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Case Report

A case of idiopathic pulmonary alveolar proteinosis

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ABSTRACT

Idiopathic pulmonary alveolar proteinosis (PAP) is a rare disease due to impaired alveolar macrophage function caused by neutralising anti-granulocyte-macrophage colony-stimulating autoantibodies. A nineteen years old male patient was admitted with the complaints of cough, sputum production, dyspnea and fever. There were bilaterally inspiratory fine crackles. The chest radiographs showed bilateral air-space consolidation. On thorax computed tomography; pre-carinal lymph nodes enlargement, ground glass opacities, septal thickening and crazy-paving appearance were determined. Bronchoalveolar lavage was performed and reported was PAP.

1. Introduction

Pulmonary alveolar proteinosis (PAP) is an unusual lung disorder of unknown etiology characterized by the accumulation of large amounts of a phospholipoproteinaceous material in the alveoli that stains positive by using the periodic acid-Schiff (PAS) method.[1,2]

More recently, the role of granulocyte-macrophage colony-stimulating factor (GM-CSF) has been described in the pathogenesis of the PAP.[2] A deficiency in GM-CSF activity results in defective macrophages and reduced clearance of surfactant from the lungs.[1,3] Anti–GM-CSF antibodies have also been found in most patients.[4]

There are three different types of PAP: congenital PAP (2% of total cases), secondary PAP (less than 10% of total cases), and acquired or adult-type PAP (90% of cases).[3,5] More than 90% of cases of PAP occur as a primary acquired disorder of unknown etiology, not associated with any familial predisposition.[4,5]

Diagnosis of the disease may be difficult with clinical sings and symptoms. Currently, there is no curative treatment of the disease.[1,2,5] We presented a case of primary PAP who had disharmony between clinical and radiological findings.

2. Case

A nineteen years old male patient was admitted to our clinic with the complaints of cough, sputum production, mild dyspnea on exertion and fever in the last 2 days. In the history of the patient, there was not any disease. The physical examination revealed bilaterally inspiratory fine crackles on auscultation. The chest radiographs showed bilateral air-space consolidation, prominent in the bases (Fig. 1a). The patient was a non smoker and had no environmental and occupational organic or inorganic dust exposure. Complete blood count revealed WBC 11.0 K/UL, RBC 4.73 M/UL, Hemoglobin 16.1 g/dl, Hematocrit 44.7%, Platelet 221 K/UL. Erytrocyte sedimentation rate was 23 mm/h, C-reactive protein 21.8 mg/L, lactate dehydrogenase (LDH) 401 U/L. Tumour markers and the other laboratory parameters were within normal limits. The serology of HIV was negative. The pulmonary function tests of the case showed FVC 4.98 L (99%), FEV1: 4.30 L (%101), FEV1/FVC: 86%, DL_{CO}: 8.21 mmol/kPa/min (70%), TLC: 6.15 L (90%), RV: 1,81 L (113%), RV/TLC: 29%. Arterial blood gases analysis presented mild hypoxemia (pH: 7.41, pCO2: 39.5 mmHg, pO2: 70.1 mmHg, HCO3: 24.7 mmol/L). Sputum examinations and cultures for M. tuberculosis and other bacteria were negative. On thorax computed tomography; pre-carinal lymph nodes enlargement, bilateral ground glass opacities, septal thickening and "crazy-paving" appearance were determined (Fig. 1b,c). The bronchoscopic appearance of airways was normal. Bronchoalveolar lavage (BAL) was performed and the appearance of BAL fluid was milky. The cytology of BAL fluid reported was consistent with PAP. Other possible diseases were excluded with clinical, laboratory and radiological examinations.

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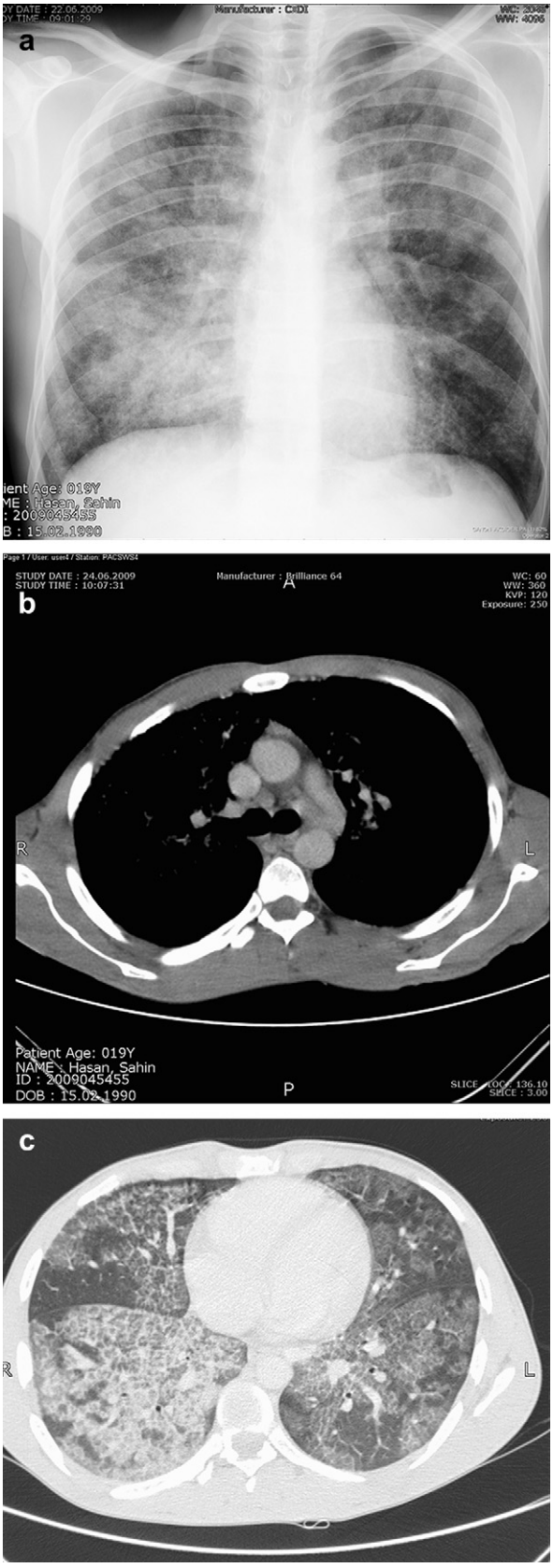

Fig. 1. a. The chest radiographs show bilateral air-space consolidation, prominent in the bases. b. There is pre-carinal lymph nodes enlargement on thorax computed tomography. c. There are bilateral ground glass opacities, septal thickening and "crazy-paving" appearance on thorax computed tomography.

3. Discussion

PAP is a disease of impaired alveolar macrophage function leading to excessive accumulation of surfactant components in the alveoli.[1]

Incidence of the disease is 4 times higher in males than females[1,5]; our case was male. Patients are typically aged 20–50 years at presentation,[1,2] our case was 19 years old. Physical findings are usually nonspecific.[1] The physical examination of our case revealed bilaterally inspiratory fine crackles. There was no definite lobar or zonal predominance on chest X-ray.[5] The chest X-ray of the case showed bilateral air-space consolidation, prominent in the bases. Although the "crazy-paving" appearance has been considered to be strongly suggestive of alveolar proteinosis, recent studies have reported that the crazy-paving pattern on thin-section CT scans is a nonspecific finding.[6,7] Bilateral ground glass opacities, septal thickening, "crazy-paving" appearance and para-tracheal lymph nodes enlargement were determined on 64 row multidetector computed tomography of the case. Lymph node enlargement is uncommon in patients with pulmonary alveolar proteinosis.[8] We are of opinion that LAP sign was coincidental because laboratory studies for infectious agents could not detect any microorganisms.

Seymour et al. reported a series of 410 cases; the median duration of symptoms before diagnosis was 7 months.[5] Interestingly the symptoms of our case started only 2 days before.

Seymour et al. reported that the mean ± SD PaO2 at diagnosis was 58.6 ± 15.8 mmHg[5] PaO2 of our case was 70 mmHg. PAP patients have a mean ± SD LDH level that is 168 ± 66% of the upper limit of the normal range.[5] The level of LDH was 401 U/L at diagnosis of our case.

Three different types of PAP have been identified: congenital, secondary and primary PAP.[2] Since no other diseases were evaluated, the patient was diagnosed as primary PAP; because, the patient was a non smoker and had no environmental and occupational exposure.

The consolidation is usually bilateral and patchy. In some patients, it is very extensive, despite relatively mild respiratory symptoms.[1] Although the clinical symptoms of our case were mild, bilateral diffuse ground glass consolidation was found in radiological examination.

On pulmonary function testing, the most common pattern seen is that of a restrictive defect, with a disproportionate reduction in diffusing capacity relative to modest impairment of vital capacity.[5] We detected normal spirometri results with mild reduction of diffusion capacity for DL_{CO} by the pulmonary function testing of our patient.

Anti–GM-CSF antibodies have been found in most patients.[2] Since Anti–GM-CSF antibodies have not been available until now in our country, we could not study on these antibodies. Serum immunoglobulin levels have been reported to be reduced in 4% of patients tested.[5] Serum immunoglobulin levels of our case were within normal limits. Also, the serum autoimmune marker levels were within normal limits.

Wang et al. suggested that actual lung tissue, obtained via transbronchial biopsy or open lung biopsy, remains the "gold standard" of diagnosis but is not necessary except in problematic cases.[9] They proposed that, when several clinical features (eg, symptoms, laboratory test results, chest radiographs, and HRCT findings) suggest PAP, BAL alone was generally sufficient to exclude other conditions.[9] According to clinical symptoms, blood gases results, radiologic findings, BAL findings and exclusion criteria for other possible diseases; our presented case was considered PAP.

Kariman et al. suggested that patients with an arterial partial pressure of oxygen (PaO2) of greater than 70 mm Hg or P(A–a)O2 gradient of less than 40 mm Hg are more likely to improve

spontaneously.[10] We planed periodic follow-up with three months intervals.

4. Conclusion

Although the radiological findings are very extensive in some PAP patients, the respiratory symptoms may be relatively mild.

Conflict of interest statement

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

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