


Transbronchial lung cryobiopsy: a novel confirmatory tool to diagnose asbestos-related pulmonary fibrosis

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Keywords

Asbestos fibre count, asbestosis, cryobiopsy.

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Received: 28 June 2018; Revised: 8 October 2018;

Accepted: 9 October 2018; Associate Editor:

Kazuhiisa Takahashi.

Respirology Case Reports, 7 (1), 2019, e00380

doi: 10.1002/rccr.2.380

Abstract

Asbestosis is diagnosed with a combination of historical, clinical and radiological findings in the absence of another cause. Histology is required when uncertainty exists, with lung biopsy via VATs being gold standard. Transbronchial cryobiopsy is becoming increasingly popular for diagnosing interstitial lung disease and may provide sufficient lung sample to demonstrate asbestosis. A 73 year old man presented with dyspnoea on a background of rheumatoid arthritis, previous methotrexate use and asbestos exposure. Examination revealed fine crackles in the mid and lower zones bilaterally without signs of pulmonary hypertension. The presence of pleural plaques and basal interstitial reticulation on HRCT was suggestive of asbestosis but histology was required to differentiate this from rheumatoid or methotrexate associated ILD. Samples of lung tissue were obtained via transbronchial cryobiopsy, demonstrating fibrosis and asbestos fibres consistent with asbestosis. Transbronchial cryobiopsy appears effective in obtaining sufficient parenchymal lung samples to diagnose asbestosis when clinical uncertainty exists.

Introduction

Asbestosis is a diffuse pulmonary fibrosis resulting from the excessive inhalation of asbestos fibres [1]. It is a slow progressing disease that has a lead time of 15–40 years from exposure until onset of symptoms [2–4]. Diagnosis is usually made on probability based on a history of asbestos exposure, clinical features of pulmonary fibrosis, absence of another cause of fibrosis, and radiological findings. Often, histological confirmation is required, such as when atypical clinical or radiological features are present or for medicolegal reasons associated with compensation. Due to insufficient tissue samples obtained via traditional bronchoscopic

transbronchial biopsy, current recommendations suggest biopsy via video-assisted thoracoscopic surgery [5]. Transbronchial cryobiopsy is an increasingly popular technique for the diagnosis of interstitial lung disease and may provide lung samples of sufficient size for the diagnosis of asbestosis.

Case Report

A 73-year-old former smoker (5 pack-years) presented for respiratory evaluation with progressive exertional dyspnoea over the course of a few years. He described heavy

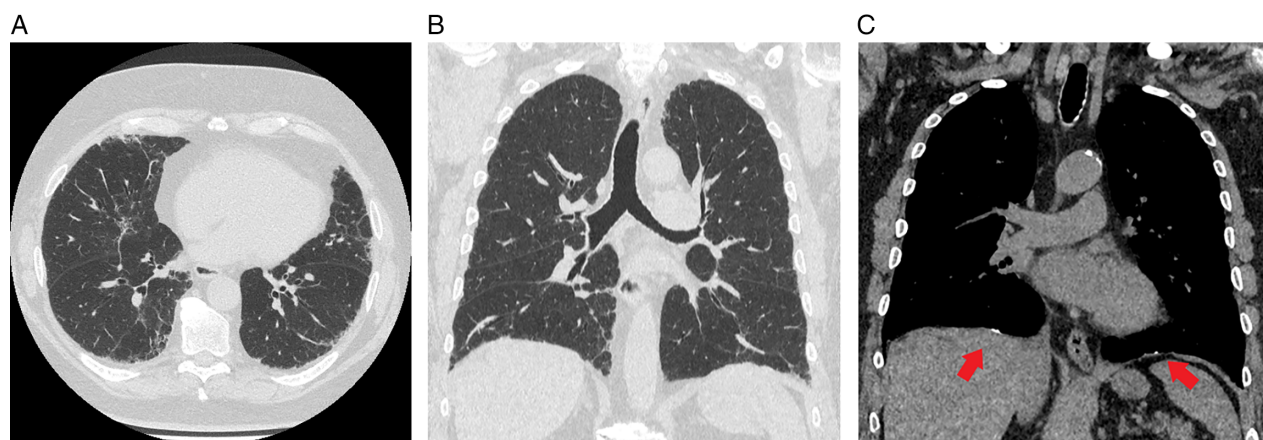


Figure 1. Axial (A) and coronal (B) high-resolution computed tomography chest views demonstrating mild subpleural reticulation. Mediastinal window (C) demonstrates diaphragmatic calcification (arrows).

occupational asbestos exposure between 18 and 55 years of age while employed on ships removing asbestos lagging from insulated pipes, rarely using protective ventilatory apparatus. Relevant medical background included rheumatoid arthritis previously on methotrexate, type 2 diabetes mellitus, hypertension, and obesity.

On examination, he was noted to be morbidly obese (body mass index 40.2), saturating 96% on room air with a respiratory rate of 24/min, and was normotensive. There was no clubbing or lymphadenopathy. Fine crackles were auscultated in the mid and lower zones bilaterally. Cardiac examination was normal, and there were no clinical features of pulmonary hypertension.

Pulmonary function tests demonstrated a forced expiratory volume in 1 second (FEV1) of 2.09 L (82.4% predicted), forced vital capacity (FVC) of 2.75 L (82.7% predicted) with FEV1/FVC ratio of 0.76, Total Lung Capacity (TLC) of 4.46 (72.2% predicted), and Diffusing capacity of the lungs for carbon monoxide (DLCO) of 12.95 (57.1% predicted), demonstrating a parenchymal restrictive process.

A high-resolution computed tomography chest showed calcified pleural plaques bilaterally, predominantly in the lower zones. Increased subpleural reticular markings at the lung bases were present, with relative sparing of upper zones. There was no obvious honeycombing (Fig. 1).

A diagnosis of asbestosis was suspected clinically, but differential diagnoses included idiopathic pulmonary fibrosis, rheumatoid arthritis, and methotrexate-associated interstitial lung disease. The presence of pleural plaques, whilst confirming asbestos exposure, was insufficient for the confirmation of asbestosis. Due to the importance of differentiating these causes, histological confirmation was sought.

The patient underwent elective rigid bronchoscopy under general anaesthesia. The central airways appeared macroscopically normal without significant endoluminal

abnormality. Bronchoalveolar lavage was performed from the right middle lobe and from the lingula, both yielding a clear, watery return. Under fluoroscopic guidance, a 1.9-mm cryoprobe was inserted into the right lower lobe basal segments (RB8, RB9 and RB10) and the lateral segment of the right middle lobe (RB4). The procedure was uncomplicated, and no pneumothorax was noted on post-procedure chest X-ray.

The bronchoalveolar lavage demonstrated bronchial cells and macrophages amidst a moderate number of neutrophils. An isolated ferruginous body was present.

Two tissue biopsies (4 mm and 6 mm across) from the right middle lobe showed alveolated lung parenchyma with mild peribronchiolar fibrosis associated with some mild type 2 pneumocyte hyperplasia. Multiple asbestos bodies were seen, with a count of at least 14 per cm² (Fig. 2).

A further four biopsies (ranging 4–7 mm across) from the right lower lobe comprised a higher proportion of bronchial wall with cartilage and peribronchial glands as well as alveolated lung parenchyma. There were also asbestos bodies present (at least 9 per cm²).

Of relevance, no significant interstitial inflammatory infiltrates/lymphoid aggregates, granulomas, vasculitis, haemorrhage, or other specific features were noted to suggest a connective tissue disease as the underlying pathology.

On the basis of this histopathology and the clinical and radiological information, a diagnosis of asbestosis was made.

Discussion

This case demonstrates the utility of transbronchial lung cryobiopsy in confirming the aetiology of asbestos-related interstitial lung disease in the presence of diagnostic uncertainty. The cryobiopsy technique allows for a larger

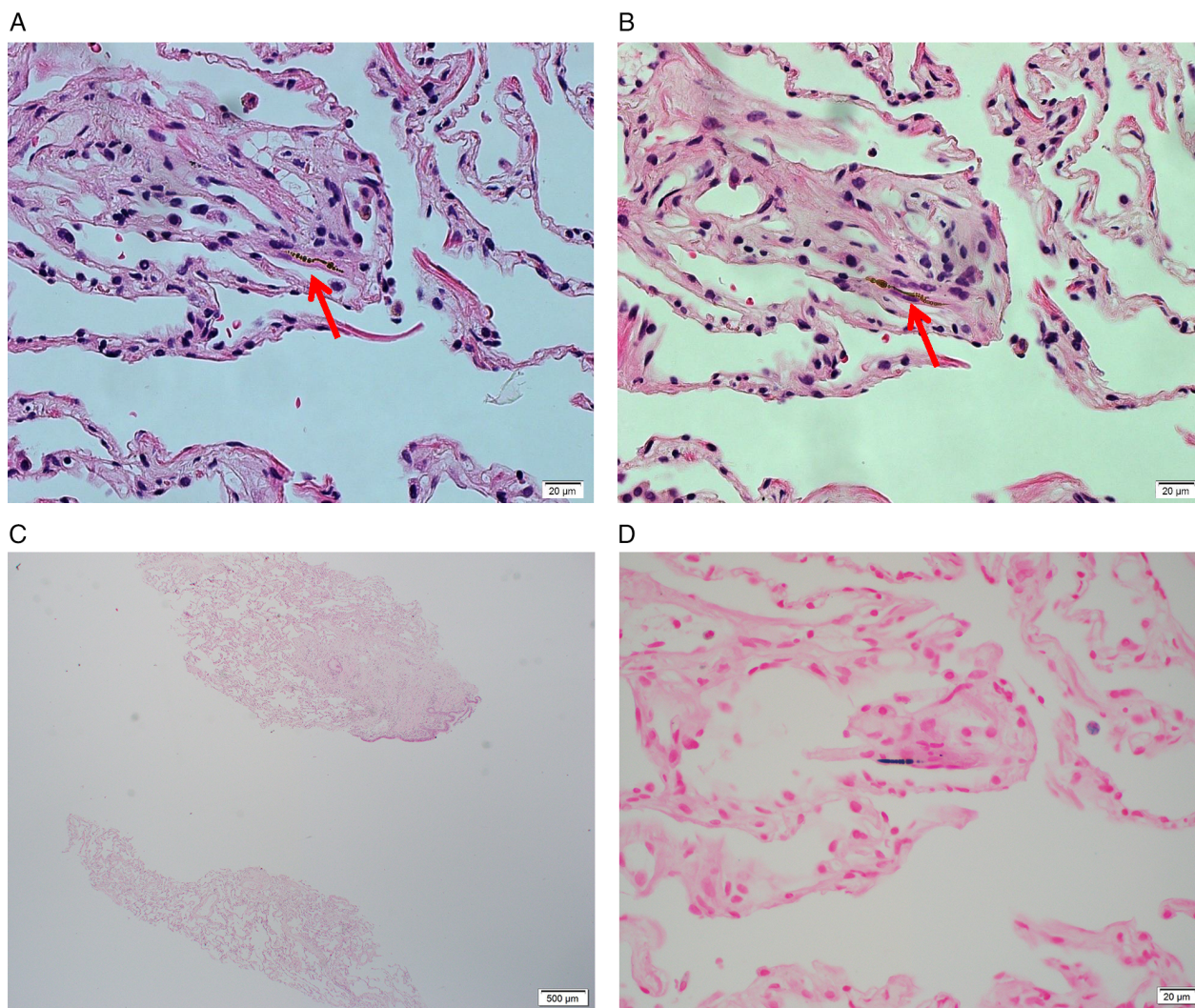


Figure 2. (A) and (B) Examples of ferruginous bodies found in the cryobiopsies of alveolar lung parenchyma from this patient. Arrows indicate the characteristic pigmented beaded bodies in the interalveolar septae. (C) Low-power view of Haematoxylin and eosin (HE) stain containing alveolar parenchyma. (D) Perls' stain highlighting asbestos body.

specimen yield, increasing the probability of sampling pathological tissue compared with conventional transbronchial biopsy [6–8].

The gold standard for diagnosis of asbestosis is made based on the presence of diffuse interstitial pulmonary fibrosis in a subpleural distribution together with the histological finding of asbestos bodies implanted in the air spaces or within regions of fibrosis. On light microscopy, the asbestos bodies appear beaded or dumbbell-shaped and can be recognized by their thin, transparent core. They form as a result of the iron-protein-mucopolysaccharide coating of asbestos fibres. Guidelines state that two or more asbestos bodies per square centimetre of a 5 μm thick lung section are required to make the diagnosis [1]. Due to variability in fibre counts within

smaller transbronchial specimens, it is currently suggested that optimal samples for analysis should comprise 2 cm^3 blocks from three anatomical sites (usually from the apical upper, apical lower and basal segments of the lung) [1].

Asbestos bodies can be formed by other substances, for example, cellulose. Electron microscopy (EM) can be used to determine if asbestos bodies contain asbestos fibres and can also determine fibre type. EM was not performed in this case, but the history of significant asbestos exposure and the finding of asbestos bodies in high numbers is likely to indicate significant asbestos exposure.

In cases of interstitial lung disease (ILD) where there is diagnostic uncertainty and a lung biopsy is required, surgical lung biopsy is the gold standard for tissue sampling as

bronchoscopic transbronchial biopsies using forceps provides too little parenchymal tissue [8]. However, surgically acquired biopsies are associated with higher morbidity and mortality when compared with bronchoscopy. Comorbidities that are often associated with ILD, such as pulmonary hypertension and hypercapnia, compound this risk and can often preclude patients from being surgical candidates.

In interstitial lung diseases, transbronchial lung cryobiopsy has been shown to improve the diagnostic yield when compared with conventional transbronchial biopsies (obtained via forceps), providing larger specimen size (often measure 0.5 cm or more in greatest diameter) without associated crush artefacts [9]. No studies to date have directly compared the diagnostic accuracy of transbronchial cryobiopsy with that of surgical lung biopsies. However, several studies demonstrate the safety and efficacy of transbronchial biopsies in the setting of diffuse parenchymal lung diseases, with lower rates of complications such as bleeding, shorter hospital stays, and improved mortality [6,7,9].

Current guidelines make recommendations for the diagnosis of asbestosis based on surgical biopsy sample sizes [1]. However, these do not reflect the increasingly available and potentially safer method of transbronchial cryobiopsy, which, as our case has demonstrated, can also provide large-enough lung samples to demonstrate asbestos bodies in sufficient numbers to be helpful in attributing the cause of pulmonary fibrosis. Further studies directly comparing the diagnostic efficacy and safety profiles between these two methods in the setting of asbestosis are needed.

To our knowledge, this is the first description of the transbronchial cryobiopsy technique to confirm a diagnosis of asbestosis. Bondue and colleagues noted the presence of asbestos fibres in a cryobiopsy specimen from a patient with a radiological pattern of Usual interstitial pneumonia (UIP) but the low fibre count dissuaded the pathologists from attributing the fibrosis to asbestos [8].

In conclusion, this case demonstrates the effectiveness of transbronchial cryobiopsy as a modality for obtaining lung parenchymal samples of adequate size to demonstrate asbestos bodies in sufficient numbers to confirm

significant asbestos exposure and to indicate asbestos exposure as the cause of pulmonary fibrosis. Current guidelines could be modified to reflect advances in biopsy techniques.

Disclosure Statement

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

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