ASBESTOS RELATED DIFFUSE PLEURAL FIBROSIS

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Diffuse pleural fibrosis (DPF), particularly when severe may cause reduction in vital capacity and contribute to respiratory disability.[1] Recently DPF has been accepted as a consequence of asbestos exposure.[2,3] We previously studied 7 cases of asbestos related DPF and reported on the pathological and mineralogical findings.[4] In this study we have extended these observations to 13 cases and also performed mineralogical analysis on tissues sampled from the central, subpleural and pleural regions of the lung. The aims of the study were to investigate the type of occupational exposure, the total mineral fibre burdens and the type and distribution of asbestos mineral fibres within the lungs associated with this form of asbestos related disease.

METHODS

The 13 cases were selected on the basis that there was a history of asbestos exposure and at autopsy the DPF was bilateral, covered more than 25% of the lung surface and exceeded 5 mm in thickness at some points. Clinical and occupational histories were obtained from the hospital notes or Medical Boarding Centres. At least one of the lungs was inflated and tissue blocks were taken for histology as follows:

1. Subpleural region of the apex of upper lobe.
2. Subpleural region of the apex of lower lobe.
3. Subpleural region of the base of lower lobe.
4. Central region of the upper lobe.
5. Central region of the lower lobe.
6. Several blocks from areas of pleural fibrosis.

The degree of parenchymal fibrosis was graded from 0 to 4 for each histological slide by an established system and an average value obtained for each case.[5,6]

For mineralogical examination samples were taken from the same areas. The mineralogical analysis was performed for the subpleural region by pooling samples adjacent to blocks 1-3, for the central region by pooling the samples adjacent to blocks 4 and 5 and the pleura by pooling the samples adjacent to the blocks from 6. The samples were divided into two, and one from each of the areas was dried to a constant weight so that the wet/dry ratio could be calculated. The remaining portions were digested in a wet state by 40% potassium hydroxide. For light microscopy: after centrifugation, the sediment was examined in a Fuchs Rosenthal chamber by phase contrast and the number of fibres and bodies counted, from which could be calculated the number per gramme of dried lung.[7] At least 100 asbestos forms were counted. For electron microscopical examination: following digestion, the final deposits were ashed at 300C for 4 hours. The suspensions were then passed through 0.2 pore sized nucleopore filters.

They were then carbon coated and examined by transmission electron microscopy. The fibres were identified by type and the number per gramme of dried lung calculated. At least 200 fibres were counted and identified for each sample. Statistical analysis was performed using the Wilcoxon ranking test for paired data.

RESULTS

The occupational details for each case are given in Table I. All were males and the age at death ranged from 47 to 80 years. Duration of exposure to asbestos varied from 1 to 35 years. In all cases macroscopical examination revealed extensive diffuse visceral pleural fibrosis which was at least greater than 5 mm but which went up to 4 cm in thickness and mimicked pleural mesothelioma in some cases. In several cases there were extensive adhesions between the visceral and parietal pleura. In some cases recognisable parietal pleural plaques were also present. Case 10 also showed severe diffuse pericardial fibrosis similar to that of the pleura. Microscopically the pleura showed mature collagen arranged in a basket weave pattern. The degree of pulmonary fibrosis for each case is given in Table I.

Total mineral fibre counts obtained by light and electron microscopy at the central, subpleural and pleural sites are given for each subject in Table II. Table III shows the mean total and specific fibre counts for each of the anatomical sites.

The total asbestos fibre count was significantly greater in the central and subpleural region than in the pleura ($p<0.01$). There were no significant differences in the distribution of chrysotile in the central, subpleural or pleural regions but there was a statistically significant difference in the distribution of amosite and crocidolite ($p<0.01$). The amosite and crocidolite levels were much lower in the pleura than in the other regions.

Table I

Ages, Occupational Histories and Histological Fibrosis Grades of 13 Cases of DPF with a History of Asbestos Exposure

SUBJECT	AGE/YRS	OCCUPATIONAL HISTORY	GRADE OF PULMONARY FIBROSIS
1	80	Pipe fitter 25 yrs	2
2	67	Engineer, 2 yrs cutting asbestos sheets	2/3
3	64	Boiler maker	1/2
4	75	Electrical welder	2
5	71	Carpenter, cutting roofing sheets	1/2
6	64	Asbestos sprayer	2/3
7	62	Boiler lagger for 33 years	1
8	64	Unloaded asbestos from sacks (4 yrs) and production of refractory slab (7 yrs)	2
9	47	Mixing and moulding blue asbestos for battery moulds for 1 yr	0/1
10	69	Marine engine fitter 35 yrs	ND
11	54	Gas fitter and plumber	0/1
12	75	Refitting ships 25 yrs	1
13	74	Ship yard joiner	2/3

DISCUSSION

We consider that the DPF in 11 of these cases is likely to have been caused by asbestos but in two it is debatable. Subject 13 had been treated for pulmonary tuberculosis nine months prior to death; the lungs showed quite severe fibrosis and very low asbestos fibre counts which were well within the range of our normal controls. Tuberculosis therefore seems the most likely cause of the pleural fibrosis in this case. Subject 11 had a very vague history of asbestos exposure and the lung asbestos counts were well within the normal control levels. The cause in this case is unknown but unlikely to be due to asbestos.

The light and electron microscopical mineral fibre counts showed a good correlation with each other but the light microscopical counts were in general two orders of magnitude lower than the electron microscopical counts. Although light visible counts obtained by phase contrast cannot give an accurate value for total lung asbestos burden, they are a useful indicator of amphibole exposure.[9,10] Small thin fibres are not visible by this method. Nevertheless, the method is inexpensive, quick and more widely available than EM analysis and in this group of cases the LM counts appeared to be a useful indicator of whether the DPF was likely to have been asbestos induced.

The total counts were generally raised above normal and in

Table II

Total Fibre Counts Obtained by LM and EM Analysis in the Central (C), Subpleural (S), and Pleural (P) Regions of the Lung

SUBJECT	LM (X 10^3)			EM (X 10^6)		
	C	S	P	C	S	P
1	102.8	76.5	5.7	10.7	25.5	2.0
2	232.7	105.5	26.7	8.4	19.0	9.2
3	79.4	131.0	7.0	18.0	19.1	7.5
4	55.6	88.5	0.65	ND	ND	ND
5	68.4	66.5	0.83	18.9	12.2	2.2
6	95000.0	5700.0	306.0	24769.5	32722.3	123.5
7	5330.0	4200.0	0	143.3	124.7	10.1
8	1210.0	1800.0	3.7	162.8	225.0	11.0
9	48.5	100.0	0	15.4	40.6	2.5
10	ND	744.0	11.5	18.6	80.3	17.0
11	12.2	7.7	3.1	21.9	13.1	3.3
12	7000.0	2500.0	0	93.9	164.5	2.1
13	0	25.0	0	26.1	32.4	13.2

Table III

Geometric (Arithmetic) Mean Asbestos Fibre Counts by Type in the Central (C), Subpleural (S) and Pleural (P) Regions of the Lung (10^6)

	Total Asbestos fibres	Chrysotile	Crocidolite	Amosite
C	36.8 (2089.3)	5.24 (9.5)	5.2 (1907.9)	6.6 (182.9)
S	50.4 (2776.5)	13.3 (56.3)	4.9 (2559.0)	7.4 (160.9)
P	6.7 (16.2)	5.5 (7.7)	0.15 (7.4)	0.05 (1.1)

the range we have seen with pleural plaques and minimal asbestosis. However, three subjects had counts which were well above this range (subjects 6, 7 and 12). Subject 6 had an extremely high count, which we have usually encountered in severe asbestosis; he was an asbestos sprayer, an occupation which may be associated with very high asbestos exposures.

The counts obtained at the various sites within the lung confirm the nonuniform distribution of asbestos as shown by others.[11] Chrysotile parenchymal levels were similar to normal controls except for subject 6. Amphibole parenchymal levels were raised above normal in all but two (subjects 11 and 13) which we consider unlikely to be caused by asbestos. The pleura contained relatively little fibre and by far the majority of this was chrysotile. Sebastien et al[12] in a previous study of asbestos fibres from the lung parenchyma and pleura of cases suffering from a variety of asbestos related diseases, found no relationship between parenchymal and pleura concentrations and the pleura contained almost exclusively chrysotile. Although amphibole fibres were found in the pleura of all but one of our cases, they were extremely sparse in number.

In conclusion the findings of this study confirm previous observations that the distribution of fibres within the lung is not uniform. It also shows that in these cases of DPF the majority of fibre within the pleura is chrysotile but small numbers of amphibole fibres are also present. Also the amount of amphibole fibres within the pleura is much less than that in the parenchyma. As in other asbestos related diseases the parenchymal levels of amphibole asbestos but not chrysotile appear raised above controls.

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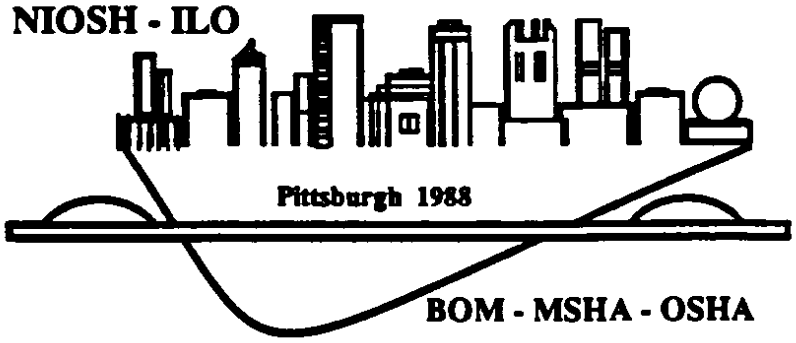
II



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