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Case Report

Comprehensive Imaging-Guided Optimization of the Surgical Management of Patients with Pulmonary Alveolar Microlithiasis

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ABSTRACT

Pulmonary alveolar microlithiasis (PAM) is a rare lung disease with poor prognosis. The only effective treatment to date, is lung transplantation in the severest cases. However, the etiology of PAM has been recently deciphered, and the treatment paradigm is shifting. We report a case of PAM and propose an optimized imaging-guided management based on the current state of the art.

History

A 46-year-old woman performed Chest X-ray and CT-scan for dyspnea (Figures 1 & 2). The diagnosis of PAM was suggested by the typical imaging pattern and confirmed by transbronchial lung biopsy. Clinical worsening of symptoms was associated with radiological worsening and documented by bone single photon emission tomography [SPECT/CT] and ventilation perfusion SPECT/CT (Figures 1 & 2). Two years after the diagnosis, a right uni-pulmonary transplantation was performed. Her clinical status improved after the transplantation, and no allograft rejection for four years. No familial case was detected.

Discussion

PAM is a rare autosomal recessive genetic disease characterized by widespread deposits of intra-alveolar minute calcium called microliths or calcospherites without disturbances in calcium and phosphorus metabolism [1]. It results from a mutation of the SLC34A2 gene that encodes a type IIb sodium-dependent phosphate transporter, which is specifically expressed in type II alveolar cells. Mutation of this protein abolishes the normal gene function and leads to phosphate deposit with calcium-phosphate microliths formations in alveolar space (Figure 3) [1-3].

While chest X ray and CT-scan could detect early microliths, the symptoms and diagnosis of PAM usually occur at an advanced stage of the disease due to a dissociation between imaging findings and clinical symptoms. Thanks to genetic advances, targeted approaches are envisioned, and monitoring kinetics of the disease appears as the current challenge for medical imaging [1, 4].

The evaluation of the kinetics of microliths deposit can be performed with CT-scan, 18F-FDG PET/CT and bone SPECT/CT. CT-scan allows to evaluate the pulmonary microliths burden, as well as the kinetics of the worsening between several time points. However, this is challenging in severe cases with high concentrations of microliths, like in our case

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but could be performed quantitatively by semi-automatic software due to the high difference in density between calcium deposit and air in the lung. Alternatively, 18F-FDG positron emission tomography [PET/CT] and bone SPECT/CT will measure precisely disease activity at a single time endpoint (Figure 1) and might be valuable prognostic and predictive tools. 18F-FDG PET is a sensitive tool for the detection of inflammation sites. Interestingly, 18F-FDG PET could monitor the activity of macrophages, which play a key role in the degradation of outdated surfactant (Figure 3) [5]. Bone SPECT/CT uptake will occur in case of presence of calcium salts in communication with the systemic circulation and can therefore be negative in few cases [6].

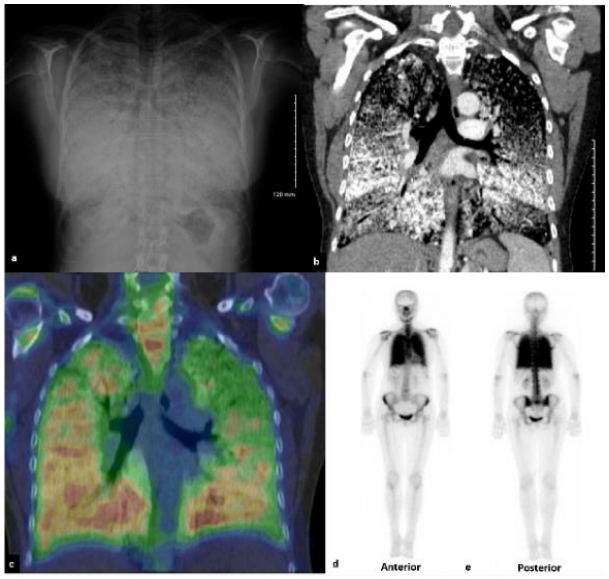

Figure 1: Imaging findings of Chest radiography, **a)** & **b)** coronal CT-scan reconstruction at mediastinal window show diffuse, scattered, bilateral areas of micronodular calcifications, producing a "sandstorm" appearance. **c)** & **d)** HDP-Tc99m SPECT/CT reveals high symmetrical pulmonary uptake (similar to bone) due to phosphate-calcium accumulation.

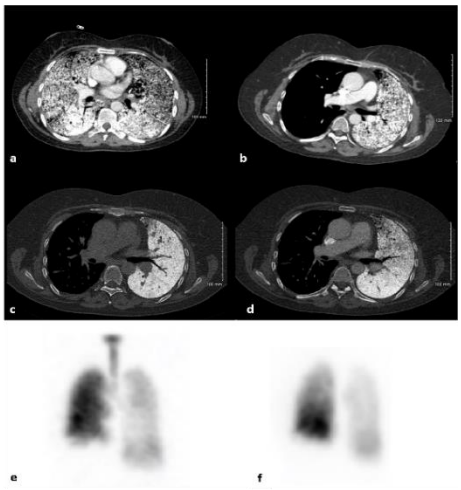

Figure 2: a) & **b)** Axial CT image at mediastinal window and **c)** & **d)** bone window. **a)** Axial baseline Chest CT image shows bilateral diffuse intra-alveolar as well as interlobular septal calcifications; **b)** Contrast-enhanced CT imaging one year after right pulmonary transplantation. Right transplanted lung appears more expanded than the restrictive left native lung involved by PAM; **c)** & **d): c)** Three years after right lung transplantation expiration **d)** and inspiration acquisitions show density changes between expiration and inspiration phase; **e)** & **f): e)** Planar images of ventilation after KRYPTON inhalation and **f)** perfusion after injection of 150MBq of technetium PULMOCIS, three years after transplantation. Left lung shows diffuse decrease in ventilation and perfusion: the relative perfusion contribution was 77.6% and 22.4% for the right and left lungs, respectively.

The evaluation of the impairment of ventilation and perfusion is a key metric to monitor the disease and to guide lung transplantation decision. Acquisition of deep breath-hold inspiration and expiration CT-scans will allow a monitoring of total and regional lung ventilation function capacity (Figure 2). Finally, ventilation perfusion SPECT/CT allows to directly assess how microliths impair total and regional ventilation and subsequently perfusion (Figure 2). Ventilation perfusion SPECT/CT is mostly used for pre-transplantation screening and post-transplantation follow-up due to its availability and cost.

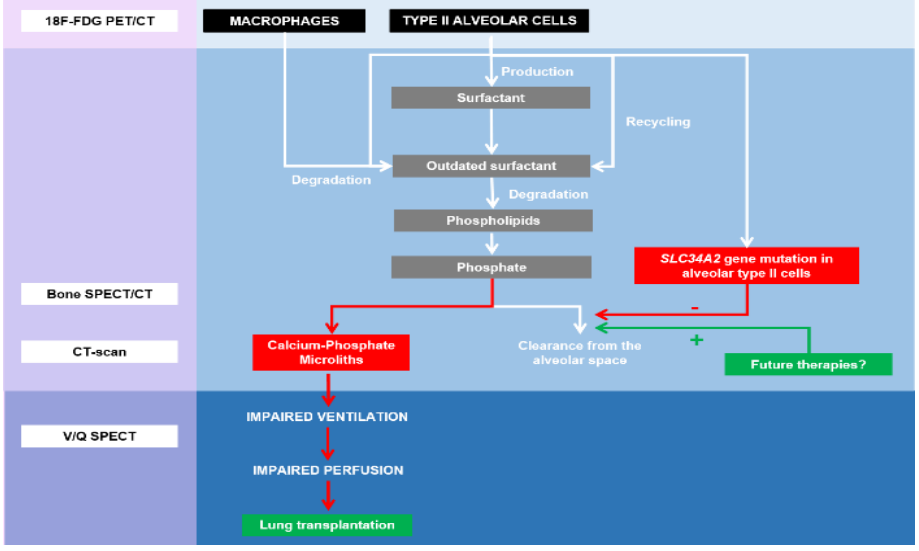

Figure 3: Proposal of a comprehensive imaging-guided optimization of the management of patients based on pulmonary alveolar microlithiasis actionable pathways.

Recent discovery of molecularly actionable mutations raises hope for new therapies targeting phosphate metabolism or the protein altered by the gene mutation. In this context, multimodal imaging could gain an important place for screening, staging, follow-up, and precision medicine approaches. Our proposed imaging-guided management was designed to fit the current knowledge of PAM actionable pathways and is stratified according to the temporal and spatial evolution of the disease (Figure 3).

Competing Interest

None.

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