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LETTERS TO THE EDITOR

Idiopathic pleuroparenchymal fibroelastosis with suggestive biopsy of pulmonary carcinoma – Case report

To the Editor,

Idiopathic pleuroparenchymal fibroelastosis (IPPFE) is an uncommon and recently defined condition characterized by fibrosis and thickening of dense and subpleural lung parenchyma, mainly in the upper lobes,[1] presenting with clinical course similar to chronic fibrosing interstitial pneumonias.[2] Thickening of visceral pleura combined with collagenic and intra-alveolar fibrosis and septal elastosis in abrupt transition to remaining lung parenchyma[3] compose an overlapping pattern with other interstitial pneumonias, where bad prognosis, different therapeutic options and knowledge of this entity are essential in medical practice.

An 82-years-old male was referred to the Pulmonology Department due to right thoracic pain and episode of haemoptysis. A computed tomography (CT) scan showed a solitary pulmonary lesion in the upper right lobe (Fig. 1), with 18-fludeoxyglucose uptake on positron emission tomography-computed tomography.

A transthoracic needle biopsy was performed and lung parenchyma with mild septa enlargement due to fibrosis was observed with one edge exhibiting a group of atypical cells in acinar arrangement together with large eosinophilic cells with hyperchromatic nuclei. Immunohistochemistry studies were positivity for cytokeratin 7 (SP52), cytokeratin 5/6 (D5/16B4), vimentin (V9) and thyroid transcription factor (TTF1, SP141) – all from Ventana, AZ-USA; Periodic acid-Schiff (PAS) was also positive. The diagnosis of probable adenosquamous carcinoma was proposed, taking into consideration the available representative factors.

Additional study of the patient was made: atrial fibrillation, smoking habits and dyslipidaemia were his pathological conditions. Physical evaluation, blood tests and respiratory function tests were normal (forced expiratory volume — FEV1 = 96.7%). An upper right lobectomy and mediastinal lymphadenectomy was performed.

We received a RULobectomy of 133 g weight gross and measuring 20 cm × 10.5 cm × 3.5 cm with areas of irregular visceral pleura that on cut surface revealed pleural thickening and subpleural dense tissue with a nodule measuring 3 cm × 2.5 cm × 3 cm; a caveated lesion with 1.5 cm was also detected, surrounded by dense lung parenchyma.

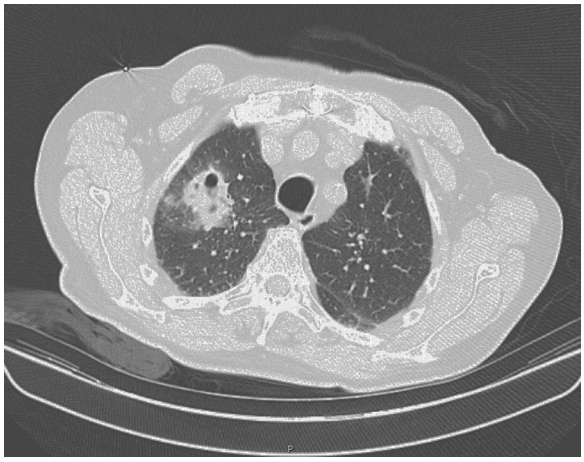

Figure 1 Computed tomography (CT) showing solitary pulmonary lesion in the upper right lobe. The lesion has irregular boundaries and a caveated component is exhibited.

Microscopically there was pleural thickening, with collagenous fibrosis (MT), and subpleural architectural distortion with elastosis and intra alveolar fibrosis (MT, EVG), with curled, short and randomly oriented elastic fibres. There were alveolar spaces and bronchioles imprisoned by the lesion, with bronchial associated lymphoid tissue hyperplasia and marked reactive changes in the epithelium (Fig. 2). The caveated lesion showed giant multinucleated cells, foreign body type, surrounded by fibroelastic band. In the periphery of the lesion, there was organizing pneumonia with inflammatory myofibroblastic polyps. An abrupt transition to the remaining lung parenchyma was registered, which showed emphysema and constrictive bronchiolitis.

The patient was revaluated three weeks after surgery. A chest X-ray showed minimal pneumothorax that disappeared in two weeks, without need for chest drainage.

IPPFE is an exceptional clinicopathological syndrome with its own radiological and histological features; there are fewer than 100 cases reported in the literature, first referred in 1992 by Amitani et al.[4] and later characterized by Frank et al. in 2004[5]; nowadays it is classified as a rare idiopathic interstitial pneumonia (IIP) by the updated American Thoracic Society/European Respiratory Society (ATS/ERS) classification.[1]

Clinically IPPFE does not show age or gender predilection and is not related to smoking, it presents normally with exertional dyspnoea and dry cough. Body weight loss may

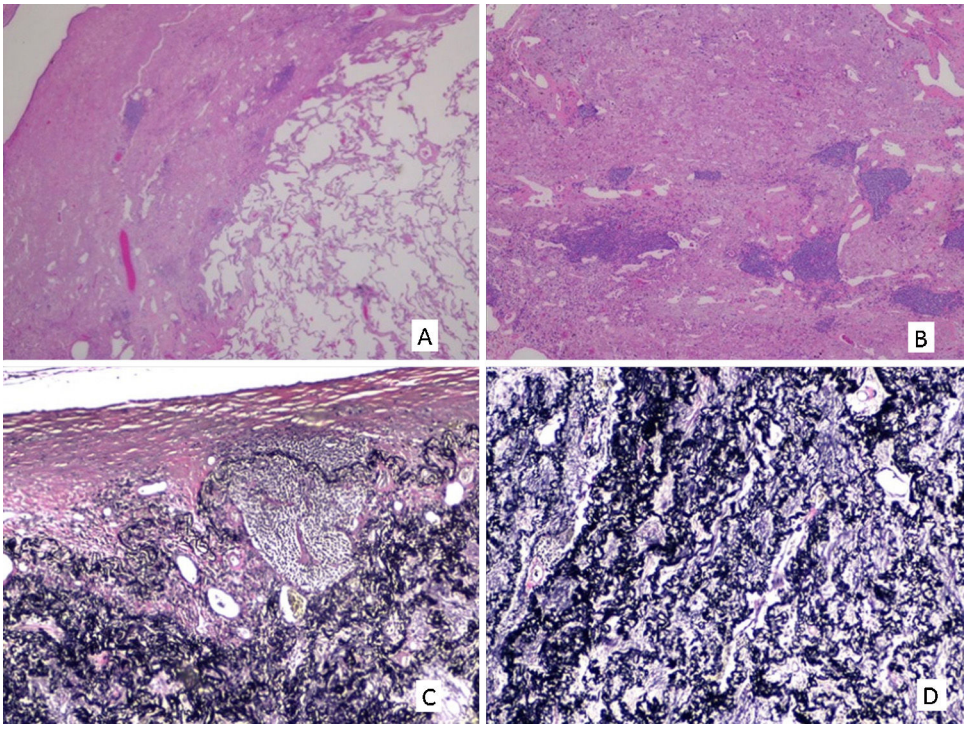

Figure 2 Dense pleural and subpleural fibrosis with abrupt transition to non-affected pulmonary parenchyma (A, H&E 20×); subpleural elastosis and intra alveolar fibrosis with alveolar spaces and bronchioles imprisoned by the lesion, with bronchial associated lymphoid tissue hyperplasia (B, H&E 40×); diffuse and severe elastosis with curled, short and randomly oriented elastic fibres (C and D, EVG 100× and 200×).

be registered and chest pain can occur as a consequence of pneumothorax.[2] Patients with IPPEF exhibit disease progression in 60%, with death from disease occurring in 40%.[1]

Classical histology presents upper zone fibrosis of the visceral pleura, homogenous and prominent subpleural fibrosis and alveolar septal elastosis, with preservation of pulmonary parenchyma away from pleura and abrupt transition of affected to normal tissue; however these findings may not appear or be absent in small biopsies.[3] In our case, classical histological elements were present, but the entrapped respiratory spaces with epithelial cells exhibiting marked reactive cellular atypia provided a diagnostic pitfall in transthoracic biopsy.

Radiological patterns may contribute to definite diagnosis with upper lobe pleural thickening and subpleural fibrosis and less/absent lower lobe involvement on high resolution computed tomography (HRCT),[2,3] without reference to defined nodular pattern as seen in this case.

The main differential diagnoses are connective tissue diseases, asbestosis, fibrosing sarcoidosis, radiation/drug induced diseases and normal interstitial pneumonia, the latter mainly in biopsies[6]; the absence of occupational exposure to dusts and the histological combination of intra-alveolar fibrosis and septal elastosis should favour IPPFE diagnosis.[3]

Up till now therapeutic schemes have not shown efficacy in IPPFE, as it is refractory to steroids/immunosuppressive agents, but survival may reach 11 years in lung-transplantation associated cases; supporting care may be useful and oxygen support is mandatory in advanced stages as well as infection control.[2,7]

IPPFE is a distinct and well characterized entity with aggressive and rapidly progressive course and poor prognosis. The intense fibroelastosis may be associated with prominent inflammatory and reactive changes, making the differential diagnosis with other IIPs challenging and occasionally mimicking oncologic diseases, especially in small biopsies, with actual case reflecting a possible nodular pattern.

Conflicts of interest

The authors have no conflicts of interest to declare.

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Neonatal respiratory failure due to ABCA3 deficiency

Respiratory distress syndrome (RDS) is due to surfactant deficiency and commonly occurs in preterm neonates. Recent studies indicate that mutations in the gene encoding for the ATP-binding cassette protein A3 (ABCA3) are a significant cause of neonatal respiratory distress in full-term neonates with surfactant deficiency.[1]

We present the clinical course of a male newborn with homozygous ABCA3 gene mutation, who was kept alive for 2 months with extracorporeal life support. He was the second child of Romanian parents in Portugal, had had no prenatal care assessment until 34 weeks when infectious screening showed negative serologies and vaginal group B *Streptococcus* carriage. Eutocic delivery at 36 weeks of gestational age, weighed 2880 grams and had Apgar score 9/10/10. Fifteen minutes after delivery the newborn developed respiratory distress and was started on Continuous Positive Airway Pressure and on antibiotics. A left-sided pneumothorax was diagnosed, treated successfully with thoracocentesis, allowing for spontaneous breathing with oxygen therapy (5 l/min).

At 36 h of life the chest X-ray (CXR) showed respiratory distress syndrome type II and surfactant was administered. Around 40 h of life, due to increasing dyspnea, he was started on high frequency oscillatory ventilation and inhaled nitric oxide and transferred to a level III Neonatal Intensive Care Unit, but clinical deterioration continued. On day 5 he had severe pulmonary hypertension and refractory respiratory failure and our extracorporeal membrane oxygenation (ECMO) referral center *retrieved him on veno-arterial ECMO*.

After 2 weeks of ECMO and persistent interstitial opacity on the CXR (Fig. 1), the infectious etiology was questioned and further investigation was undertaken. Computed tomography revealed diffuse reticular-nodular infiltrates and ground glass opacity in the lungs. Bronchoalveolar lavage revealed a mixed inflammatory pattern, without signs of alveolar proteinosis and tested negative for cytomegalovirus, *Legionella pneumophila*, *Pneumocystis jirovecii* and fungus.

Considering these clinical and imaging findings, negative culture results and absence of response to antibiotics, the most likely scenario was that of an interstitial lung disease, namely a surfactant protein disorder. Blood was sent for genetic tests and specific treatment was empirically started: prednisolone, hydroxychloroquine and azithromycin.

An improvement in the lung volumes on day 41 propelled a therapeutic trial with lung surfactant. During the following 12 h lung volumes increased to around 6 ml/kg and the interstitial opacity on CXR decreased. Unfortunately the effect did not last more than 12 h. The experience was repeated 24 h later with similar results.

On day 56 the genetic test results came through: DNA sequencing demonstrated a homozygous mutation in ABCA3 gene: c.3997_3998del (p.Arg1333Glyfs*24).Empiric treatment was discontinued and, on day 61, following a comprehensive discussion with the parents, intensive care was withdrawn.

After death lung and skin biopsies were performed, with written consent from the parents. The lung biopsy revealed chronic pneumonitis of the infant (Fig. 2).

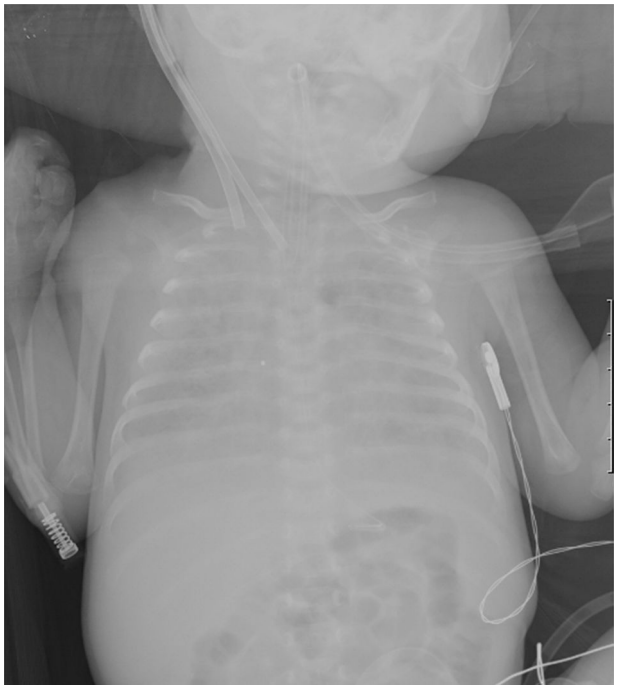

Figure 1 Chest radiograph. Persistent image of bilateral reticulogranular pattern after 2 weeks of ECMO.