

Transbronchial lung biopsy (TBLB) in diagnosing pulmonary alveolar proteinosis (PAP): forgotten role in Australia?

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Abstract

Transbronchial lung biopsy (TBLB) is uncommonly performed in non-malignant conditions because of its low sensitivity and small tissue samples. It is not routinely performed in Australia to investigate idiopathic pulmonary fibrosis, although it can be a useful adjunct in obtaining tissue diagnosis in selected conditions in interstitial lung disease (ILD). A 52-year-old non-smoker received a living unrelated renal transplant in January 2014 but developed insidious onset of dyspnea on exertion 1 year later. Computed tomography of the thorax showed bilateral persistent ground glass opacifications with a characteristic crazy paving pattern, although *Pneumocystis jirovecii* pneumonia was more concerning. He was treated as *Pneumocystis jirovecii* pneumonia but his initial bronchoscopy failed to confirm either diagnoses. He then went on to TBLB that showed the presence of periodic acid–Schiff staining material. We conclude that TBLB is a useful adjunct to obtain histological diagnosis of ILD in carefully selected patients with appropriate radiological indications.

Introduction

Transbronchial lung biopsy (TBLB) is uncommonly performed in interstitial lung disease (ILD) and various non-malignant conditions because of its low tissue yield and small tissue samples in defining histological patterns [1]. In a recent Australian survey [2], only 1% of respondents in 2012–2013 would routinely perform TBLB to investigate idiopathic pulmonary fibrosis (IPF). Nonetheless, TBLB is helpful in certain pathological processes involving centrilobular and peribronchial regions [3]. Pulmonary alveolar proteinosis (PAP) is an example of these processes with its typical radiological findings including ground glass opacities, parenchymal consolidation, and reticuloseptal reticulations leading to a non-specific but characteristic crazy paving pattern. Open lung biopsy (OLB) is unnecessary to diagnose the condition, and TBLB is a useful adjunct although bronchoalveolar lavage (BAL) fluid analysis is often sufficient for its diagnosis [4]. We describe a case

of PAP with typical radiological features and failure of an initial BAL to confirm its diagnosis but TBLB did. The case report should remind clinicians that TBLB should be considered as an alternative to OLB in patients with appropriate radiological and clinical indications.

Case Report

A 52-year-old non-smoker man from New South Wales, Australia, became a recipient of living unrelated renal transplant in January 2014. His initial course was complicated by BK virus infection that resolved 3 months afterward. He had no history of any respiratory illnesses but developed insidious onset of dyspnea on exertion 12 months post-transplantation. There were no constitutional symptoms or features to suggest infection, and he had minimal respiratory symptoms otherwise. He continued his work as a tradesperson despite his respiratory symptoms without significant issues. Cardiopulmonary examination

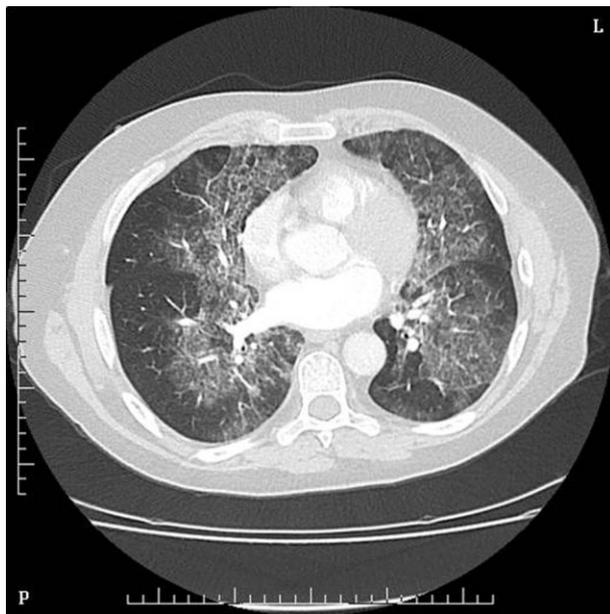


Figure 1. Computed tomography of the thorax showing ground glass opacifications.

remained unremarkable without hypoxia. A computed tomography of the thorax (Fig. 1) demonstrated diffuse ground glass opacifications with a perihilar zonal predominance with a crazy paving pattern reported, but *Pneumocystis jirovecii* pneumonia (PJP) appeared to be concerning in the context of immunosuppression. He was on appropriate PJP prophylaxis during the post-transplant period. His blood tests and connective tissue screening were unremarkable except a creatinine of 128, which is his baseline renal allograft function. Echocardiogram was normal. His lung function test demonstrated mild airflow obstruction and normal lung volumes with mild impairment of gaseous exchange. A 6-min walk test documented the absence of post-test desaturation. He was initially managed for PJP and given clindamycin and primaquine, but bronchoscopy with BAL fluid analysis failed to establish a diagnosis. Macroscopic appearance of the BAL fluid was also normal. Given the absence of microbiological evidence to suggest infection, TBLB was performed to evaluate the histological pattern of his radiological changes. TBLB showed periodic acid–Schiff positive stained, granular eosinophilic material in alveoli consistent with PAP (Fig. 2). The procedure was well tolerated without any significant complications. An extensive search was in progress to determine the etiology of his PAP, while he opted for a conservative management approach with ongoing clinical monitoring due to the mild degree of symptoms (disease severity score of 1).

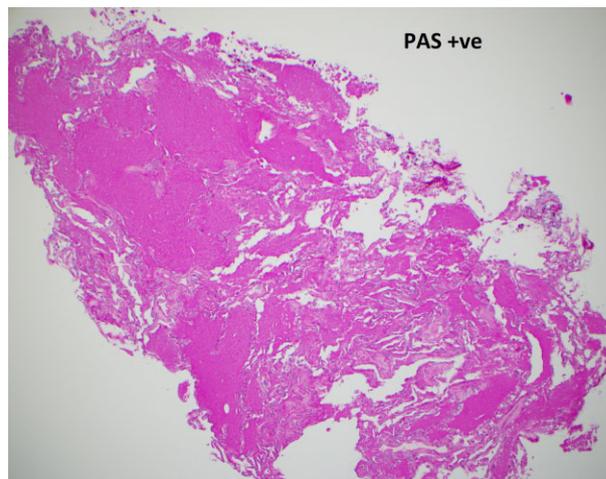


Figure 2. Transbronchial lung biopsy showing periodic acid–Schiff (PAS) positive eosinophilic material in alveoli.

Discussion

TBLB was described by Andersen et al. [5] to obtain parenchymal tissue via flexible bronchoscope to investigate diffuse interstitial lung disease. Radiological indications for TBLB included alveolar opacifications, reticulonodular perilymphatic changes, “tree-in-bud” pattern, and the presence of the “bronchus sign” [3]. It is also useful in conditions where small lung fragments are adequate for tissue diagnosis, such as granulomatous diseases, cryptogenic organizing pneumonia, diffuse alveolar damage but inadequate for IPF, non-specific interstitial pneumonitis, and desquamative interstitial pneumonia [1]. The size limitations of its parenchymal tissue obtained subsequently led to the procedure carried out less frequently over time. This was reflected in a recent Australian survey revealing a decrease in the routine use of TBLB to diagnose IPF from 18% of the correspondents in 1999 to 1% in 2012–2013, in accordance with changes in international IPF guidelines [2]. More recently, the use of transbronchial lung cryobiopsy (TBLC) generated renewed interest in the technique [1] due to the ability of TBLC to obtain larger lung fragments to assist histological interpretation.

PAP is characterized by defective surfactant clearance by alveolar macrophages, leading to alveolar accumulation of lipoprotein-rich material correlated as ground glass opacity radiology. This is superimposed with reticulations from interstitial disease resulting in a crazy paving pattern. Although this pattern is characteristic of PAP, it is non-specific and is found in a wide variety of lesions, including cardiogenic pulmonary edema, alveolar hemorrhage, pulmonary infection, exogenous lipid pneumonia, or bronchioloalveolar carcinoma [4]. Our case report clearly

demonstrated that TBLB could establish a diagnosis when BAL failed to do so. Indeed, in a cohort of 248 patients 34.1% and 58.7% of PAP cases were diagnosed by TBLB and BAL, respectively [4]. Our patient had typical radiological features, but both the macroscopic appearance of his initial BAL and cytology was not suggestive. We postulate that the initial BAL was sampled in a zone without significant lipoprotein-rich material, despite the area being abundant of ground glass changes radiologically.

To conclude, our case report demonstrated that TBLB has its place in the diagnosis of ILD especially when there are non-specific, diffuse changes which in turn would allow higher yield of sampled tissue. In carefully selected cases with radiological and clinical indications, we believe that it can be considered as an alternative to OLB despite OLB being readily available in Australia. This is especially important when BAL fails to establish a diagnosis.

Disclosure Statements

No conflict of interest declared.

Appropriate written informed consent was obtained for publication of this case report and accompanying images.

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