Flexible bronchoscopy was done to exclude tuberculosis, *Pneumocystis carinii* and fungal infections. Broncho-alveolar lavage was negative for TB and Fungus using molecular biology techniques. Tran's bronchial biopsy shows inflammatory changes minimal improvement in dyspnea and hypoxia achieved.

After 1 month of hospital admission a new CT scan was done and showed persistent diffuse Ground glass opacities. His physicians put their final diagnosis as idiopathic pulmonary fibrosis without histopathological confirmation. They put him on supplemental oxygen, prednisolone (200 mg/a day) and azathioprine (100 mg/a day).

After 4 months, the patient still dyspnic and his oxygen saturation declined more and more.

Chest X-ray has been done (Figure 1), and shows bilateral interstitial and alveolar infiltrates. His laboratories revealed normal values except for LDH (1400).

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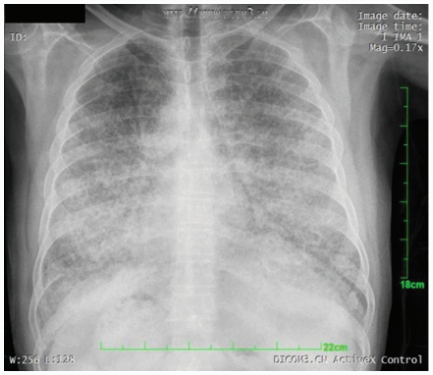

Figure 1: Chest X-ray shows bilateral interstitial and alveolar infiltrates.

Arterial bold gases showed acute or chronic respiratory failure. The next step was certainly obvious, chest computed tomography (Figure 2). Chest CT showed bilateral interlobular and intralobular septal thickening with diffuse ground glass opacities which are widely known as "Crazy paving pattern".

The differential diagnosis of this pattern includes Pulmonary alveolar Proteinosis (the most important), pulmonary edema, infections, pulmonary hemorrhage, cryptogenic organizing pneumonia, bronchoalveolar carcinoma, sarcoidosis and non-specific interstitial pneumonia as well. Flexible Bronchoscopy was done and bronchoalveolar lavage showed this milky, white, and full of proteins fluids (Figure 2) which lead us to the diagnosis of Pulmonary Alveolar Protenosis (PAP). In order to confirm the diagnosis, surgical lung biopsy was done (Figure 3). The pathological study confirmed the diagnosis of Pulmonary Alveolar Protenosis (PAP) (Figure 4).

The patient has undergone WHOLE- LUNG- LAVAGE which is the best proven treatment in this case. He showed us significant clinical improvement two days after the procedure. Chest x-ray did not improve significantly after two weeks of WHOLE- LUNG-LAVAGE. So, other treatment sessions are scheduled later to reach the best benefit desired.

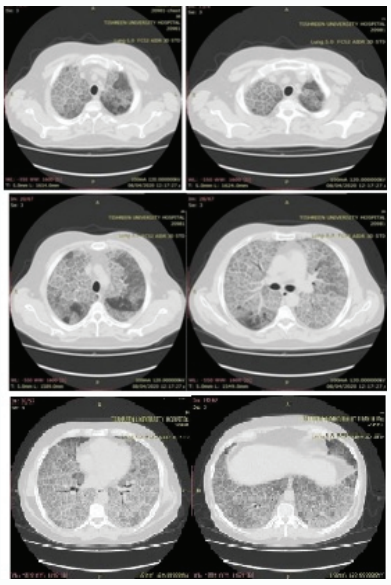

Figure 2: CT of the chest demonstrates bilateral interlobular and intralobular septal thickening with diffuse ground glass opacities which is widely known as "Crazy Paving Pattern".

Figure 3: Milky, full of proteins BAL.

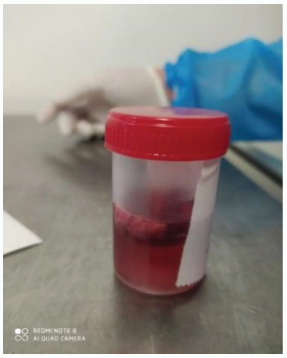

Figure 4: Surgical lung biopsy.

Discussion

Pulmonary Alveolar Proteinosis is a rare diffuse lung disease, characterized by accumulation of proteinaceous particles within alveoli and alveolar macrophages due to disturbances in surfactant balance [4]. Most patients are men who have a history of tobacco consumption and the mean age at the time of diagnosis is 39 years old [2]. The median period before diagnosis is about 7 months after the beginning of the symptoms [3]. Granulocyte Macrophage Colony Stimulating Factor (GM-CSF) was determined as very important causative factor of the disease. The discovery of its role lead us to understand most of the pathophysiology of PAP. Abnormal macrophage function, anti-GM-CSF autoimmunity (the most important: 90% of cases) and other genetic impairment in surfactant production are the cause of most adult cases [4]. Impairment in gas exchange is the most important consequence of the disease and it may lead to respiratory failure which can lead to death without proper treatment [4]. The disease was first described in 1958 by Rosen and colleagues, and our understand of the disease has developed considerably [4]. The prevalence of the disease is estimated by 0.36-3.7 cases per million population [3]. There are three types of the disease: auto immune, secondary and congenital form the type that was previously called "Idiopathic PAP" is now well known as Auto immune PAP, which is caused by GM-CSF antibodies [5]. Secondary type is accompanied with hematologic cancers, drugs, inhalation of fumes or toxins and sometimes infections [5]. Its pathophysiology is partial deficiency of GM-CSF and macrophage impairment [5]. It is important to know that is the prognosis of this type is really related to the prognosis of the underlying disease [5]. The congenital type is due to mutation and gene disorders and thus the GM-CSF has a diminished role there [3]. Clinical presentations

varies from asymptomatic old patient with primary type to the death of neonates in congenital PAP [1]. The most important symptoms are Dyspnea, dry or productive cough, fatigue, weight loss often start many months before the diagnosis. Fever and hemoptysis are less common and many times they come with super infections [1]. The physical examination is unremarkable in many cases but crackles and cyanosis may occur [1]. Chest X-ray demonstrates bilateral, symmetric infiltrates [1]. CT scan of the chest demonstrates diffuse ground glass opacities with septal thickening and sub pleural sparing [1]. This type of radiographic appearance called "CRAZY PAVING PATTERN". The gold standard remains "Surgical lung biopsy" also false negative could be noticed some times because of the errors in sampling [3]. Open biopsy is not always required as we can make the right diagnosis using clinical suspicion, radiographic findings and milky Bronchoalveolar Lavage (BAL) [2]. The fluid contains of large amount of granular acellular eosiphilic proteinaceous materials with abnormal macrophages "Foamy type" with diastase resistant PAS-positive intracellular inclusions [3]. Lung biopsy shows near complete filling of the alveoli and terminal bronchioles with surfactant [3]. The best treatment is absolutely Whole Lung (WLL) Lavage for now. WLL was used to treat patients with PAP in 1964, we used only 3 litters of normal saline mixed with heparin and acetylcysteine under local anesthesia [6]. The efficacy and safety improved significantly using general anesthesia and about 50 letter of normal saline [6]. Patients may need a second session of WLL after 18 months due to surfactant accumulation, and some of them do not need other sessions of WLL after first treatment after 5 years in some studies [6]. GM-CSF inhalation therapy was first described in Japan in 2000. This treatment may produce a full remission of the disease [6]. Therapy may last for 6 months to get better benefit of it [1]. Although, GM-CSF failed to treat severe cases due to excessive amount of proteins in alveoli [6]. Some studies suggest a combination therapy. So, we can use GM-CSF inhalation therapy after WLL [6]. The most type expected to benefit from GM-CSF inhalation therapy is auto immune type then secondary type, as well as the congenital type may not have great benefit there [3].

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Consent

Written informed consent was obtained from the patient for publication of this case report.

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