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Non-malignant chest *x* ray changes in patients with mesothelioma in a large cohort of asbestos insulation workers

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ABSTRACT To assess the prevalence of non-malignant chest *x* ray abnormalities in cases of mesothelioma 184 cases of mesothelioma (72 pleural and 112 peritoneal) which had occurred in a cohort of asbestos insulation workers followed up since 1967 were studied. Chest *x* ray films of satisfactory quality, on which the presence or absence of non-malignant radiological changes indicating interstitial pulmonary fibrosis or pleural fibrosis or both, could be assessed with a high degree of certainty were available. In some cases (20% for pleural mesothelioma, 11·6% for peritoneal mesothelioma) non-malignant radiological changes were not radiologically detectable. Parenchymal interstitial fibrosis (small irregular opacities) only was found in a proportion of cases (25·4% of pleural mesotheliomas, 12·5% of peritoneal mesotheliomas). Pleural fibrosis only was detected in 17% of cases of pleural mesothelioma and 27% of cases of peritoneal mesothelioma. Most patients had both parenchymal and pleural fibrosis. Although these results tend to indicate that in peritoneal mesothelioma the proportion of pleural fibrosis is significantly higher, these findings might have been due to the fact that in most cases of pleural mesothelioma non-malignant changes were interpreted in one hemithorax only. In 46 cases (21 pleural, 25 peritoneal) in which sufficient lung tissue was available histopathology of lung parenchyma indicated the presence of interstitial fibrosis; in 20 (43·5%) of these the chest *x* ray film had been read as negative. Thus the absence of radiologically detectable small opacities on the chest *x* ray film does not exclude the existence of interstitial pulmonary fibrosis in cases of mesothelioma among insulation workers. With lower levels of exposure (such as in family contacts of asbestos workers) it is conceivable that mesothelioma might occur in the absence of interstitial pulmonary fibrosis.

Mesothelioma, pleural and peritoneal, occurred in 356 members of a large cohort[1] of asbestos insulation workers. Non-malignant abnormalities on the chest *x* ray film indicating the presence of interstitial pulmonary fibrosis, pleural fibrosis, and pleural calcifications, preceding the development of the malignant mesothelioma or detectable on the hemithorax opposite to that in which the tumour developed, were of interest, given the widely accepted opinion that mesothelioma can occur after relatively short and low exposure to asbestos[2–5] (R Lilis *et al*, VI International Pneumoconiosis Conference, Bochum, May 1983, abstracts pp16, 30).

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POPULATION AND METHODS

Mesothelioma had occurred in 356 members of a large cohort of 17 800 insulation workers in the United States and Canada, established in 1967.[1 6] The diagnosis of malignant mesothelioma was ascertained by thorough review of pathology in all cases by one of us (YS).

In 184 cases chest *x* ray films of satisfactory quality were available for review: 112 cases of peritoneal mesothelioma and 72 of pleural mesothelioma. The chest *x* ray films were interpreted for non-malignant abnormalities of the lung parenchyma, or of the pleura, by following the criteria of the International

Table 1 *Peritoneal mesothelioma (n = 112)*

	No	%	
Presence of non-malignant pulmonary and pleural abnormalities			
None	13	11·6	
Parenchymal interstitial fibrosis only (small irregular opacities)	14	12·5	
Pleural fibrosis only	30	26·8	
Parenchymal and pleural fibrosis	55	49·1	
Parenchymal interstitial fibrosis (irregular opacities)			
Profusion			
0/0–0/1	43	38·4	
1/0–1/2	45	40·2	61·6%
2/1–2/3	20	17·8	
3/2–3/3	4	3·6	

Classification of Radiographs of Pneumoconioses.[7]

In the 112 cases of peritoneal mesothelioma the full chest *x* ray film was interpreted for non-malignant abnormalities (parenchymal or pleural, or both). In most of the 72 cases of pleural mesothelioma the interpretation of non-malignant radiological pleuropulmonary changes were made on the hemithorax contralateral to that in which the tumour had developed (60 cases); in 12 cases full chest *x* ray films preceding the mesothelioma by a relatively short period (several years) were available and were used for interpretation.

Findings in the 112 cases of peritoneal mesothelioma were compared with those in the 72 cases of pleural mesothelioma.

Results

PERITONEAL MESOTHELIOMA

Radiological changes indicating the presence of interstitial pulmonary fibrosis (small irregular or rounded opacities, or both) or pleural fibrosis were absent in 13 (11·6%) of the 112 cases of peritoneal mesothelioma. Pleural fibrosis was present in one or more locations in 76·0% of all cases: chest wall, tangential, or face on, or both, and diaphragmatic plaques.

In 30 (26·9%) cases changes consistent with pleural fibrosis were the only abnormalities detected, whereas in 55 (49·1%) small irregular opacities indicating the presence of interstitial fibrosis were associated with pleural fibrosis (table 1).

Small, mostly irregular but sometimes also rounded opacities were radiologically detectable in 69 (61·6%) cases; the majority, almost two thirds, showed opacities of type s (according to the ILO classification), and in one third of cases the predominant shape and size of radiologically detectable small opacities was t. The profusion of radiologically detectable small opacities was 1/0–1/2 in 45 cases (40·2%), 2/1–2/3 in 20 cases (17·8%), and reached a 3 grading (3/2–3/3) in only four cases (table 1).

Tangential pleural fibrosis was found with similar prevalence on the right in 44 (39·4%) and on the left in 50 (44·6%) cases. The extent and width of tangential pleural fibrosis were also similar. Pleural fibrosis face on was a relatively frequent finding, present in one third of all cases affecting the left hemithorax (in cases of right pleural mesothelioma). The extent (1, 2, or 3) of pleural fibrosis face on was relatively evenly distributed; for tangential pleural fibrosis, extents 1 and 2 were more prevalent than extent 3, and widths A and B were more prevalent than width C (table 2).

Circumscribed pleural fibrosis was found roughly twice as often as diffuse pleural fibrosis (table 3).

Diaphragmatic plaques (table 4) were observed with a similar frequency on the right and on the left hemidiaphragms, in almost half of cases (47·3% right diaphragmatic plaques and 49·1% left). They were radiologically non-detectable in 39 (34·9%) cases, bilateral in 35, present on the left only in 20, and on the right only in 18. The costophrenic angle was blunted in less than 20% of cases, both on the right and on the left hemithorax (table 4). Pleural

Table 2 *Peritoneal mesothelioma: tangential pleural fibrosis (in profile) and face on (n = 112)*

Pleural fibrosis (tangential)	*Right*		*Left*		*Pleural fibrosis (face on)*	*Right*		*Left*	
	No	%	*No*	%		*No*	%	*No*	%
None	68	60·7	62	55·3	None	83	74·1	74	66·1
Present	44	(39·4)*	50	(44·6)*	Present	29	(25·9)*	38	(33·9)*
Extent 1	17	15·2	20	17·9	Extent 1	10	8·9	12	10·7
2	23	20·5	24	21·4	2	11	9·8	12	10·7
3	4	3·6	6	5·3	3	8	7·1	14	12·5
Width A	20	17·9	22	19·6					
B	18	16·1	22	19·6					
C	6	5·4	6	5·4					

*No (%) out of 112 cases of peritoneal mesothelioma.

Table 3 *Peritoneal mesothelioma (n = 112)*

*Pleural fibrosis**							
Right				*Left*			
Circumscribed		*Diffuse*		*Circumscribed*		*Diffuse*	
No	%	*No*	%	*No*	%	*No*	%
32	28·6	13	11·6	35	31·2	20	17·9

*Includes pleura face on.

calcifications were not radiologically detected in 67 cases (59·8%); they were bilaterally present in 27 (24·1%) and in more cases, 14 (12·5%) on the left than on the right, four (3·6%).

PLEURAL MESOTHELIOMA

Seventy two cases of pleural mesothelioma had chest *x* ray films satisfactory for interpreting non-malignant pleural and parenchymal changes, either on the hemithorax opposite to the tumour (in 60 cases) or on the full chest *x* ray film that had preceded the development of mesothelioma by several years. The malignant mesothelioma had developed on the right side in 43 (59·7%) cases and on the left in 27 (37·5%); in two cases the primary site remained unidentified (table 5). The contralateral site was interpreted in 35 cases of right pleural mesothelioma and in 25 cases of left mesothelioma, whereas the full chest *x* ray film was read in eight cases of right and two of left mesothelioma (table 5).

In 14 cases (19·7%) there was absence of radiologically detectable non-malignant abnormalities (table 6). Parenchymal changes only (small irregular or rounded opacities) were found in 18 (25·4%) cases, a higher proportion than that of cases with peritoneal mesothelioma (12·5%). Pleural fibrosis only was present in 12 (16·9%) cases of pleural mesothelioma, whereas an association between parenchymal and pleural fibrosis was the most frequent occurrence in 27 (38%) cases.

Small parenchymal opacities, mostly irregular but also rounded, indicating interstitial pulmonary fibrosis, were detected in 45 (62·5%) cases with pleural mesothelioma. The profusion of small opacities was 1/0–1/2 in 35 (48·6%) and 2/1–2/3 in 10 (13·9%) cases. As with peritoneal mesothelioma, the predominant type of small irregular opacities was s (in 62·7% of cases) followed by t in 21 (35·6% of cases).

The prevalence of tangential fibrosis (tables 7 and 8) approached 50% for both the right and left hemithorax (somewhat higher than in peritoneal mesothelioma). Diffuse pleural fibrosis was much less frequent (25% of all cases of pleural fibrosis) than circumscribed pleural fibrosis (table 9). Pleural fibrosis face on was again found relatively often in 16 (22·2%) cases. Pleural diaphragmatic plaques were found with a much lower prevalence (45·8%) than in the cases of peritoneal mesothelioma where it was 65·2%. There is a strong possibility that the unilateral chest *x* ray film interpretation for non-malignant radiological changes had a significant influence on this lower prevalence of diaphragmatic plaques detected in pleural as compared with peritoneal mesothelioma. Blunting of the costophrenic angle was found with similar frequency (18·1% of cases).

Pleural calcifications were found with a higher

Table 4 *Peritoneal mesothelioma*

	No	%
Diaphragmatic pleural plaques:		
None	39	34·8
Bilateral	35	31·2
Left	20	17·9
Right	18	16·1
	112	100·0
Costophrenic angle blunted:		
Right	21	18·7
Left	22	19·6

Table 5 *Pleural mesothelioma (n = 72)*

Location of tumour *Hemithorax*	*No*	%
Right	43	59·7
Left	27	37·5
Side unindentified	2	2·8

Interpretation of chest x ray films of pleural mesothelioma for non-malignant pulmonary and pleural abnormalities

	Right pleural mesothelioma	*Left pleural mesothelioma*
Contralateral	35	25
Full chest *x* ray film (preceding malignant mesothelioma)	8	2

Table 6 *Pleural mesothelioma (n = 72)*

	No	%	
Non-malignant radiological abnormalities:			
None	14	19·7	
Parenchymal changes (small irregular opacities) only	18*	25·4*	
Pleural fibrosis only	12	16·9	
Parenchymal and pleural fibrosis	27	38·0	
Interstitial pulmonary fibrosis (small irregular opacities):			
Profusion category:			
0/0–0/1	27	37·5	
1/0–1/2	35	48·6	62·5%
2/1–3/4	10	13·9	

*One chest *x* ray film was unreadable for parenchymal changes.

Table 7 *Pleural mesothelioma (n = 72)*

Chest x ray interpretations for pleural abnormalities

	Right hemithorax (left tumour) (n = 25)	*Left hemithorax (right tumour) (n = 35)*	*Total chest x ray (preceding tumour) (n = 12)*	*Total*	
				No	*%*
Pleural fibrosis (tangential)	8	17	7 (3)*	32	(44·4)
Pleural fibrosis face on	3	11	2 (2)*	16	(22·2)
Pleural diaphragmatic plaques	10	15	8 (5)*	33	(45·8)
Costophrenic angle	5	3	5 (1)*	13	(18·1)

*Bilateral pleural fibrosis present.

prevalence (20%) on the right hemithorax (in the case of left mesothelioma) and on the left (34·3%) hemithorax (in the case of right mesothelioma) than was the case with peritoneal mesothelioma, where the corresponding prevalences were 3·6 and 12·5%. There were, nevertheless, an additional 24·1% of cases of peritoneal mesothelioma with bilateral pleural calcifications.

In 46 of the 184 cases (21 pleural, 25 peritoneal) lung tissue was available for histopathology assessment of interstitial fibrosis. Whereas in 20 (43·5%) of the 46 the radiological interpretation was negative (small opacities 0/0 in 8, 0/1 in 12 cases), histopathological evidence of interstitial fibrosis was present in all.

Table 8 *Pleural mesothelioma (n = 72)*

Pleural fibrosis: tangential

	Right No	*Left No*
Extent 1	5 (2)*	6 (1)*
2	7 (3)*	13 (1)*
3	1 (0)*	3 (3)*
Width A	6 (2)*	7 (2)*
B	4 (3)*	12 (2)*
C	3 (0)*	3 (1)*
Total	13	22

*Cases in which full chest x ray films preceding the malignant pleural mesothelioma were available (total number = 12).

Discussion and conclusions

The relations between both pleural fibrosis and radiologically detectable interstitial fibrosis with the type of mesothelioma—pleural or peritoneal—were tested by using chi-square statistics. Pleural changes were found in 76% of the cases of peritoneal mesothelioma and in only 55% of cases of pleural mesothelioma ($\chi^2 = 8{\cdot}74$; $p = 0{\cdot}003$). Therefore, there seemed to be an association between type of mesothelioma and pleural fibrosis, with cases of peritoneal mesothelioma having a greater frequency of pleural changes. Nevertheless, this apparent higher prevalence of pleural fibrosis among the cases of peritoneal mesothelioma might be, at least in part, due to the fact that in most cases of pleural mesothelioma non-malignant changes were interpreted in one hemithorax only. With regard to parenchymal changes, no association with type of mesothelioma, peritoneal or pleural, was found ($\chi^2 = 0{\cdot}058$; p = ns).

As was shown by the comparison of radiological parenchymal abnormalities and histopathological changes, the absence of radiologically detectable small opacities on the chest *x* ray film does not exclude the existence of interstitial pulmonary fibrosis in cases of mesothelioma among insulation workers.

Table 9 *Pleural mesothelioma (n = 72)*

Pleural fibrosis: circumscribed and diffuse

	Right hemithorax (left tumour) (n = 25)	*Left hemithorax (right tumour) (n = 35)*	*Total chest x ray (preceding tumour) (n = 12)*	*Total No*
Pleural fibrosis circumscribed	6	15	6 (1)*	27
Pleural fibrosis diffuse	3	2	4 (0)*	9

*Bilateral pleural fibrosis was present.

Similar findings have recently been reported in cases of lung cancer from the same cohort.[8]

The possibility still exists that mesothelioma due to past exposure to asbestos might occur in the absence of interstitial pulmonary fibrosis in subjects with lower levels of asbestos exposure than that which characterised insulation work in the past. The findings in this study of cases of mesothelioma from the cohort of asbestos insulation workers cannot be extrapolated to lower levels of exposure that are known to have resulted in cases of mesothelioma among, for example, family contacts of workers exposed to asbestos.[9]

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