Asbestosis occurring after brief inhalational exposure: usefulness of bronchoalveolar lavage in diagnosis

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ABSTRACT   A case of clinically and radiologically typical asbestosis manifesting in a 55 year old man occurred 36 years after a brief exposure period of less than one year. A transbronchial lung biopsy was performed but the samples were considered non-diagnostic. The diagnosis was supported by the use of bronchoalveolar lavage to obtain alveolar samples and scanning electron microscopy-energy dispersive x ray analysis of fibres found in the bronchoalveolar lavage fluid which showed a predominance of amosite.

Asbestosis is usually associated with chronic inhalational exposure and occurs after a long latent period.[1] The finding of asbestos bodies and fibres in the lung indicates exposure to asbestos dust.[2][3] The present case illustrates the occurrence of asbestosis in a patient who had had brief and limited exposure to asbestos material many years before the development of symptoms and objective findings. Fibreoptic bronchoscopy with transbronchial biopsy and bronchoalveolar lavage (BAL) established the presence of asbestos bodies which confirmed the exposure and aided the diagnosis.

Case report

A 55 year old oil company executive was evaluated in 1986 because of a productive cough. He never smoked cigarettes. He had known exposure to asbestos for one year or less in 1949 and 1950 (about six months each year). At that time he worked as a chemical engineer trainee ("co-op") for a company that manufactured pipe insulation containing asbestos. He worked in an office building away from the factory site and was not aware of any exposure to asbestos dust and rarely went to the factory site. When he visited the factory he did recall being exposed occasionally to asbestos dust and he never wore a protective mask. He was in the Army Chemical Corps from 1954 to 1956 but was not aware of any exposure to asbestos then. In his current occupation as a chemical engineer for a refinery he had no known exposure to any asbestos material and

primarily did "executive" work in an office building. Although there was demolition or remodelling periodically of rooms and offices in the building, he rarely visited these areas. There was no other significant occupational and environmental exposure history.

A physical examination showed bibasilar inspiratory "Velcro" type crackles that were more audible on the left side. Recent chest radiographs were characterised by a "B" reader as bilateral small parenchymal opacities (UICC/ILO classification,[4] 1/1), diffuse pleural thickening on the right chest wall, pleural plaques on the left chest wall, and pleural calcification above the right diaphragm (fig 1). A chest CT scan was not carried out. Previous outside chest radiographs obtained in 1970 (fig 2), 1977, 1979, and 1982 showed a progression of abnormalities; chest films before 1970 were not available. Recent pulmonary function testing results are presented in the table. The forced expiratory volume in one second (FEV_1),[5] the forced vital capacity (FVC),[5] the FEV_1/FVC ratio,[6] and the total lung capacity (TLC)[7] are shown. A single breath diffusing capacity (DCO)[8] adjusted for haemoglobin and the alveolar volume (V_A) are also given. The arterial blood gases on room air were pH 7·41, pCO_2 42, and pO_2 87. A lung compliance study indicated that static compliance[9] was decreased at 0·112 l/cm H_2O and that the elastic recoil pressure[10] was increased at 44·4 cm H_2O (measured at 55% predicted TLC).

The following were normal or negative: electrolytes, glucose, BUN, creatinine, liver enzymes, packed cell volume, haemoglobin, white cell count, urine analysis, antinuclear antibodies, and rheumatoid factor. Results of sputum analyses for acid fast organisms and
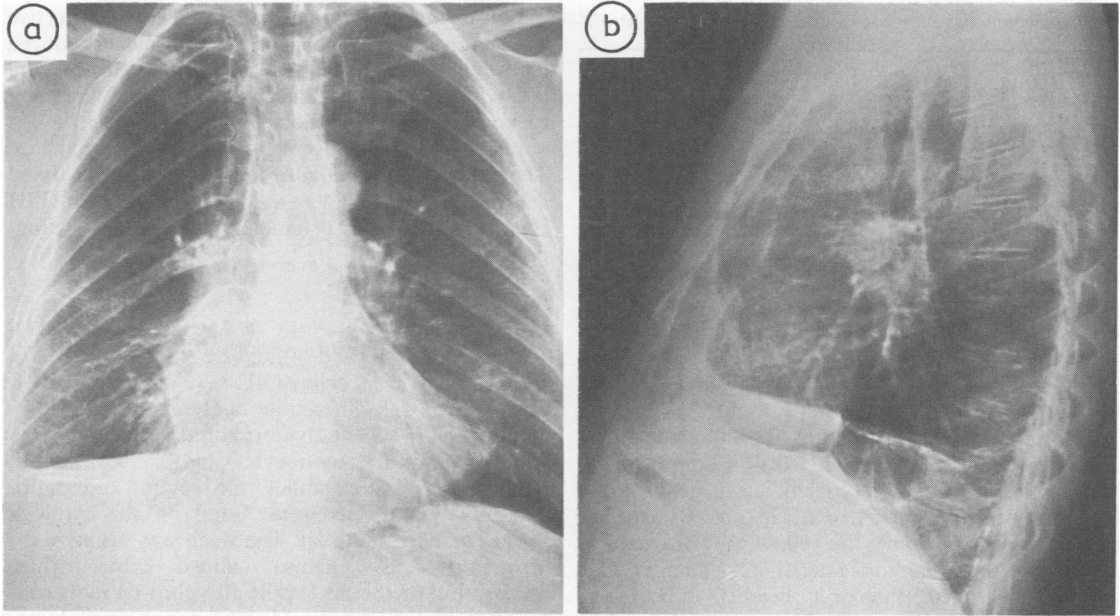
Fig 1 (A) & (B)   *1986 chest radiographs showing bilateral pleural thickening, calcification on both hemidiaphragms, and pleuropericardial adhesions.*

and neoplasia were negative. Asbestos bodies were not evident on the sputum cytology examination. The patient would only consent to bronchoscopy as an aide to elucidate the diagnosis.

Methods and materials

Bronchoscopy was performed with a TR model flexi-

ble fibreoptic bronchoscope (Olympus Corporation of America, New Hyde Park, NY). One right middle lobe segment was lavaged with 150 ml of physiological saline in 50 ml aliquots after which transbronchial lung biopsies were performed.

The BAL fluid retrieved was prepared for analysis by a standard protocol.[11] Briefly, it was pooled and spun at 250Xg for 10 minutes. The cell pellets were
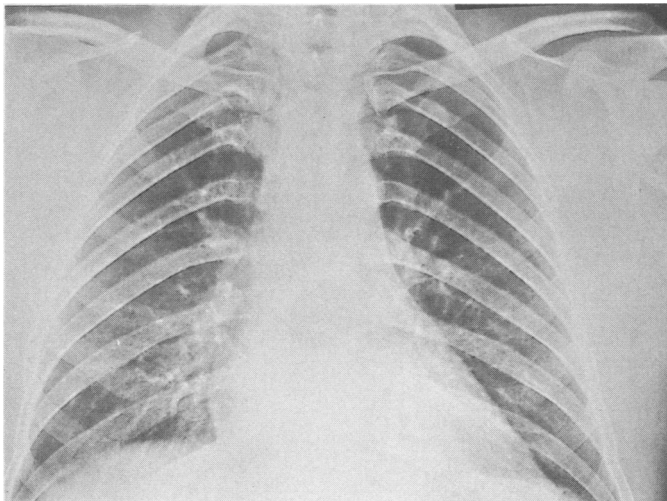
Fig 2   *1970 chest radiograph showing pleural plaque in right mid-lung region.*

Pulmonary function

	Observed	% of Predicted
FEV₁ (l)	1·91	61
FVC (l)	2·49	58
FEV₁/FVC₁ (%)	77	
TLC (l)	3·24	54
DCO (ml/min/mm Hg)	17·5	65
Vₐ (l)	3·28	54

combined and resuspended in RPMI 1640 (Gibco, Grand Island, NY). Several cytocentrifuge slide preparations were made (spun at 22·4Xg) and stained with Giemsa. The cell differential count was then determined by examination of 300 cells. A total cell count from a fixed BAL aliquot was determined microscopically with a haemocytometer.

The remaining cell mixture was filtered on to cellulose membrane (Millipore Corporation, Bedford, MA; porosity, 0·45 μm). Hypochlorite digestion of the BAL cells was performed in order to quantify asbestos bodies.[12] Asbestos bodies are yellow brown structures measuring 20–150 microns long and 2–5 microns wide and have "clubbed" ends or a "beaded" appearance, or both.[13] After air drying, the filters were mounted on glass slides and the slides studied with an optical microscope. A manual count of the entire filter for asbestos bodies was performed. Lavage material was also sent to the UCLA Medical Center clinical cytology laboratory for processing. The transbronchial lung biopsies were processed by the clinical pathology laboratory.

For scanning electron microscopy-energy dispersive x ray analysis (SEM-EDXA),[14] the cell pellet produced on the glass slide in the cytocentrifuge was treated as a tissue section and transferred from the slide to a carbon disc using acrylic medium. This procedure is applicable to any cytocentrifuge prepared specimens. The particles (fibrous and non-fibrous) are analysed within the macrophages in the specimen.[15] NIOSH standards (75–0043 for amosite) were used for comparison.[14]

Results

There was a 67% yield of fluid return from the BAL, with 41 × 10⁶ total cells or 41 × 10⁴ cells/ml of BAL fluid return. Cell differential analysis indicated 84% macrophages, 1·8% polymorphonuclear cells, 13·2% lymphocytes, 1·0% monocytes, and 0% eosinophils. Numerous asbestos bodies, histiocytes, and multinucleated giant cells were found on the cytology smears of BAL material. The wash was negative for malignant cells. Giemsa stained cytocentrifuge preparation of the BAL cells also showed numerous asbestos bodies (fig 3). Manual counting of hypochlorite digestion of BAL specimens identified about 13·4 asbestos bodies per ml of BAL fluid volume or 26·4 asbestos bodies per 1 × 10⁶ BAL cells. The transbronchial lung biopsy specimens were non-diagnostic. An asbestos body was found in one small specimen and an area of minimal fibrogenesis was noted in another biopsy specimen.
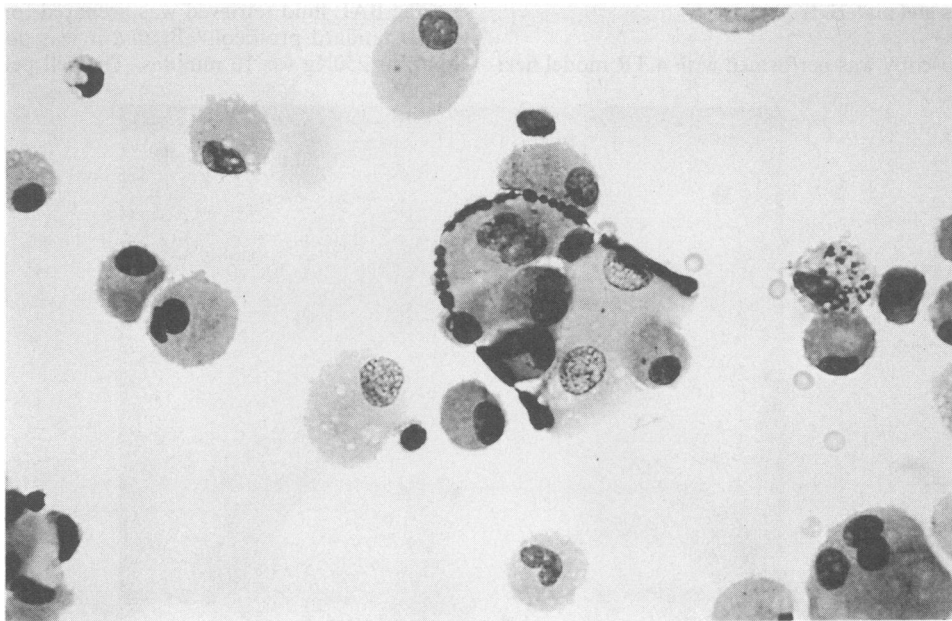

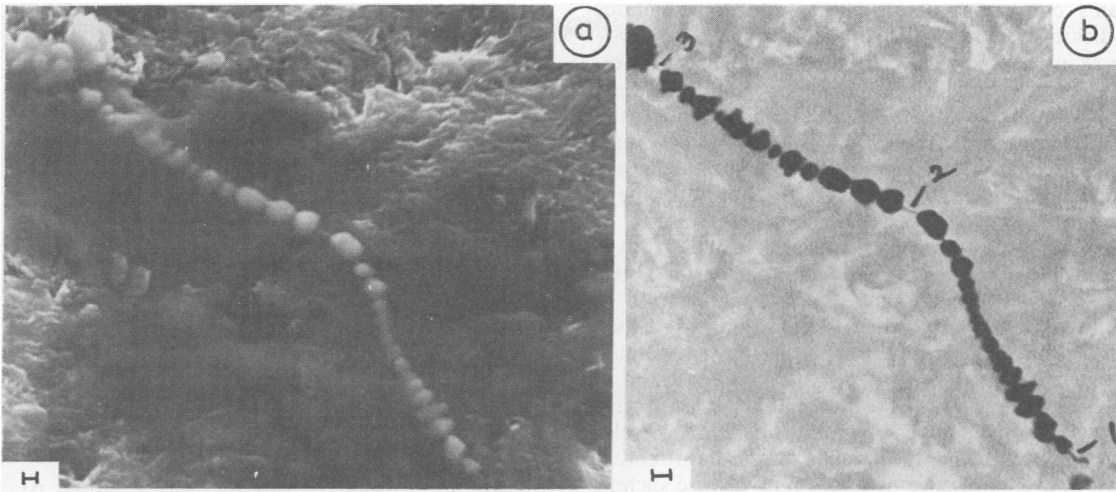Fig 3 *Giemsa stain of BAL specimen showing curved asbestos body.*

Fig 4 *Scanning electron microscope images of an asbestos body within an alveolar macrophage obtained by lavage. Magnification marker represents 1·0 micrometer. (A) Secondary electron image shows dark outline of macrophage. (B) Backscattered electron image of asbestos body within alveolar macrophage. Energy dispersive x ray analysis was done on areas marked.*

The SEM-EDXA analysis of the BAL specimens showed numerous inorganic particulates. The fibre core of the asbestos bodies (fig 4) was shown by EDXA to be consistent with amosite.

Discussion

Although the clinical assessment of the pathological response to exposure to asbestos is available, attributing the abnormalities directly to such exposure may often be difficult. The assessment of asbestos related lung disease may be difficult because the patient may be unaware of the risks of exposure to asbestos or may be uncertain of the exposure. The periods of exposure, the amount of exposure, or the types of fibres inhaled may also be unknown to the patient. Furthermore, because of the long latent period, asbestos related pulmonary abnormalities may appear to occur "suddenly" in a previously healthy individual.

One index of exposure that has been advocated is the finding of asbestos bodies in lung specimens.[16-18] Sputum analysis for asbestos bodies is not very sensitive.[19] Biopsy procedures such as transbronchial lung biopsies, percutaneous needle lung biopsies, and open lung biopsies are fraught with risks and, except in the last, the samples obtained may be too small to make an adequate analysis. One technique that has recently come into clinical use to evaluate other types of pulmonary diseases is BAL.[20] BAL has recently been found to be a useful adjunct to confirm asbestos exposure,[21 22] although it does not yield a direct tissue diagnosis.

The SEM-EDXA analysis of BAL cells allows examination for inorganic particulates. In addition,

asbestos bodies and fibres can be identified and quantified.[23 24]

Although asbestos related lung diseases—for example, mesotheliomas—may occur after a brief or low dose exposure, this case illustrates the occurrence of another asbestos related lung disease—that is, asbestosis—after a brief known exposure period. The BAL cell differential analysis was within the normal limits as defined by prior BAL controls.[11] The transbronchial lung biopsies were not revealing and considered non-diagnostic, but the surprising find of numerous asbestos bodies in the BAL specimens substantiated the exposure. De Vuyst *et al* performed a quantitative analysis of BAL specimens and recently reported that more than half the subjects who had definite asbestos exposure and more than one third of the subjects with probable exposure had from 1 to 99 asbestos bodies per ml of BAL specimen.[21 22] More than three quarters of the subjects with a clinical diagnosis of asbestosis and only one third of those with pleural disease reported by De Vuyst *et al* had greater than 10 asbestos bodies per ml of BAL specimen. Although our patient's history suggested that he had only a small cumulative asbestos exposure, the BAL specimen clearly showed a raised lung burden of asbestos which strengthened the diagnosis of asbestosis. The extensive pleural changes also suggested that he may have had significant exposure to asbestos. Many cases of radiographically detected bilateral pleural thickening are thought to be due to exposure to asbestos often undetected by routine history.[25] The presence of interstitial disease radiologically (and restrictive disease physiologically) also led to the diagnosis of asbestosis as the best possible explanation for this

man's pulmonary abnormalities. Since ferruginous bodies may be associated with other inhaled silicates— for example, talc[13]—a SEM-EDXA analysis was performed to confirm the presence of asbestos fibres, most of which were amosite. The predominance of amosite fibres detected by SEM-EDXA was also substantiating information for exposure. Amphibole asbestos such as amosite has been a major asbestos fibre type in commercially used asbestos in the United States.[26]

We have shown another clinical use for BAL. It is helpful in substantiating exposure to asbestos fibres. Analysis of the BAL such as the quantification of asbestos bodies and SEM-EDXA analysis helped confirm the exposure. Recent studies have attempted to associate the number of asbestos bodies found in BAL with the severity of asbestos lung disease.[16-18] De Vuyst and others have shown that there is a correlation between the number of asbestos bodies found in BAL and the presence of severe lung disease such as asbestosis in individuals at risk for asbestos related lung diseases.[21 22]

In conclusion, we have found BAL a useful means of detecting asbestos exposure when the exposure history is in doubt. Although it may be an extreme example of biological monitoring, BAL has been shown to have a clinically useful role in a variety of diseases—for example, idiopathic pulmonary fibrosis (IPF) or sarcoidosis.[20] This present case illustrates that in many cases of IPF BAL may also be useful to substantiate the presence of asbestos fibres or other inorganic substances, or both, when lung biopsy analysis, as in our case, is unavailable or inadequate. We emphasise that the findings of BAL do *not* make the diagnosis of asbestosis, which is established on the basis of exposure history, clinical, radiological, and physiological data (and by histopathology, when available), and by the exclusion of other possible aetiologies for restrictive lung disease.

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References

1 Becklake MR. Asbestos-related diseases of the lung and other organs—their epidemiology and implications for clinical practice. *Am Rev Respir Dis* 1976;**114**:187–227.

2 Utidjian MD, Gross P, de Treville R. Ferruginous bodies in human lungs. *Arch Environ Health* 1968;**17**:327–33.

3 Churg A, Warnock ML. Asbestos fibers in the general population. *Am Rev Respir Dis* 1980;**122**:669–78.

4 International Labour Office. *Guidelines for the use of ILO inter-national classification of radiographs of pneumoconiosis*. Rev ed. Geneva: International Labour Office, 1980. (Occupational safety and health series No 22.)

5 Detels R, Tashkin DP, Simmons MS, *et al*. The UCLA population studies of chronic obstructive respiratory disease. 5. Agreement and disagreement of tests in identifying abnormal lung function. *Chest* 1982;**82**:630–8.

6 Goldman HI, Becklake MR. Respiratory function tests. Normal values at median altitudes and the prediction of normal results. *American Review of Tuberculosis* 1959;**79**:457–67.

7 Cotes JE. *Lung function. Assessment and application in medicine*. Oxford: Blackwell, 1979.

8 Dinakara P, Blumenthal WS, Johnston RF, Kauffman LA, Solnick PB. The effect of anemia on pulmonary diffusing capacity with derivation of a correction equation (note). *Am Rev Respir Dis* 1970;**102**:956–9.

9 Schlueter DP, Immekus J, Stead WW. Relationship between maximal inspiratory pressure and total lung capacity (coefficient of retraction) in normal subjects and in patients with emphysema, asthma and diffuse pulmonary infiltration. *Am Rev Respir Dis* 1967;**96**:656–65.

10 Turner JM, Mead J, Wohl ME. Elasticity of human lungs in relation to age. *J Appl Physiol* 1968;**25**:664–71.

11 Barbers RG, Gong H, Tashkin DP, Oishi J, Wallace JM. Differential examination of bronchoalveolar lavage (BAL) cells in cigarette tobacco and marijuana smokers. *Am Rev Respir Dis* 1987;**135**:1271–5.

12 Williams MG, Dodson RF, Corn C, Hurst GA. A procedure for the isolation of amosite asbestos and ferruginous bodies from lung tissue and sputum. *J Toxicol Environ Health* 1982;**10**: 627–38.

13 Craighead JE, Abraham JL, Churg A, *et al*. The pathology of asbestos associated diseases of the lungs and pleural cavities. Diagnostic criteria and proposed grading schema. *Arch Pathol Lab Med* 1982;**106**:544–96.

14 Abraham JL, Burnett BR. Quantitative analysis of inorganic particulate burden in situ tissue sections. *Scanning Electron Microscopy* 1983;**2**:681–96.

15 Mason GR, Abraham JL, Hoffman L, Cole S, Lippman M, Wasserman K. Treatment of mixed-dust pneumoconiosis with whole lung lavage. *Am Rev Respir Dis* 1982;**126**:1102–7.

16 Churg A, Wiggs B, Depaoli L, Kampe D, Stevens B. Lung asbestos content in chrysotile workers with mesothelioma. *Am Rev Respir Dis* 1984;**130**:1042–5.

17 Churg A. Asbestos fiber content of the lungs in patients with and without asbestos airways disease. *Am Rev Respir Dis* 1983;**127**:470–3.

18 Roggli BL, Pratt PC. Numbers of asbestos bodies on iron stained tissue sections in relation to asbestos body counts in lung tissue digest. *Hum Pathol* 1983;**14**:355–61.

19 Roggli VL, Greenberg SD, McLarty JW, *et al*. Comparison of sputum and lung asbestos body counts in former asbestos workers. *Am Rev Respir Dis* 1980;**122**:941–5.

20 Hunninghake GW, Gadek JE, Kawanami O, Ferras VJ, Crystal RG. Inflammatory and immune processes in the human lung in health and disease. Evaluation by bronchoalveolar lavage. *Am J Pathol* 1979;**97**:149–206.

21 De Vuyst P, Jedwab J, Dumortier P, Vandermoten G, Weyer RV, Yernault JC. Asbestos bodies in bronchoalveolar lavage. *Am Rev Respir Dis* 1982;**126**:972–6.

22 De Vuyst P, Dumortier P, Monlin E, Yourassowsky N, Yernault JC. Diagnostic value of asbestos bodies in bronchoalveolar lavage fluid. *Am Rev Respir Dis* 1987;**136**:1219–24.

23 Rubin ID, Maggiore CJ. Elemental analysis of asbestos fibers by means of electron probe techniques. *Environ Health Perspect* 1974;**9**:81–94.

24 Langer AM, Mackler AD, Pooley FD. Electron microscopical investigation of asbestos fibers. *Environ Health Perspect* 1974;**9**:63–80.

25 Abelda SM, Epstein DM, Gefter WB. Pleural thickening: its significance and relationship to asbestos dust exposure. *Am Rev Respir Dis* 1982;**128**:621–4.

26 Hueper WC. Occupational and non-occupational exposure to asbestos. *Ann NY Acad Sci* 1965;**132**:184–95.