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CASE REPORT

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An unusual case of interstitial lung disease: Revisiting peribronchiolar metaplasia interstitial lung disease (PBM-ILD)

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Abstract

Peribronchiolar metaplasia (PBM) is a histological finding of uncertain significance commonly seen in interstitial lung disease (ILD). PBM is thought to be secondary to small airway injury from insults such as tobacco smoke and other environmental exposures. The term PBM-ILD has been proposed for patients with ILD where PBM is the major histologic finding, however a lack of radiographic changes supportive of ILD in previously reported cases has limited recognition of the diagnosis. We present a rare case of welding-associated ILD with clinical, radiographic, and histologic evidence consistent with the proposed definition of PBM-ILD. We outline an approach to its consideration as a diagnosis based on our experience through multidisciplinary discussion.

KEYWORDS

bronchiolar fibrosis, idiopathic pulmonary fibrosis, interstitial lung disease, occupational lung disease, peribronchiolar metaplasia

INTRODUCTION

Peribronchiolar metaplasia (PBM) is a non-specific histologic finding with unclear clinical significance that is commonly reported in interstitial lung disease (ILD).[1–3] It is characterized by a fibrotic and proliferative extension of bronchiolar epithelia into perialveolar septae, and understood to be secondary to pulmonary insults, such as tobacco smoke.[1,2,4,5] A case series of idiopathic interstitial pneumonias (IIP) with PBM-dominant histology first proposed the term PBM-ILD.[3] PBM-ILD was defined as unclassified ILD with PBM as the sole histologic explanation for symptoms. However, as HRCTs in this series were predominantly normal, beyond mosaic attenuation, its recognition as a diagnosis has remained limited.[6,7] We present a rare case of welding-associated ILD with PBM as the sole histologic explanation for the clinical and radiographic presentation.

CASE REPORT

A 57-year-old Sri Lankan man with hypothyroidism, dyslipidemia, and a prior label of eosinophilic pneumonia was assessed in our ILD clinic in September 2020. His queried diagnosis of eosinophilic pneumonia had been based on recurrent presentations with cough, bronchoscopy from 2014 which showed modestly elevated eosinophils of 19%, and initial response in lung function to steroids. However, when symptoms and radiologic evidence of ILD persisted despite ongoing steroid therapy in the setting of an eosinophil level that had not met the threshold necessary for a confident diagnosis of eosinophilic pneumonia, he was referred to our clinic to investigate alternate etiologies.

During initial consultation, he endorsed worsening dyspnea over 6 months and cough with white sputum. He denied infectious, cardiac, and constitutional symptoms. He was a lifetime non-smoker. He had a 30-year history of occupational welding fume exposure, though always wore personal protective equipment at the workplace. There were no organic or inorganic pneumotoxic exposures, pneumotoxic drug use, symptoms of connective tissue disease (CTD), or family history of ILD.

Physical examination was unremarkable beyond diffuse bibasilar inspiratory crackles. Pulmonary function testing in September 2020 showed severely reduced forced vital

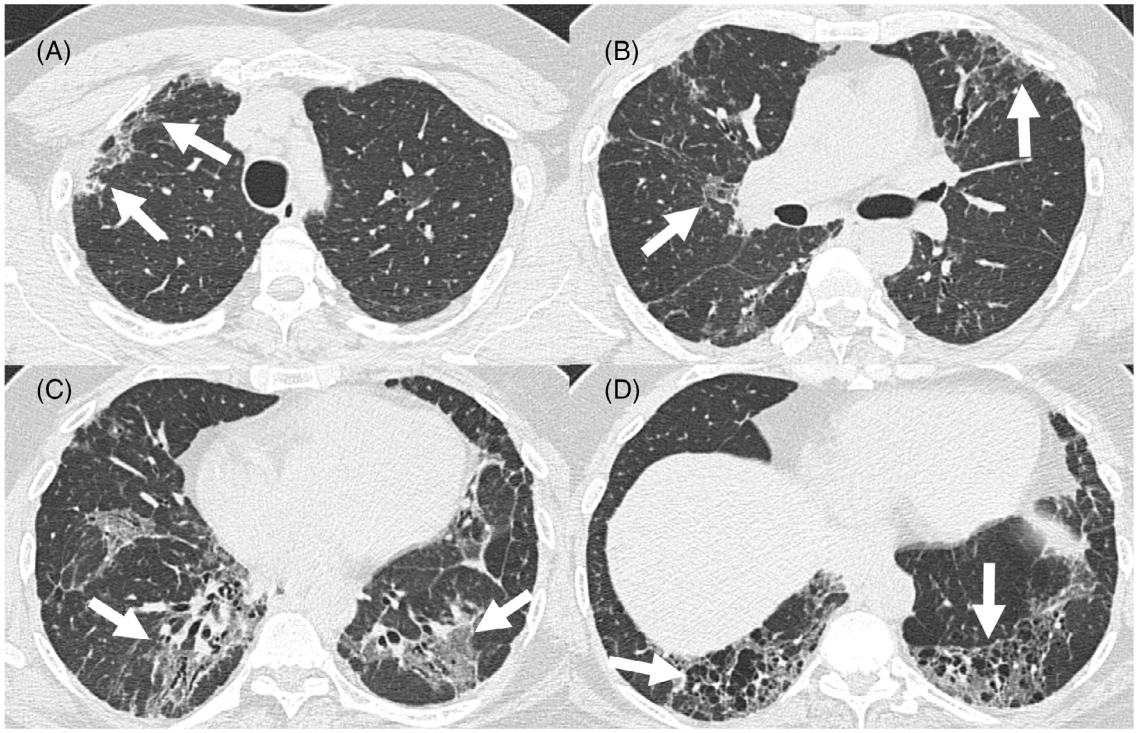

FIGURE 1 Fibrosing interstitial lung disease in a 57-year-old man with worsening dyspnea and a history of welding fume exposure. Transverse images of the lung demonstrate mild fibrosis at the apices (arrow, A) and mid lung (arrows, B) that is predominantly peripheral and reticular with mild ground glass opacity. In the lower lung zones, the fibrosis is strikingly peribrochovascular (arrows, C) with confluent ground glass opacity, traction bronchiectasis, and architectural distortion. Cystic formations are evident amongst the fibrosis at the extreme lung bases (arrows, D)

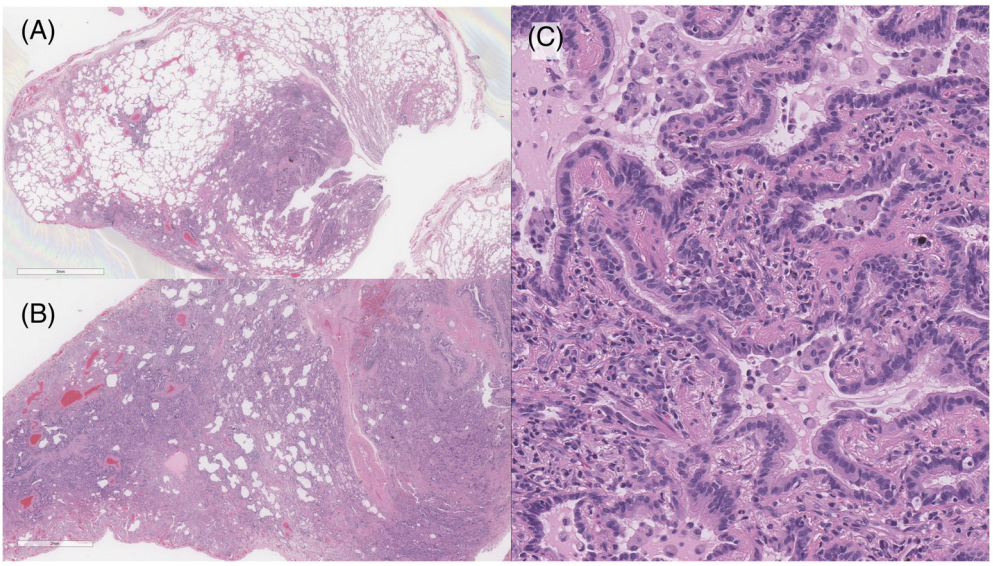

FIGURE 2 Extensive peribronchial metaplasia can be seen in both the left upper lobe (a) and left lower lobe (B), with more diffuse involvement seen from sections of the lower lobe. Peribronchiolar metaplasia is characterized by metaplastic bronchiolar epithelium into adjacent alveolar spaces with retention of cilia (C)

capacity of 2.3 L (48% predicted; FEV1/FVC 83%) and normal resting DLCO of 17.9 ml/min/mmHg (92% predicted). He reached 585 meters (104% predicted) on a 6-min walk test with a resting saturation of 100% and minimum saturation of 90% on room air. CBC, liver enzymes, renal function, and C-reactive protein were within normal range. CK was mildly elevated (288 U/L; normal upper limit 241 U/L). ANA, ENA, rheumatoid factor, anti-CCP, and ANCA serology were negative. Myositis panel showed weakly positive anti-Mi-2-alpha.

Serial HRCTs were performed. In 2014, bilateral peribronchovascular ground glass opacities in upper and middle lung zones were observed, which was most consistent with an alternative diagnosis to usual interstitial pneumonia (UIP). This persisted on imaging in 2018, with new subpleural reticulation, peri-bronchovascular traction, and cystic bronchiectasis. HRCT in May 2021 showed progressive fibrosing ILD (Figure 1).

Video-assisted thoracoscopic (VATS) surgical lung biopsy of left upper and lower lobes in 2019 showed extensive PBM (Figure 2).

The differential considered (in order of likelihood) at multidisciplinary discussion (MDD) was welding-associated PBM-ILD, idiopathic PBM-ILD, fibrotic nonspecific interstitial pneumonia (NSIP), and chronic fibrotic hypersensitivity pneumonitis (HP) without an identified organic antigen. Occult CTD-related ILD was discussed to be less likely through MDD, as there were no signs or symptoms of CTD and a weakly positive anti-Mi-2 antibody in isolation is a nonspecific finding.

Management was decided through MDD. Given the minimal inflammatory infiltrates on biopsy and no symptomatic, physiologic, or radiologic response to steroids, anti-inflammatory therapy was discontinued. Anti-fibrotic therapy was recommended for the progressively fibrosing phenotype, for ongoing ILD clinic follow-up with consultation from an occupational lung disease specialist.

DISCUSSION

ATS/ERS guidelines for IIPs (2013) describe PBM-ILD to "probably represent a form of small airway disease" based on lack of consistent parenchymal radiographic evidence in previous reports. We present a histopathologically unusual case of welding-associated ILD with PBM as the sole explanation for the progressive fibrosis on HRCT.

PBM is commonly reported in ILD, including HP, UIP, NSIP, respiratory bronchiolitis, and desquamative interstitial pneumonia.[1,4,7,8] However, these diagnoses also demonstrate additional histopathologic features, such as coincident fibroblastic foci, honeycomb change, bronchiolocentric fibrosis, and/or widespread cellular inflammation.[8–11] In the present case, upper and lower lobe lung biopsy showed extensive PBM, but with minimal cellular interstitial pneumonia and cellular bronchiolitis, and a lack of poorly formed non-necrotizing granulomas to suggest that this was HP.

The 30-years of welding was highlighted during MDD. ILD with metal exposure includes bronchiolitis obliterans, subacute fibrosing alveolitis, and chronic interstitial pneumonia, the last of which can be consistent with a pneumoconiosis called giant cell interstitial pneumonia (GIP).[12–14] Metal arc welding aerosolizes metal oxides and toxic gases which deposit into airways to increase risk of pulmonary disease.[15] No histopathologic evidence of GIP was observed in our case, suggesting against a diagnosis of hard-metal lung disease, however the exposure was recognized as possibly contributory during MDD. Our literature review yielded one previously reported case of welding-associated PBM-ILD, wherein a 44-year-old male with welding and asbestos exposure was diagnosed with interstitial pneumonia with PBM-predominance on biopsy.[3] However, no HRCT findings were reported to support this diagnosis.

Narrowing the differential in "unclassifiable" ILD remains challenging but a priority to alleviate patient distress and facilitate early intervention in this progressive and irreversible disease. The present case contributes to sparse literature on the clinical relevance of PBM in ILD. More data is required to understand whether PBM-ILD is truly an independent entity or a marker of inhalation injury and other ILD. As in our case, its diagnosis may be appropriate in rare cases with consistent clinical, radiographic, and histologic evidence with no alternate explanation based on MDD. The phenotype of this case suggests against the utility of long-term anti-inflammatory therapy, although its role in acute exacerbation remains unclear. Reports of similar cases will have much to contribute to classifying the unclassifiable in ILD literature, and the query of PBM-ILD as a unique diagnosis.

AUTHOR CONTRIBUTIONS

All authors contributed to the conception and interpretation of the work, in addition to the drafting and revision of the present report.

CONFLICT OF INTEREST

Jolene Fisher reports grants from the Canadian Pulmonary Fibrosis Foundation and the University of Toronto, and personal fees from Boehringer-Ingelheim and AstraZeneca, outside the submitted work. Shane Shapera reports honoraria for speaking engagements and participation in advisory boards with Boehringer-Ingelheim, Hoffman-La Roche and AstraZeneca. Micheal McInnis reports personal fees from Bayer and Boehringer-Ingelheim, outside the submitted work.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICS STATEMENT

The authors declare that appropriate written informed consent was obtained for the publication of this manuscript and accompanying images.

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