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Abstract

Pulmonary alveolar proteinosis (PAP) is a rare disorder, in which lipoproteinaceous material accumulates within the alveoli. We report a case of a 27-year-old male patient with acute worsening of breathlessness over the last 7–8 months and cough with desaturation up to 79% on room air. Contrast-enhanced computerized tomography of the thorax revealed unilateral diffuse crazy-paving pattern likely PAP. Transbronchial lung biopsy confirmed the diagnosis of PAP. The present case highlights the unusual presentation of PAP with unilateral involvement. To the best of our knowledge, this is the first reported case of unilateral PAP from India with a biopsy diagnosis and resolution with whole lung lavage.

Keywords: Biopsy, Breathlessness, Contrast-enhanced computerized tomography, High-resolution computed tomography, Lipoproteinaceous, Pulmonary alveolar proteinosis, Whole lung lavage.

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Abbreviations used in this Article

PAP = Pulmonary alveolar proteinosis, CE = Contrast enhanced, CT = Computed tomography, HRCT = High-resolution computed tomography, WLL = Whole lung lavage, PaO_2 = partial pressure of oxygen, GM-CSF = Anti-granulocyte monocyte-colony stimulating factor

Introduction

Pulmonary alveolar proteinosis is a rare disease that is characterized by abnormal accumulation of pulmonary surfactant proteins in the lung's gas-exchange area, as these are not properly removed. The incidence of PAP is higher in males than in females and usually presents in young and middle-aged adults (20–50 years of age).[1] Clinical presentation is usually with non-specific respiratory symptoms, such as dyspnea or a minimally productive cough. Approximately one-third of patients may be asymptomatic.[1]

On imaging, PAP is classically associated with the bilateral crazy-paving pattern on computed tomography (CT) of lungs. Whole lung lavage (WLL) should be considered in patients with deteriorating lung function and in cases with progressively worsening symptoms. It is still the most effective treatment for PAP.[1] Though the most common presentation of the disease is bilateral, in this report, we present a case of a 27-year-old male patient diagnosed as a case of unilateral PAP and describe its management.

Case Report

A 27-year-old male, a shopkeeper by occupation, with no comorbidities presented to our institution with acute worsening of breathlessness and cough with desaturation. The patient had a history of progressive breathlessness for the last 7–8 months. Patients were on multiple courses of antibiotics with steroids and inhalers. High-resolution CT (HRCT) of the thorax done 5 months ago, showed right-sided ground-glassing with interstitial septal thickening (Fig. 1). The patient was diagnosed as having acute viral fever (RT-PCR for COVID-19 negative) and was managed conservatively. The patient came to us with increased intensity of breathlessness and cough. Arterial oxygen saturation of 79% on room air. Contrast-enhanced computerized tomography (CECT) of the thorax revealed unilateral diffuse ground glassing with septal thickening in a crazy-paving pattern, suggesting PAP. Routine blood chemistry, antinuclear antibody (ANA) profile, vasculitic markers, and coagulation profile were within normal limits. The patient could not do (a pulmonary function test) due to breathlessness. Arterial blood gas analysis revealed hypoxia with a partial pressure of oxygen (PaO_2) of 53 mm Hg on room air.

Bronchoscopy showed turbid, milky-colored aspirate (Fig. 2), which on keeping for 30 min showed sedimentation. Transbronchial lung biopsy from the right lower lobe (Fig. 3) was suggestive of PAP. Whole lung lavage from the right lung was done in our case, as he was symptomatic with a saturation of 79% on room air. The postoperative patient was kept on a ventilator overnight. The procedure was done under general anesthesia using a double-lumen ET tube, and about 10 L of fluid was used. Post-operatively patient was stable with oxygen saturation of 94% on room air. The blood sample for anti-granulocyte monocyte-colony stimulating factor (GM-CSF) was normal. Post-operative chest radiograph post-lavage (Fig. 4B) showed improvement. The pulmonary function test suggests moderate restriction. The patient was discharged in a stable condition without any domiciliary oxygen.

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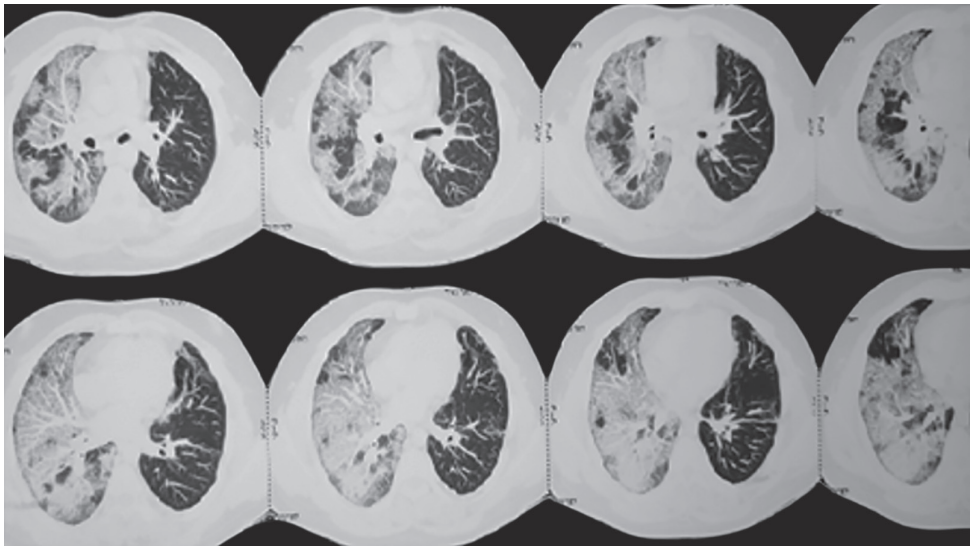


Fig. 1: High-resolution computed tomography thorax showed right-sided, ground-glassing with interstitial septal thickening (left lung is almost normal)

Fig. 2: Turbid milky effluent with sediments (serial collection shows clearing of fluid)

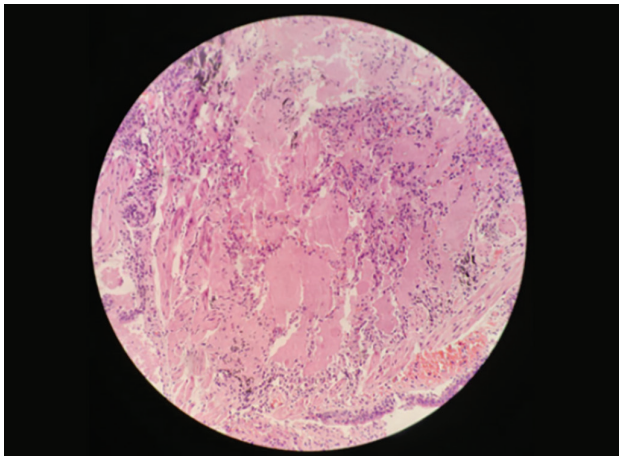


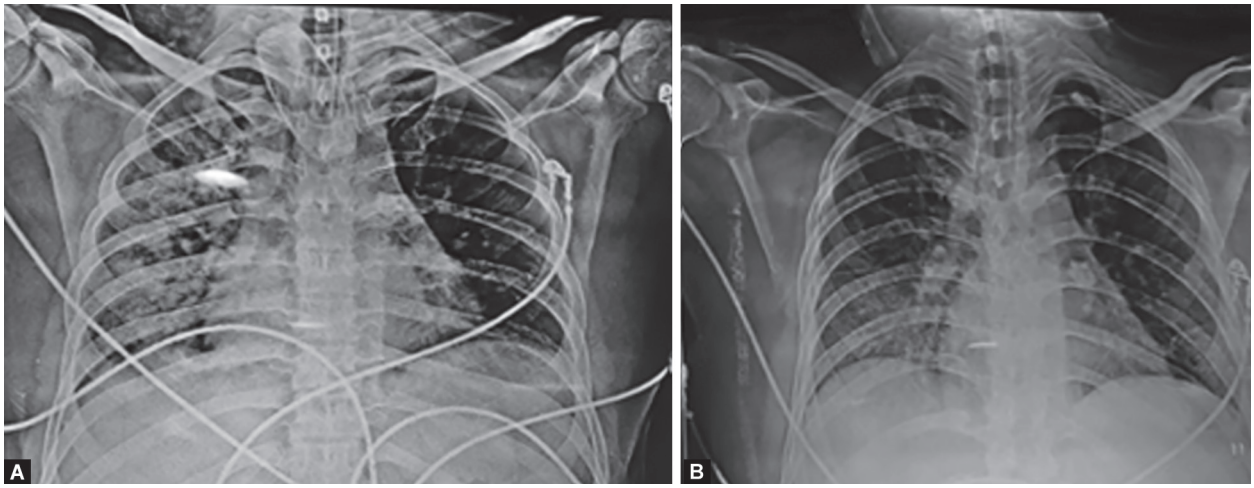
Fig. 3: Transbronchial lung biopsy shows amorphous eosinophilic material in alveolar spaces in a patchy fashion. At places, alveolar spaces are collapsed with focal mild thickening of the interstitium. No inflammation is seen

Discussion

Pulmonary alveolar proteinosis, first described by Rosen et al.[2] in 1958, is a rare pulmonary disease with a worldwide distribution. In contrast to adult PAP, which is usually caused by an autoimmune process,[1] most PAP cases in children and adolescents are caused by genetic defects leading to the abnormal synthesis of alveolar surfactant.[3] Because of the rarity of PAP, it is difficult to estimate its true incidence and prevalence. Initial studies reported the prevalence of autoimmune PAP at 3.7 cases per million.[2]

In most reported series there has been a male preponderance, with a male-to-female ratio of 2.1:1 to 2.7:1, and the usual duration of symptoms prior to diagnosis is around 7–10 months.[2] Similarly, our case was the male patient, he presented with the symptoms for the last 7–8 months.

The diagnosis of PAP should be established on the basis of the combination of clinical symptoms, lung function, radiology, and evidence of the accumulation of surfactant lipids and proteins in alveolar spaces.[4]



Figs 4A and B: Chest radiograph (postero-anterior view) (A) Pre lavage and (B) Post lavage (next day)

The commonest chest radiographic presentations in patients with PAP are bilateral symmetrical alveolar opacities located centrally in the mid and lower lung zones, often in a "batwing" distribution. The commonest CT chest presentation is patchy ground-glass opacities. Interlobular septal thickening is seen in about 85% of the patients. Crazy paving refers to the pattern of septal thickening with interspersed ground-glass opacities.[1] Contrast-enhanced computerized tomography thorax of our case revealed patchy areas of ground-glassing with septal thickening involving a majority of the right lung only.

Histology of lung tissue is a useful adjunct in diagnosis,[1] and our patient's specimen showed amorphous eosinophilic material in alveolar spaces with focal mild thickening of the interstitium. Biopsy was suggestive of PAS-positive material, suggestive of PAP.

The unilateral presentation of the disease is rarely reported with only a few case reports having been published in the literature.[5–8] A case series of 34 cases from Mayo Clinic USA in 1987 showed only 5 cases of unilateral pulmonary infiltrates.[5] Another study from Tunisia[6] reported a case of unilateral PAP which was resolved with conservative treatment. Nosaka et al.[7] from Japan reported a case of solitary pulmonary nodule, which was resected with suspicion of malignancy and was diagnosed with PAP on biopsy. Two cases of unilateral PAP were described by Oh et al.[8] from Korea in 2014, and both of the patients improved with conservative therapy.[8]

According to available studies in the literature, there are no consensual guidelines for the management of PAP, and decisions are primarily based on the severity of the disease and type of PAP. Whole lung lavage is the primary treatment of choice, since it was first described in the 1960s, and for a long time, considered the "standard of care".[2] It was first described by Ramirez and colleagues in 1965[9] and further modified by Wasserman and co-workers in 1968. Specific indications include a definitive histologic diagnosis and one of the following: resting PaO_2 <65 mm Hg (at sea level), alveolar-arterial O_2 gradient ≥40 mm Hg, measured shunt fraction >10–12%, or severe dyspnea and hypoxemia at rest or on exercise.[10]

More recently, therapy with GM-CSF has been attempted. Although a positive effect of GM-CSF has been shown in PAP, its long-term safety has not been determined, and the optimal dose, the optimal duration of treatment, and the optimal route of GM-CSF remain unclear.[11]

Conclusions

To the best of our knowledge, our case represents the first diagnosed case of unilateral PAP from India. It highlights that the diagnosis of PAP should be considered in patients with atypical presentation, also if the radiological and clinical features are suggestive and can be confirmed by bronchoscopy and biopsy. Our case is also unique in the sense that the patient was symptomatic with unilateral involvement and showed a satisfactory response with therapeutic whole lung lavage.

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