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A CASE OF PULMONARY ALVEOLAR PROTEINOSIS IN A MIDDLE AGED FEMALE.

General Medicine

Dr. Divya Joshi 3rd Year Resident, Department of General Medicine, SVPIMSR, NHLMMC, Ahmedabad.

Dr. Anand Shah* 2nd Year Resident, Dept. of General Medicine, SVPIMSR, NHLMMC, Ahmedabad. *Corresponding Author

Dr. Bhargav Prajapati 3rd Year Resident, Dept. of General Medicine, SVPIMSR, NHLMMC, Ahmedabad.

Dr. Ami Parikh Professor and Head of Department of General Medicine, SVPIMSR, NHLMMC, Ahmedabad

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 57 years old female patient was admitted with complaints of non productive cough and dyspnoea at rest. 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.

KEYWORDS

GM-CSF, Whole Lung Lavage, Crazy Pavement Appearance

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 using the periodic acid-Schiff (PAS) method.

More recently, the role of granulocyte-macrophage colony-stimulating factor (GM-CSF) has been described in the pathogenesis of the PAP. A deficiency in GM-CSF activity results in defective macrophages and reduced clearance of surfactant from the lungs.Anti–GM-CSF antibodies have also been found in most patients. 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).More than 90% of cases of PAP occur as a primary acquired disorder of unknown etiology, not associated with any familial predisposition.

Diagnosis of the disease may be difficult with clinical signs and symptoms. Currently, there is no curative treatment of the disease. The disease can be controlled by repeated whole lung lavage.

CASE REPORT

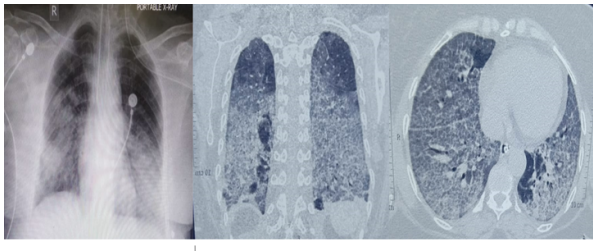
A 57 year old Hindu female, with no comorbidities and nil addictions presented to the Emergency department of a tertiary care hospital with breathlessness on minimal exertion with non productive cough for 3 months. One week before the current presentation she developed dyspnea at rest with no complaints of fever, cold, pedal edema, orthopnea and paroxysmal nocturnal dyspnea. She gave no history of joint pain, Raynaud's phenomenon, dryness of the mouth or eyes, rashes, muscle weakness or bleeding. She had no significant occupational or allergen exposure history. She had visited a couple of private hospitals where she was evaluated for H1N1 influenza, report of which came negative and was treated for Interstitial lung disease with oral steroids.

On admission patient was tachypneic, tachycardic with oxygen saturation of 63% on room air with lung auscultation revealing B/L Inspiratory fine crackles. She required continuous non-invasive positive pressure ventilation(Bi-PAP).

INVESTIGATIONS

Her blood and radiological investigations were done and the relevant investigations are as follows; her haemogram was normal with normal leukocyte count and normal liver and renal function tests.

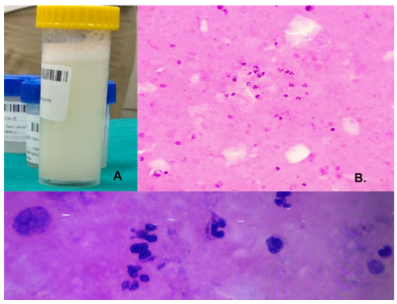
INVESTIGATION	VALUE	INVESTIGATION	VALUE
HEMOGLOBIN (g/dl)	13.9	**TOTAL LEUCOCYTE COUNT(/cumm)**	10500 (75/20/4/1/0)
PLATELET (lakh/cumm)	3.62 lakh	**ANA BY IF**	NEGATIVE
PROCALCITONIN (ng/ml)	<0.01	**SERUM BETA D GLUCAN**	NEGATIVE
TSH(mIU/L)	2.26 (0.4-4)	**SERUM ACE LEVELS**	NORMAL
LDH(U/L)	870 (140-280)	**ESR(mm/hr)**	23(0-20)
CRP(mg/dl/)	<0.6	**SERUM CALCIUM(mg/dl)**	8.2(8.5-10.5)
SERUM TROP-I	<0.01	**VIRAL MARKERS(HIV/HBsAG/HCV)**	NEGATIVE
SERUM PROTEIN(g/dl)	6.8	**Serum Albumin(g/dl)**	4.0



CHEST-XRAY(PORTABLE):BI LATERAL FLUFFY OPACITIES IN LOWER ZONES WITH SPARING OF CP ANGLES.

HRCT-THORAX S/O SYMMETRICAL GROUND GLASS HAZZINESS WITH INTRA AND INTERSTITIAL SEPTAL THICKNESS(CRAZY PAVEMENT APPEARANCE) NOTED IN B/L LUNG FIELDS, S/O PULMONARY ALVEOLAR PROTEINOSIS. MPA:AA>1, S/O PULMONARY ARTERIAL HYPERTENSION.

In view of Chest X ray and HRCT Thorax findings(s/o pulmonary alveolar proteinosis), the patient was advised to undergo Broncho alveolar lavage(BAL) as a diagnostic and therapeutic intervention. First BAL was done and 200-300ml of fluid was removed, the fluid had a milky white appearance which was PAS positive. BAL cytology revealed alveolar foamy macrophages with PAS positive eosinophilic hyaline globules and background showing abundant proteinaceous material mixed with inflammatory cells. BAL cytology with PAS stain was suggestive of pulmonary alveolar proteinosis. BAL Culture was negative and TB gene Xpert from BAL fluid was also negative.



A. BAL FLUID- MILKY WHITE APPEARANCE.

B. BAL CYTOLOGY-(LOW POWER)

C. BAL CYTOLOGY(HIGH POWER)

On confirming the diagnosis she was advised repeated whole lung lavage with injection of GM-CSF 250microgram subcutaneously daily.

The patient agreed for the same and was subjected to 2 cycles of whole lung lavage. The patient improved clinically and radiologically. She was discharged with stable vitals on minimal oxygen support. She was advised regarding need for supplemental oxygen therapy at home and was advised to continue taking injection GM-CSF subcutaneously for six months. Patient was advised follow up after 15 days. She was counselled about the disease progression and was explained regarding the need for whole lung lavage in the future.

DISCUSSION:

PAP is a disease of impaired alveolar macrophage function leading to excessive accumulation of surfactant components in the alveoli. Incidence of the disease is 4 times higher in males than females,our case be ing female. Patients are typically aged 20–50 years at presentation, our case being 53 years old. Physical findings are usually nonspecific. The physical examination of our case revealed bilateral inspiratory fine crackles. The“crazy-paving” appearance has been considered to be strongly suggestive of alveolar proteinosis. Bilateral ground glass opacities, septal thickening, “crazy-paving” appearance and paratracheal lymph nodes enlargement were determined on 64 row multidetector computed tomography of the case.

Seymour et al reported a series of 410 cases; the median duration of symptoms before diagnosis was 7 months.The symptoms of our case started 3 months ago.

Seymour et al. reported that the mean ± SD PaO2 at diagnosis was 58.6 ± 15.8 mmHg5 PaO2 of our case was 55 mmHg. PAP patients have a mean ± SD LDH level that is 168 ± 66% of the upper limit of the normal range. The level of LDH was 870 U/L at diagnosis of our case. Three different types of PAP have been identified: congenital, secondary and primary PAP.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. Anti–GM-CSF antibodies have been found in most patients. Our patient could not afford Anti - GMCSF antibodies hence we could not study on these antibodies. Serum immunoglobulin levels have been reported to be reduced in 4% of patients tested. 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.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. According to clinical symptoms, blood gases results, radiologic findings, BAL findings and exclusion criteria for other possible diseases; our presented case was considered PAP.

CONCLUSIONS:

With repeated whole lung lavage, the patient can lead a relatively normal life.Clinical and radiological suspicion is imperative for initiating early treatment in the course of the disease. Whole lung lavage remains the gold standard treatment for PAP.

Although the results of the study of GM-CSF augmentation are compelling, the efficacy of this treatment will remain unproven until randomized, controlled trials have been conducted.

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