

Respiratory bronchiolitis-interstitial lung disease: A rare complication of smoking

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Abstract

A 58-year-old male and a 52-year-old female, both active smokers, presented an incidental finding of bilateral miliary, centrilobular, diffuse ground glass-like opacities on their chest CT. The differential diagnosis is broad and includes miliary tuberculosis and vasculitis and could be ruled out after bronchoalveolar lavage and transbronchial biopsies. Lung cryobiopsy revealed interstitial and intraalveolar accumulation of brownish pigmented alveolar macrophages with small, fine-granular, anthracotic particles, i.e. “smokers macrophages”. The diagnosis of bronchiolitis-interstitial lung disease was retained at the institutional multidisciplinary ILD-board. Partial and complete remission was observed after smoking cessation.

Keywords

Bilateral miliary; CT; Tuberculosis; Lung.

Introduction

Respiratory bronchiolitis-interstitial lung disease (RB-ILD) is classified as smoking-related diffuse parenchymal lung disease. Most patients with RB-ILD are current or former cigarette smokers, suggesting that cigarette smoking plays a crucial role in the aetiology. There are only few reports of RB-ILD occurring in non-smokers who were exposed to tobacco smoke [1]. The role of cigarette smoking is further supported by the improvement in disease manifestations after smoking cessation. CT-imaging in RB-ILD often demonstrates diffuse, fine reticular or nodular opacities with preserved lung volumes [2]. The incidence of RB-ILD is unknown, but generally thought to be rare. RB without ILD is frequently found in smokers who receive lung biopsy for another reason, e.g. for suspicion of lung cancer and might consist of one end of the spectrum of the disease manifestation [3].

Case Presentation

A 58-year-old male patient underwent chest CT to rule out bilateral cervical necrotizing fasciitis.

Diffuse, bipulmonary, miliary, non-solid opacities were discovered as an incidental finding. The patient was in fair clinical condition, had no B-symptoms and was of stable weight. He was an active smoker with 60 pack years. Lung auscultation revealed vesicular breath sounds over all lung fields. Oxygen saturation was 98% under room air. Pulmonary function tests showed normal dynamic and static lung volumes with reduced carbon monoxide diffusion capacity. Sputum, bronchoalveolar lavage and blood cultures were taken to rule out miliary tuberculosis. The Ziehl-Neelsen-staining, PCR and later the definitive cultures for mycobacteria were all negative. Bronchoscopy did not show any relevant macroscopic abnormalities apart from a slight non-specific mucosal inflammation. Transbronchial cryobiopsies revealed interstitial and intra-alveolar accumulation of slightly brownish pigmented alveolar macrophages with small, fine-grained, anthracotic particles – so-called “smokers macrophages” - and discrete focal micronodular interstitial fibrosis predominantly in the perivascular locations matching centrilobular areas (Figures 2 & 3). The histological changes were primarily reminiscent of smoking-associated changes. Thus, the probable association between smoking and his interstitial lung pathology was corroborated.

The second case was a 52-year-old female with active cigarette smoking of 20 pack years. She initially presented on the emergency unit with acute right-sided thoracic pain that had been occurring for 1 week. The patient was in good general condition and afebrile. She had no dyspnoea nor cough. Her clinical examination revealed ubiquitous vesicular breath sounds. A contrast-enhanced chest CT was performed to rule out pulmonary embolism. Due to the diffuse, bilateral, multiple, partly cystic nodularities with some subpleural predilection the differential diagnosis included eosinophilic granulomatosis with polyangitis. Also in her case, an increased BAL cellularity mainly consisting of alveolar macrophages with fine-granular and yellowish-brown cytoplasm inclusions could be detected. She had a blood leukocytosis of 15.5 (norm <10) G/l and a CRP of 189 (norm <10) mg/l, but turned out to be negative for ANA, ANCA and rheumatoid factor. To definitively confirm or rule-out a vasculitis a thoracoscopic wedge resection was performed. In her case no signs of vasculitis were identified.

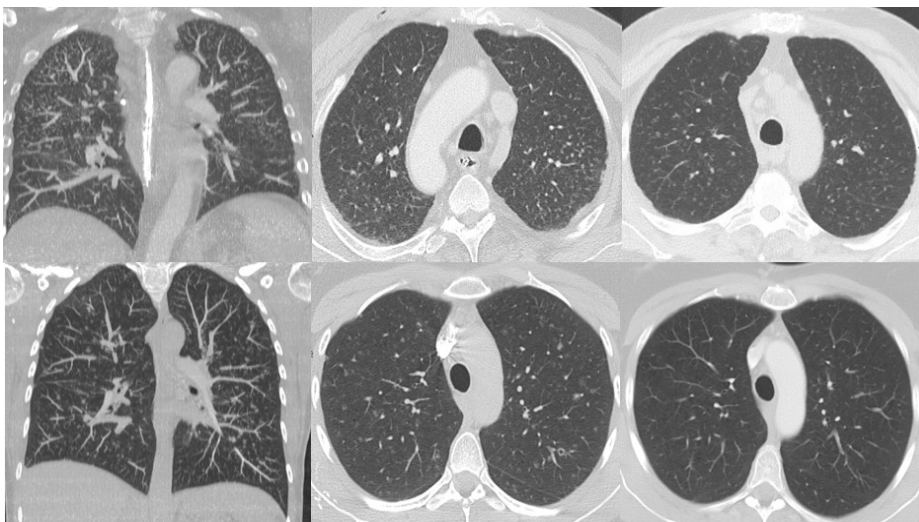


Figure 1: Thoracic CT-morphology of respiratory-bronchiolitis-interstitial lung disease in 2 incidental cases – presence of upper-lobe predominant, diffuse, bipulmonary, miliary, centroacinary, non-solid opacities with (partial) remission after smoking cessation. Axial (left) and coronal (middle) at initial presentation and follow-up after smoking cessation (left) chest CT images in an 58-year old male patient (top row) and in an 52-year-old female patient (bottom row).

Both cases were discussed at the institutional multidisciplinary decision board for interstitial lung diseases and the consensus diagnosis of RB-ILD was retained. Consistent smoking cessation was recommended in both cases. At the 6 month-follow-up, the first patient could not consequently stop smoking - so he finally accepted referral to our smoking cessation clinic. The second patient consistently stopped smoking. Her follow-up CT showed normal findings, thus, complete remission of her RB-ILD (Figure 1). She had mild, non-reversible obstructive ventilatory defect compatible with COPD GOLD 1, but her CO diffusion capacity slightly improved compared to the previous examination.

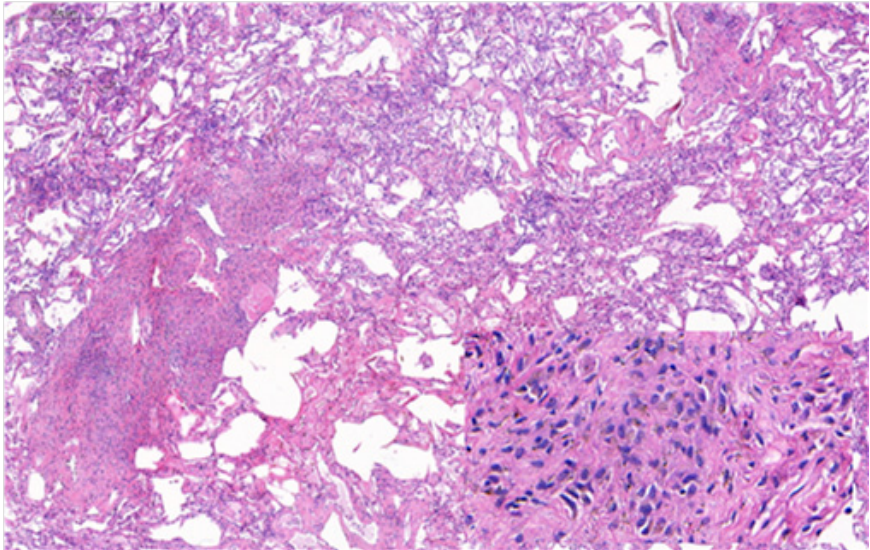


Figure 2: Lung cryobiopsy reveals multilocular peribronchovascular nodular formations of small micronodular histiocyte-rich and mild locular fibrosis. The alveolar architecture is intact and appears only artificially rarified (Haematoxylin-Eosin-staining, scale top right corner). Insert (bottom, right) with detailed representation of the micronodular histiocyte-rich fibrosis area with the so-called “smoker macrophages”.

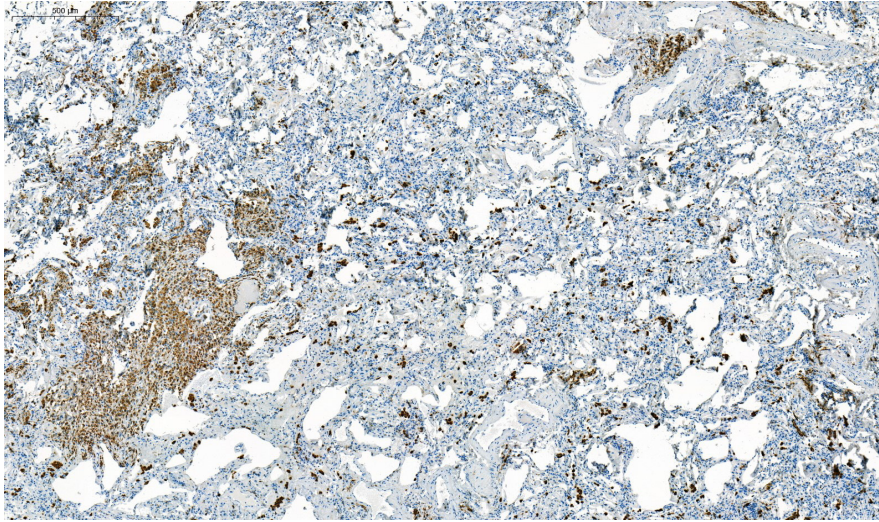


Figure 3: Immunohistochemistry for histiocytes (CD68) of the same histologic location shows histiocytic-rich fibrotic intraalveolar and interstitial nodules.

Discussion

In active smokers with diffuse bipulmonary miliary non-solid nodularities, apart from many differential diagnoses, respiratory bronchiolitis-interstitial lung disease (RB-ILD) should be considered. Within the interstitial lung diseases, RB-ILD is classified as a smoking-related disease and one of the “Idiopathic Interstitial Pneumonias” [4]. In RB-ILD, smoking leads to an accumulation of brownish pigmented alveolar macrophages with small, fine-granular, anthracotic particles, so called “smokers macrophages” within the lumen of respiratory bronchioles with variable degree of interstitial fibrosis and an accompanying peribronchiolar infiltrate of lymphocytes and histiocytes/smokers macrophages [5].

In our first case, we found diffuse miliary ground glass opacities with upper lobe-predominance. After TB was ruled out, the presence of the so-called smoker’s macrophages confirmed smoking-associated lung damage. An association was found in the Literature between the degree of cytoplasmic pigmentation of macrophages and the number of pack-years smoked, and between the presence of peribronchiolar fibrosis and the number of pack-years [3]. RB-ILD can successfully be stabilized or even remit after smoking cessation. Also, persistent smokers usually experience a relatively stable clinical course. Treatment with oral corticosteroids was able to lead to transient improvement in selected cases, but is not a standard for RB-ILD [6].

Conclusion

In oligosymptomatic active smokers with diffuse bipulmonary miliary groundglass nodularities respiratory bronchiolitis-interstitial lung disease should be considered and is likely to improve after smoking cessation.

Acknowledgements

We thank Dr. med. Jan Kellner, Senior Physician in Radiology at Cantonal Hospital St. Gallen for the valuable cooperation.

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Manuscript Information: Received: June, 10 2022; Accepted: July 01, 2022; Published: July 15, 2022

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Citation: Isic E, Rassouli F, Rodriguez R, Jorg-Thomas K, Brutsche M. Respiratory bronchiolitis-interstitial lung disease: A rare complication of smoking. Open J Clin Med Case Rep. 2022; 1870.

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