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Pulmonary Alveolar Microlithiasis: A Rare Case with Characteristic Radiological Findings

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Abstract: ***Background**: Pulmonary alveolar microlithiasis (PAM) is an extremely rare autosomal recessive lung disease characterized by intra-alveolar accumulation of calcium phosphate microliths. The condition demonstrates pathognomonic radiological features with striking clinical-radiological dissociation. **Case Presentation**: We report a case of PAM discovered incidentally in an asymptomatic patient during routine trauma evaluation following a road traffic accident. Chest radiography revealed the characteristic "sandstorm" appearance with diffuse bilateral micronodular opacities. High-resolution computed tomography (HRCT) demonstrated pathognomonic features including diffuse ground-glass attenuation, calcified interlobular septa creating a "crazy-paving" pattern, subpleural cysts, and bilateral pleural calcifications. The micronodules showed random distribution with lower lobe predominance, particularly in posterior segments of lower lobes and anterior segments of upper lobes. **Management and Outcome**: The diagnosis was established based on characteristic imaging findings without requiring invasive procedures. The patient remained completely asymptomatic despite extensive bilateral lung involvement, demonstrating the classic clinical-radiological dissociation typical of PAM. Genetic counseling and family screening were recommended given the autosomal recessive inheritance pattern. **Conclusion**: This case emphasizes the importance of recognizing PAM's pathognomonic radiological features, particularly the sandstorm appearance on chest radiography and crazy-paving pattern on HRCT. Early recognition allows for confident non-invasive diagnosis, appropriate genetic counseling, and long-term monitoring without unnecessary invasive procedures.*

Keywords: Pulmonary Alveolar Microlithiasis, Tomography, X-Ray Computed, Lung Diseases, Calcinosis, Incidental Findings

1. Introduction

Pulmonary alveolar microlithiasis (PAM) is an extremely rare autosomal recessive lung disease characterized by the widespread intra-alveolar accumulation of calcium phosphate microliths throughout the lung parenchyma.[1,2] Since the first description by Harbitz in 1918, fewer than 1,022 cases have been reported in the medical literature worldwide, making it one of the rarest respiratory disorders encountered in clinical practice.[3] The disease demonstrates a slight male predominance globally, though regional variations exist, with most cases being diagnosed in the second through fourth decades of life.[4]

The pathogenesis of PAM is attributed to mutations in the SLC34A2 gene, located on chromosome 4p15.2, which encodes the type IIb sodium-phosphate cotransporter (NPT2b) expressed in alveolar type II cells.[5,6] This transporter plays a crucial role in phosphate homeostasis by facilitating the uptake of phosphate from alveolar spaces, and its dysfunction leads to local phosphate accumulation and subsequent microlith formation.[7] The genetic basis of PAM was definitively established in 2006, with nearly all genetically tested patients demonstrating pathogenic variants in SLC34A2.[5,8]

One of the most striking features of PAM is the remarkable clinical-radiological dissociation, where patients often remain asymptomatic or minimally symptomatic despite extensive radiological abnormalities.[9,10] This characteristic has led to many cases being discovered incidentally during routine chest imaging performed for unrelated conditions. When symptomatic, patients typically present with progressive dyspnea on exertion and dry cough, usually manifesting in the third or fourth decade of life.[2,4]

Radiologically, PAM presents with pathognomonic features that make it relatively straightforward to diagnose in typical cases. Chest radiographs demonstrate a characteristic "sandstorm" appearance with diffuse, bilateral micronodular opacities that are most prominent in the lower lung zones.[11] High-resolution computed tomography (HRCT) provides superior detail, revealing the classic "crazy paving" pattern with ground-glass attenuation, septal thickening, and calcified interlobular septa, which is considered virtually pathognomonic for the condition.[10,12]

The prognosis of PAM varies considerably, with some patients remaining stable for decades while others progress to respiratory failure and cor pulmonale. Currently, no effective medical therapy exists, and lung transplantation remains the only definitive treatment option for patients with end-stage disease.[13] Given the rarity of this condition and its unique radiological presentation, we present this case to contribute to the understanding of PAM and emphasize the importance of recognizing its characteristic imaging features for accurate diagnosis.

2. Case Report

A patient presented to the emergency department following a road traffic accident (RTA). As part of the routine trauma workup, a chest X-ray was performed to evaluate for potential thoracic injuries. The patient was hemodynamically stable with no acute respiratory distress at presentation.

The chest X-ray revealed an unexpected and striking finding of diffuse bilateral pulmonary opacities with a characteristic "sandstorm" or "sand-like" appearance throughout both lung fields. The opacities consisted of innumerable tiny, punctate calcifications scattered diffusely across the lung parenchyma, predominantly affecting the lower and middle zones. The cardiac silhouette and diaphragmatic contours remained

visible, though the extensive calcifications created an overall hazy appearance of the lungs. No acute traumatic changes such as pneumothorax, hemothorax, or rib fractures were identified.

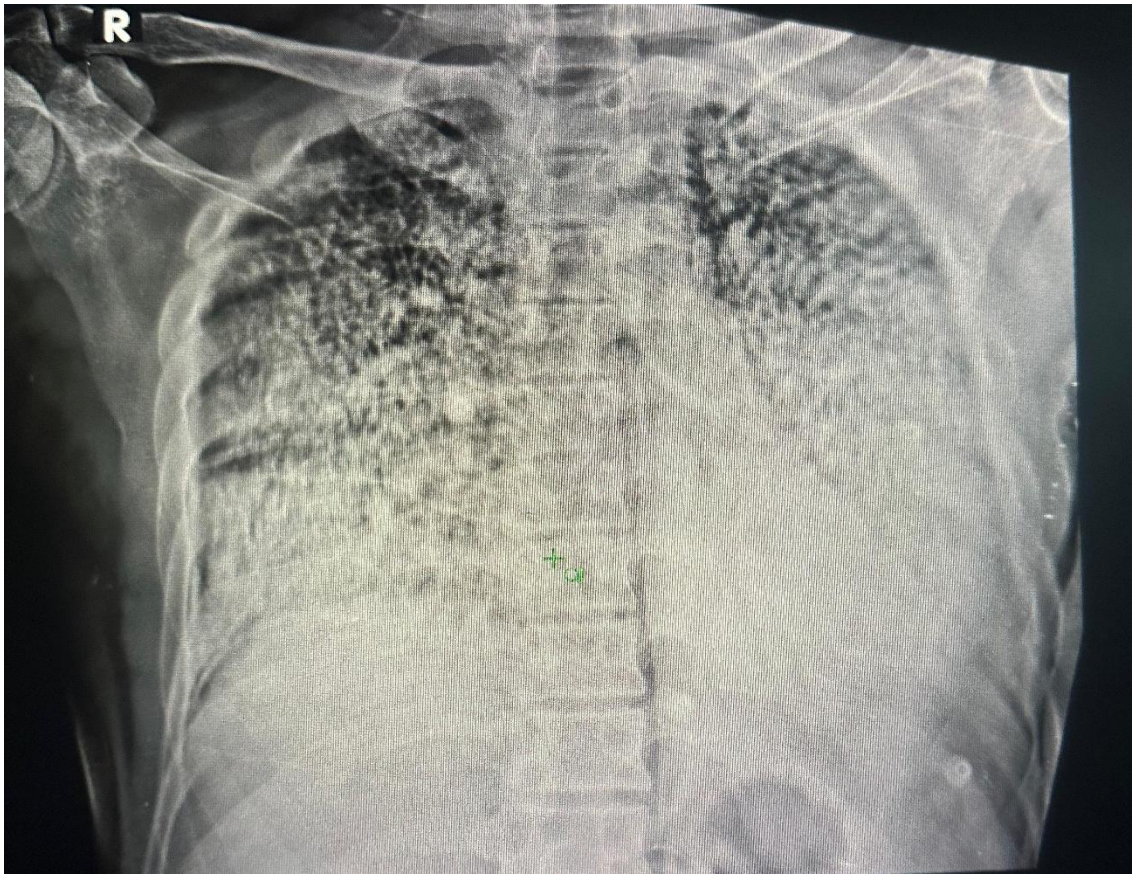

Figure 1: Frontal chest radiograph demonstrating the characteristic "sandstorm" appearance of pulmonary alveolar microlithiasis with diffuse bilateral micronodular opacities predominantly affecting the lower and middle lung zones, with preservation of cardiac and diaphragmatic contours.

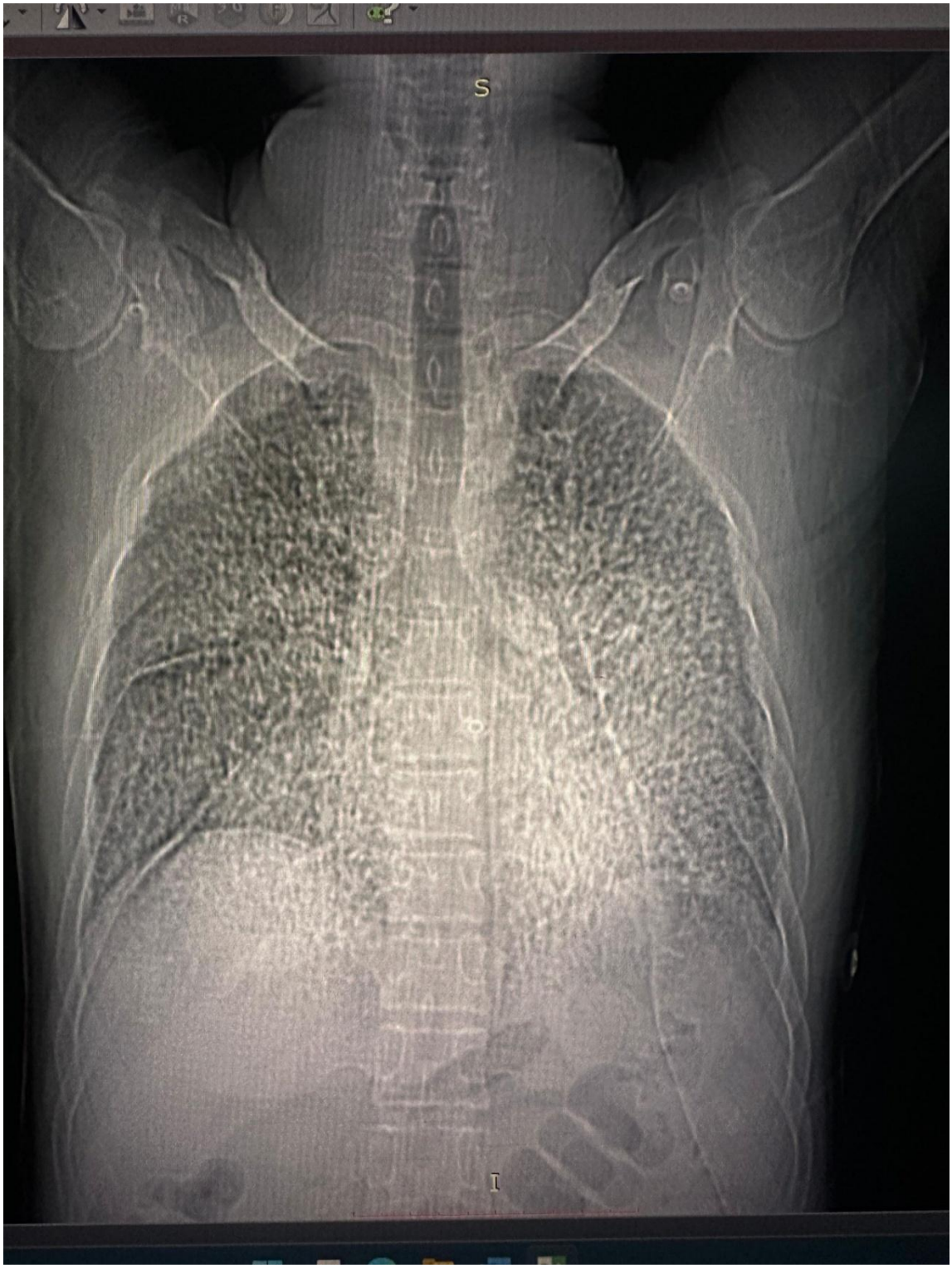

Figure 2: Coronal reconstruction of chest radiograph showing the extensive bilateral distribution of calcified micronodules throughout both lung fields, creating the pathognomonic sand-like appearance characteristic of pulmonary alveolar microlithiasis.

Given the unusual chest X-ray findings, an HRCT thorax with contrast was performed for further characterization. The CT examination confirmed the presence of extensive bilateral pulmonary abnormalities consistent with the plain radiographic findings.

The scan demonstrated diffuse, variable-sized, hyperdense micronodular airspace opacities scattered throughout the bilateral lung parenchyma. These calcified micronodules were most extensively distributed in the posterior segments of the lower lobes and anterior segments of the upper lobes, with relative subpleural sparing noted. The micronodules showed a characteristic random distribution pattern without respect to secondary pulmonary lobules.

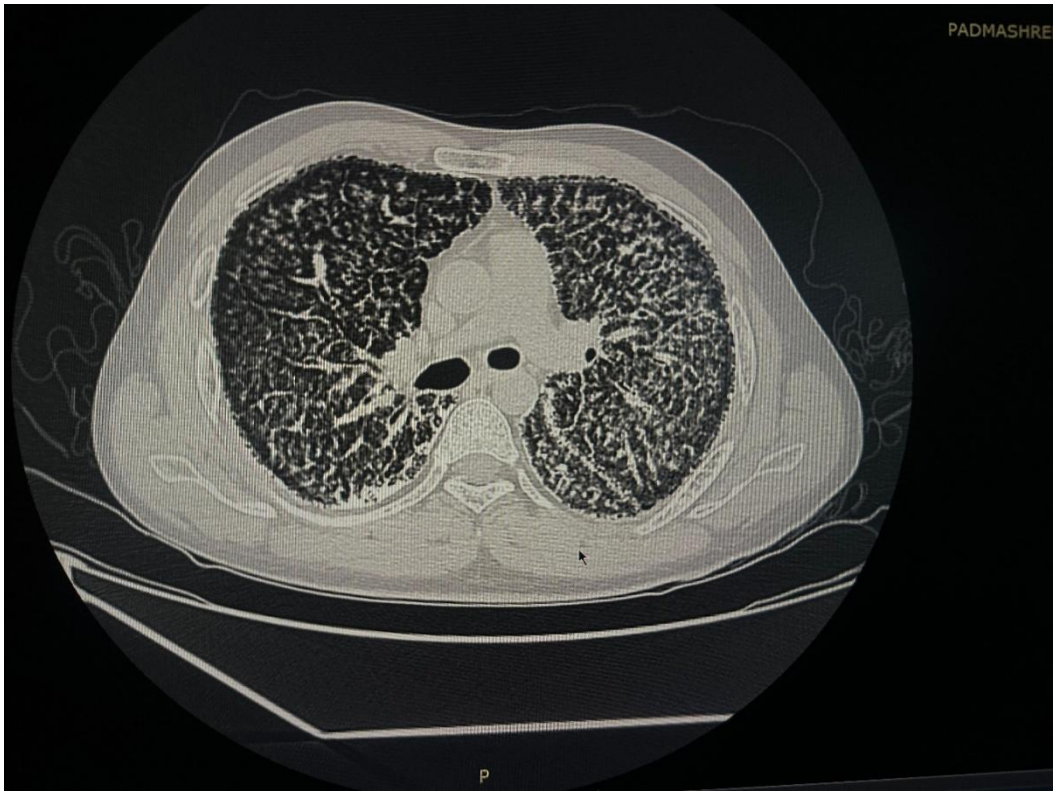

Figure 3: Axial high-resolution computed tomography (HRCT) image at the level of the lower lobes demonstrating the classic "crazy-paving" pattern with ground-glass attenuation, calcified interlobular septa, subpleural cysts, and randomly distributed calcified micronodules characteristic of pulmonary alveolar microlithiasis.

Significantly, there were multiple punctate calcific changes noted in the interlobular septae of bilateral lung parenchyma and the axial interstitium, creating a distinctive reticulonodular pattern. This septal calcification was particularly prominent and represented one of the pathognomonic features of the condition. The combination of airspace micronodules and septal calcification produced areas of ground-glass attenuation with superimposed septal thickening, consistent with a "crazy-paving" pattern.

Multiple subpleural cysts were observed in bilateral lung parenchyma, which is a recognized feature in advanced cases. Few interlobular discrete and confluent septal calcifications were noted in bilateral lung parenchyma, along with bilateral pleural calcifications, indicating disease progression.

No pleural or pericardial effusion was identified. A few subcentimeter-sized pretracheal, paratracheal, and subcarinal lymph nodes were noted, which were within normal limits. The visualized cardiac structures, great vessels, trachea, and main stem bronchi appeared normal with no evidence of calcification or other abnormalities.

The imaging findings were most consistent with Pulmonary Alveolar Microlithiasis (PAM). The characteristic combination of diffuse bilateral calcified micronodules, septal calcification, crazy-paving pattern, and subpleural cysts in an otherwise asymptomatic patient created a virtually pathognomonic radiological picture. The differential diagnosis of sarcoidosis was considered but deemed less likely given the extensive calcification pattern and distribution.

The striking radiological abnormalities contrasted markedly with the patient's asymptomatic clinical presentation, demonstrating the classic clinical-radiological dissociation characteristic of PAM. This incidental discovery during trauma evaluation highlights the importance of thorough radiological assessment and the potential for identifying rare conditions during routine imaging studies. The absence of respiratory symptoms despite extensive bilateral lung involvement is typical of early to intermediate stages of PAM, where patients may remain asymptomatic for decades despite progressive radiological changes.

The case emphasizes the critical role of imaging, particularly HRCT, in diagnosing PAM and differentiating it from other causes of diffuse pulmonary calcification. The pathognomonic imaging features obviated the need for invasive diagnostic procedures, allowing for confident radiological diagnosis in this case.

3. Discussion

This case exemplifies the characteristic presentation of pulmonary alveolar microlithiasis (PAM) as an incidental finding during routine imaging, highlighting the remarkable clinical-radiological dissociation that defines this rare condition. Our findings align closely with the extensive literature on PAM, while also demonstrating several key diagnostic features that distinguish it from other diffuse lung diseases.

The incidental discovery of PAM during trauma evaluation in our asymptomatic patient is consistent with the literature, where PAM is frequently identified as an unexpected finding

on routine chest imaging performed for unrelated conditions. In the comprehensive review by Mariotta et al. of 576 cases, symptoms were absent in more than half of the patients, with dyspnea, cough, and chest pain reported in the remaining cases.[14] Similarly, Ch'ng et al. reported a case of a 24-year-old male whose PAM was discovered during a pre-employment chest radiograph, despite being completely asymptomatic, which mirrors our patient's presentation.[15]

The striking clinical-radiological dissociation observed in our case is a pathognomonic feature of PAM. Chu et al. described this as "the hallmark of this disease" characterized by striking dissociation between radiological findings and mild clinical symptoms.[16] In their case report of a 35-year-old woman discovered post-motor vehicle accident, they noted complete calcification of the lungs on radiographic images with relatively mild clinical presentation, similar to our patient who demonstrated extensive bilateral calcified micronodules with septal thickening yet remained completely asymptomatic.[16] This dissociation is consistent with the natural history of early to intermediate-stage PAM where patients may remain asymptomatic for decades despite progressive radiological changes.

The radiological features in our case demonstrated the classic pathognomonic appearance of PAM. The "sandstorm" appearance on chest radiography, characterized by innumerable tiny calcified micronodules, is virtually diagnostic of PAM. Ch'ng et al. described this as showing "classic sandstorm-like appearance of pulmonary alveolar microlithiasis with symmetrical pattern of diffuse fine micronodules in both lungs and partial obscuration of heart border". This finding was prominently displayed in our patient's initial chest X-ray.[15]

The HRCT findings in our case were particularly comprehensive, demonstrating multiple characteristic features of PAM. In the landmark study by Francisco et al., analyzing HRCT findings in 13 PAM patients, the most frequent findings reported were diffuse ground-glass attenuation and subpleural linear calcifications, with other findings including small parenchymal nodules, calcifications along interlobular septa creating the crazy-paving pattern, and subpleural cysts.[17] Our case exhibited all these cardinal features, including the pathognomonic crazy-paving pattern, which consists of ground-glass attenuation with superimposed septal thickening.

The presence of subpleural cysts in our patient is significant, as these thin-walled cysts located in subpleural spaces may determine the presence of a radiolucent line between the calcified parenchyma and adjacent ribs, described as the "black pleural sign" on chest radiography. In the series by Francisco et al., subpleural cysts were observed in 11 patients (84.6%), making this a highly characteristic finding.[17] The study also found linear subpleural calcifications in 9 patients (69.2%), which were prominent in our case.

The characteristic imaging features in our case were sufficiently pathognomonic to establish the diagnosis without requiring invasive procedures. Francisco et al. concluded that "the typical HRCT findings in PAM are so characteristic that, when present, can rule out the need for lung biopsy".[17] This approach is supported by their study demonstrating that the diagnosis of PAM can be confirmed based on HRCT findings alone, often avoiding the need for lung biopsy. The combination of bilateral calcified micronodules, septal calcification, crazy-paving pattern, and subpleural cysts created a virtually pathognomonic radiological picture in our case.

Similarly, Deniz et al. in their HRCT study of 10 patients found that tomographic alterations were predominant in the inferior and posterior portions of the lungs, with the medial aspects appearing more heavily involved.[18] This distribution pattern was exactly what we observed in our patient, with lower lobe predominance of the calcified changes.

The primary differential diagnosis considered in our case was sarcoidosis, which can occasionally present with similar bilateral micronodular patterns. However, several key features distinguished our case from sarcoidosis. In contrast, our patient showed the characteristic lower lobe predominance typical of PAM, with extensive calcification that is uncommon in sarcoidosis.

The differential diagnosis with miliary tuberculosis was also important to consider, particularly given the diffuse micronodular pattern. Additionally, the clinical-radiological dissociation in our asymptomatic patient strongly favored PAM over active tuberculosis.

Our case contributes to the growing body of literature on PAM from various geographic regions. The comprehensive review by Mariotta et al. documented 576 cases worldwide, with most cases originating from Europe (42.7%) and Asia (40.6%).[14] The countries involved were fifty-one, with twelve of them attributed with at least ten cases each (Bulgaria, France, Germany, India, Italy, Poland, Spain, Russia, Japan, Turkey, USA, ex-Yugoslavia).[14] The age of our patient and the incidental discovery align with the typical presentation patterns described in this literature.

In their series, Mariotta et al. found that 35.8% of patients were less than 20 years old, while 88.2% were less than 50 years old, and family history for the disease was found in one-third of the patients.[14] Our patient's age falls within the typical range for PAM diagnosis.

The prevalence of characteristic imaging features in our case is consistent with published series. Deniz et al. emphasized that HRCT findings of PAM were not fully described in the current literature at the time of their study, and they found that the incidence of PAM is high in certain countries such as Turkey, Italy, and USA.[18] They noted that patients with PAM usually show sand-like micronodular infiltration particularly marked at lower zones predominantly at paracardiac areas in their chest X-rays, exactly as demonstrated in our patient.

Francisco et al. noted that in general, the findings predominated in the lower third of the lungs, which corresponds precisely with our patient's imaging.[17] They emphasized that due to the marked dissociation between radiological features and clinical presentation of PAM, the diagnosis is sometimes based only on radiological findings.

The incidental discovery of PAM in our case during trauma evaluation highlights the importance of thorough radiological assessment in all clinical scenarios. The early recognition of PAM allows for appropriate counseling regarding the natural history, genetic implications, and the need for family screening.

Francisco et al. emphasized that once a patient is diagnosed with PAM, family members should be screened by means of chest radiography, and parents should be advised that future daughters and sons are also at risk of developing the disease.[17] This genetic counseling aspect is crucial for comprehensive patient care, given the autosomal recessive nature of PAM.

The case also illustrates the evolution of PAM understanding. Kashyap and Mohapatra noted that PAM is a rare autosomal recessive disease with high penetrance, in which concretions composed of calcium phosphate fill alveolar spaces, despite normal serum calcium and phosphorus, and absence of any systemic disease of calcium metabolism.[19] They emphasized that over 1000 cases were reported worldwide, especially in Mediterranean countries, and that the disease is typically diagnosed accidentally between 30 and 50 years of age with no significant gender differences found.

While our case demonstrated classic radiological features that allowed confident diagnosis without tissue confirmation, it represents a single case report. Delic et al. emphasized the importance of radiologic-pathologic correlation in their comprehensive review, noting that PAM should be considered in patients with severe radiological features and relatively mild clinical presentation, especially in the presence of family history or consanguinity.[20] The long-term follow-up of such patients remains important to monitor disease progression.

4. Conclusion

This case demonstrates the characteristic presentation of PAM as an incidental finding with pathognomonic radiological features that allow confident diagnosis without invasive procedures. The striking clinical-radiological dissociation, typical HRCT findings including the crazy-paving pattern and subpleural cysts, and the patient's asymptomatic status are all consistent with published literature on this rare condition. Early recognition of PAM is crucial for appropriate genetic counseling and long-term monitoring, emphasizing the importance of radiological expertise in identifying this rare but distinctive disease.

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