Radiation associated malignant pleural mesothelioma

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Abstract

Malignant pleural mesothelioma of epithelial type developed in a 24 year old woman, 20 years after radiotherapy for Hodgkin's disease. This case and a review of published cases indicate that radiation may induce malignant mesothelioma.

Malignant mesothelioma is not invariably associated with past exposure to asbestos[1] and other causes have been suggested.[2] We report a case of a 24 year old teacher who developed malignant pleural mesothelioma 20 years after radiotherapy for Hodgkin's disease, and give details of nine published cases of radiation associated malignant pleural mesothelioma.

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Case report

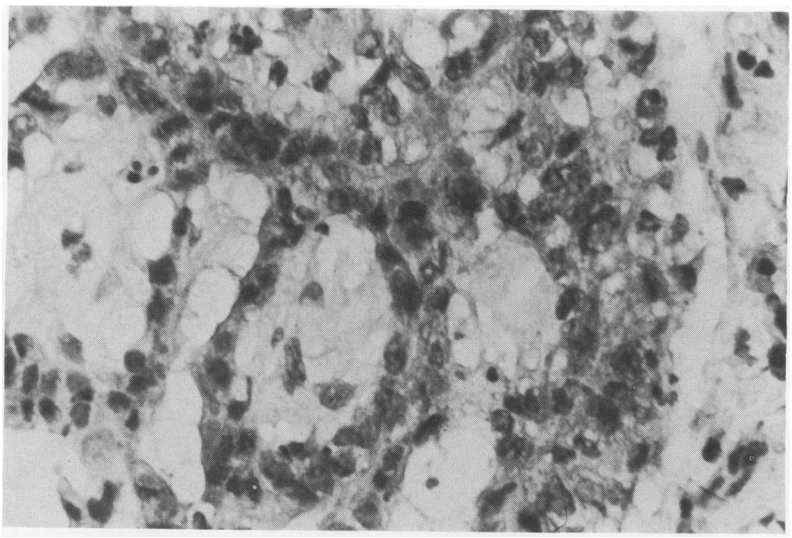
A 24 year old teacher was admitted to hospital with a persistent right pleural effusion. No history of occupational or environmental exposure to asbestos was elicited from the patient or her close relatives.

When she was 7 months old the diagnosis of Hodgkin's disease had been established by pathological examination of a cervical lymph node. At the age of 4 years the patient received irradiation to the right neck and supraclavicular region and the right axilla. The lymphadenopathy regressed and the patient remained symptom free. At the age of 11 years pathological examination of a right cervical skin lesion had shown basal cell carcinoma.

When she was admitted to hospital on this occasion she was noted to have pulmonary distress on mild exercise. The right lung field was dull to percussion and breath sounds were substantially decreased over the same area. The chest radiograph showed right pleural thickening with an effusion and mediastinal shift to the left. Computed tomography of the thorax showed a large right pleural effusion. Several solid masses with a density of soft tissue were noticed in the right lower lung field attached to the pleura. After aspiration of a large serous effusion the pleura and lungs were inspected with a mediastinoscope. Multiple minute polypoid masses were seen attached to the mediastinal pleura. The appearances of a frozen section were compatible with a malignant neoplasm. Talcum powder (30 ml) was insufflated into the pleural space. Follow up chest radiography and computed tomography showed a moderate localised effusion. The patient is alive at two years.

Pathological features Haematoxylin-eosin stained sections showed strands of polygonal and cuboidal cells in a glandular and papillary pattern. The nuclei were large and hyperchromatic with prominent nucleoli. A loose hypocellular stroma was present between the cell strands.

Immunohistochemical procedures showed the tumour cells to be positive for prekeratin (figure), weakly and focally positive for vimentin, and negative for carcinoembryonic antigen. These findings were interpreted as consistent with a diagnosis of diffuse malignant mesothelioma of epithelial type.



Positive staining of tumour cells with prekeratin antibodies.

Discussion

Although asbestos exposure is considered to be the major risk factor for the development of malignant mesothelioma, reports have varied in the proportion of patients with a history of exposure.[1] Walker *et al* estimated that the proportion with reported exposure ranged from 16% to 77%.[3] Several reasons might be suggested for this reported variation, such as the long latency period from onset of asbestos exposure to the development of malignant mesothelioma and the fact that even short term exposure to asbestos might be harmful. Thus the validity of an occupational and environmental history is frequently questionable, particularly when taken indirectly from relatives and not from the patient. The establishment of a diagnosis of malignant mesothelioma is also difficult.

In this case the occupational history was taken from the patient and her parents and not from distant relatives, and the diagnosis of malignant mesothelioma was confirmed by experienced pathologists. This case shows certain similarities to 10 cases of malignant mesothelioma without asbestos exposure described by Hirsch *et al*[4]; the patients were younger, asbestos related radiographic changes were absent, the tumour was exclusively epithelial in type, and the patients

Radiation associated malignant pleural mesothelioma: published reports

Reason for irradiation	*Age (y) at irradiation*	*Dose (rad)*	*Age (y) at diagnosis*	*Histological type*	*Ref*
Hodgkin's disease	27	?	34	Sarcomatous	1
Opacity in lung	*	9·5	57	Epithelial	4
Breast carcinoma	30	4600	40	Epithelial	5
Cosmetic irradiation	29	3400	55	Epithelial	5
Wilms' tumour	2	1500	16	Epithelial	6
Wilms' tumour	5	3300	21	Epithelial	7
Thorotrast	18	?	43	?	8
Wilms' tumour	3	?	44	Epithelial	9
Wilms' tumour	6	3400	22	?	9
Hodgkin's disease	4	3600	23	Epithelial	†

*Cumulative exposure of 9·5 rad over 26 years.
†Present case.
Conversion to SI units: 1 rad = 0·01 Gy.

survived longer than those with malignant mesotheliomas associated with asbestos exposure.

The association between radiation exposure and the subsequent development of malignant pleural mesothelioma has been reported by several authors[5–9] (table). In the present case the mesothelioma developed in the right chest, whereas radiation was given to the right cervical and axillary regions. Antman *et al* reported two cases of pleural mesothelioma following Wilms' tumour in childhood.[9] In one patient the mesothelioma developed on the opposite side to the tumour, in an area outside the radiation port, as in this case. In a study of radiation associated second malignancies 12 were found to have arisen at the edge of the prescribed treatment field and not directly within radiation therapy ports.[10] Thus the carcinogenic effects of irradiation might be at a site remote from the structure or organ irradiated.

Although the possibility of asbestos exposure cannot be completely excluded in the cases reported as radiation related malignant mesothelioma, these cases as well as animal studies indicate that radiation might induce malignant mesothelioma. This calls for further epidemiological studies of patients receiving radiotherapy or occupational groups exposed to radiation for long periods to assess the risk of malignant mesothelioma resulting from radiation. Other agents that have been suggested as inducers of malignant mesothelioma include man made mineral fibres, metals (beryllium), organic chemicals, and viruses.[2] Thus in patients with a suspected malignant mesothelioma a careful history should be taken to include exposure to agents such as radiation in addition to asbestos.

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