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Case Reports

Two Cases of Malignant Mesothelioma after Exposure to Asbestos¹

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SUMMARY

Malignant mesothelioma occurred in 2 young men after exposure to asbestos. In one patient, pleural plaques were of diagnostic importance. The patient was incidentally exposed to asbestos from the clothing of his father, who was an asbestos worker. In the other patient, chrysotile asbestos was probably the carcinogen.

The importance of clinical and radiographic observation of those in personal contact with workers in the asbestos industry and the important part played by all types of asbestos dust in the production of malignancy are stressed.

Introduction

Asbestos is one of the most valuable and versatile materials extracted from the earth's surface. There are six varieties of asbestos, all silicates, which differ physically and chemically from one another: crocidolite, amosite, anthophyllite, tremolite, actinolite, and chrysotile. Crocidolite and amosite contain more iron than do the other forms. Chrysotile, commonly known as white asbestos, is largely magnesium silicate and forms 90 per cent of the world's output of the mineral. It is found principally in Canada and the

U.S.S.R. No other type of asbestos is mined in Canada.

Repeated exposure to asbestos dust leads to a number of diseases. Asbestosis is characterized by pulmonary fibrosis causing a restrictive defect with reduced vital capacity and defective gas transfer often leading to death from respiratory failure. An increased incidence of carcinoma of the bronchus is associated with asbestosis (1). An increased incidence of primary malignant tumors of the pleura and peritoneum is also associated with exposure to asbestos dust (1). The level of asbestos exposure necessary to produce such changes is not yet known. Although it is generally recognized that exposure to asbestos is dangerous, the potential of chrysotile as a carcinogen is not yet clear. A fairly common radiographic abnormality in persons exposed to asbestos is the presence of

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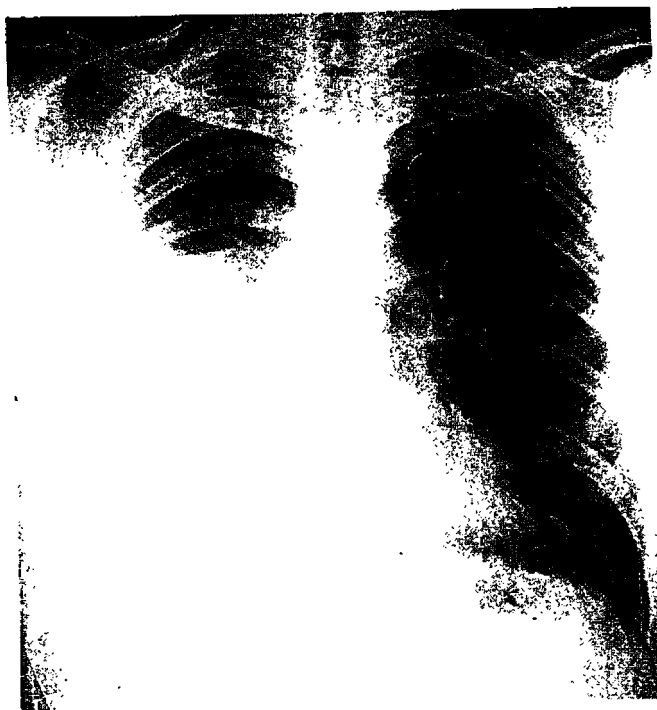


Fig. 1. Posteroanterior radiograph of chest in *Case 1* showing the presence of a large pleural effusion on the right.

pleural plaques. The degree of exposure necessary for plaque formation is not clear.

Before any serious attempt was made to protect workers from inhalation of asbestos fibers, deaths from respiratory failure were commonplace in the asbestos industry and were mainly related to the pulmonary fibrosis resulting from heavy exposure. The use of protective masks and ventilation might have resulted in decreased exposure to the dust and less severe asbestosis, so that deaths from respiratory failure have decreased, leaving workers alive long enough for the development of malignant tumors later in life. It is not possible to say whether this suggestion will be verified or whether there is a definite increase in the occurrence of such tumors.

Two cases of malignant mesothelioma of the pleura are described that illustrate certain unusual features of their causes.

CASE REPORTS

Case 1: A 31-year-old white man presented in March 1970 with a six-week history of breathlessness and a seven-month history of general weakness and malaise after an influenza-like illness. There had been no other change in his

health, no cough, hemoptysis, fever, or weight loss.

The patient was born in Glasgow, Scotland, where he had lived for the first 28 years of his life; he came to Canada in 1968. His previous employment had included work as a cable maker and die caster. He had never been occupationally exposed to asbestos dust. Occasionally he had worked with aluminum sprays and arsenic compounds. He had smoked 20 cigarettes per day for 16 years.

The patient's 68-year-old father had severe asbestosis for which he received compensation; his ill health had followed employment as a pipe lagger in Scotland. The patient's 55-year-old mother had emphysema. His only brother and two sisters were alive and well. The patient's father usually brought his overalls home from work and had often worn them home from work. No special precautions had been taken to protect the children from contact with these overalls. The mother occasionally washed the overalls.

Physical examination revealed a well nourished man with no clubbing of the fingers or lymphadenopathy. There were classic signs of right pleural effusion. A chest film (figure 1) confirmed the presence of a large right pleural effusion; on the left hemidiaphragm was a small



Fig. 2. Enlarged view of a portion of figure 1 showing a small, calcified pleural plaque on the left hemidiaphragm.

calcified, pleural plaque 2 cm in length (figure 2). No other abnormality was noted. The hemoglobin was 15.7 g per 100 ml; erythrocyte sedimentation rate (modified West), 11 mm per hour; leukocyte count, 7,800 per mm^3 with 40 per cent lymphocytes, 50 per cent neutrophils, 2 per cent segmented forms, and 8 per cent monocytes. Serum proteins and hepatic function tests were normal. Bronchoscopy revealed no abnormality. Aspirated pleural fluid was initially straw-colored, but after repeated thoracenteses, it became slightly blood-stained. No fluid samples demonstrated acid-fast bacilli on microscopy or culture. Cytologic examination revealed clumps of malignant mesothelial cells. Three pleural biopsies with an Abrams needle revealed normal pleura and connective tissue only. At open pleural biopsy (performed by Dr. Ian Munroe), 2 liters of serosanguinous fluid were removed from the right side of the chest, and it was seen that the visceral and parietal pleura were studded with pale nodules 8 mm to 2 cm in diameter. Histologic examination of these nodules revealed malignant mesothelioma. On the right side of the diaphragm was a calcified pleural plaque 8 cm in length.

At the time of the open pleural biopsy, kaolin powder was insufflated into the right pleural cavity to effect pleurodesis. Because there was a small recurrence of pleural fluid after this procedure, 20 mg of nitrogen mustard were instilled into the cavity. The effusion did not recur subsequently. The patient remained free from symptoms during the four-month follow-up pe-

riod, lost no weight, and was not anemic. After discharge from the hospital, however, slight clubbing of the fingers developed.

The patient's mother and sister were examined radiographically. Emphysematous changes were seen in the mother's chest film. In the sister's chest film a calcified pleural plaque was seen on the dome of the left diaphragm. The sister had also had no contact with asbestos other than from contact with her father.

Case 2: A 32-year-old white Canadian man presented with a history of discomfort in the right chest of six weeks' duration. The pain was pleuritic and occasionally severe. Dyspnea was not marked, and was absent at the onset of illness. There was cough with minimal mucoid sputum. The patient had lost 5 pounds in weight.

The patient had been born in Fulford, Quebec. At the age of three years, he moved to the town of Asbestos, Quebec, where he lived for the next 23 years. Asbestos is a mining town, and the patient's wife remembered it as "being continually in a haze of dust from the asbestos mines and workshops." After leaving school, the patient worked for ten years as an asbestos mine prospector in Quebec and elsewhere in Canada. For short periods, he also worked in the open pit but never performed any deep mining duties. In 1961, he moved to Vancouver, where he became a salesman at a local department store. He had been a moderately heavy smoker (20 to 30 cigarettes per day) for 14 years. As a teenager in Asbestos, he had had two pneumonic

illnesses, from which recovery was uneventful and swift. In 1963, he was believed to have had a myocardial infarction.

On physical examination, he was slim but did not appear wasted. His pulse rate was 116 beats per min and regular; his blood pressure was 120/70 mm Hg. The classic signs of a large, right, pleural effusion were present.

A chest film confirmed the presence of an effusion on the right side. No pleural plaques were seen. Hemoglobin was 15.6 per 100 ml; leukocyte count, 10,400 per mm³ with a normal differential count; erythrocyte sedimentation rate (modified West), 25 mm per hour; serum proteins were normal. Aspirated pleural fluid was initially straw-colored and contained many lymphocytes and some polymorphonuclear leukocytes. Clumps of large monocyctic cells were present and believed to be atypical pleural mesothelial cells. The sputum contained no malignant cells. Bronchoscopy was normal. At diagnostic thoracotomy (performed by Dr. Elliot Harrison), straw-colored fluid was again withdrawn. The right lung was found to be partially collapsed. The parietal pleura and the lung surface, particularly in the upper thorax, were covered with fibrin and pea-sized nodules. On the chest wall and mediastinum and extending down onto the diaphragm were yellowish, round, tumor nodules 1 cm to 3 cm in diameter. Histologic examination of samples of these nodules showed malignant mesothelioma.

The patient was treated with irradiation to the right chest in April 1968. He died in autumn of that year.

Discussion

In *Case 1*, the diagnosis of malignant mesothelioma was initially suspected because a pleural plaque was seen on the dome of the left hemidiaphragm. The presence of hyalinized and calcified plaques in persons exposed to asbestos dust is common. The plaques may be found on the visceral, parietal, or diaphragmatic pleura. Fibers of asbestos have been found in the pleura and peritoneum of persons exposed to asbestos dust (1-3). The mechanisms whereby these fibers reach the pleura and peritoneum and cause a characteristic fibrous reaction is incompletely understood. Anton (4) believed that although pleural plaques might be caused by inhalants such as talc and by specific infections, multiple pleural plaques seen on chest films are

characteristic of asbestos exposure. The degree of exposure that might induce plaque formation appears to be somewhat less than that necessary to produce asbestosis. The plaques can be found anywhere on the pleural surface but are particularly common on the diaphragmatic pleura. Although they can be seen in routine posteroanterior and lateral chest roentgenograms, oblique views are occasionally necessary to detect them. In *Case 1*, in addition to the small plaque on the left diaphragm, a large pleural plaque was found at thoracotomy on the right diaphragm; this plaque had not been seen on chest films that had included oblique views. It is likely that even the small amount of fluid remaining in the chest after aspiration had served to conceal this plaque.

There is a close relationship between the presence of pleural plaques and subsequent development of malignant mesotheliomas in those exposed to some form of asbestos dust. Thus the sister of the first patient, having been found to have a pleural plaque, must be considered to be at risk. Hourihane and co-workers (3, 5), recently described 29 patients who had been exposed to asbestos and in whom pleural plaques were the sole radiographic evidence of disease. In 5 of these patients, malignant mesotheliomas of the pleura or peritoneum subsequently developed; in addition, one patient died of carcinoma of the bronchus.

A comprehensive study by Newhouse (6) and Newhouse and Thompson (7) illustrated the importance of nonoccupational exposure to asbestos in subsequent development of malignant tumors. Among patients with mesotheliomas in the area of London, England were 9 whose only contact with asbestos was through closely related persons who worked with the mineral. It is not uncommon for pipe ladders, for example, to return home from work with a large amount of asbestos on their clothing, resulting in steady exposure of other members of the household to asbestos. *Case 1* illustrates the danger to which relatives of asbestos workers are exposed. This is probably particularly true of the children of an asbestos worker who might come into contact with their

father's overalls, and the worker's wife, who might wash these garments. Two close relatives of the first patient were examined radiographically, and one was shown to have pleural plaques.

The average time between the onset of exposure and the development of a mesothelial tumor is approximately 30 years to 35 years (6), but there are examples of induction times of 15 years or less (5). It is of interest that in the 2 patients described herein, the tumors developed at 32 years and 31 years of age, after exposure to the dust from early childhood. It is obviously important to institute regular radiographic examination of the chest not only in asbestos workers but also in their relatives.

The patient in *Case 2* had worked for many years in the Canadian mining industry and had lived in a mining town. He had been exposed only to chrysotile. As in *Case 1*, a primary malignant pleural tumor developed in the fourth decade of his life. Chrysotile is believed by some to be free of carcinogenic effect. Wagner (8, 9) has stated that one difficulty in assessing the dangers of chrysotile is that most workers are exposed to a mixture of asbestos fibers and other chemical agents. Data reported by Wright (10) referring to work by MacDonald and associates² suggest that the incidence of primary malignant tumors of the pleura is not increasing in Canada, where chrysotile is mined. Wright (10) suggested that chrysotile is associated less with malignant mesothelial tumors than other types of asbestos. Smith and co-workers (11) showed experimentally that chrysotile alone was not carcinogenic to hamsters unless combined with the hydrocarbon 3,4 benzpyrene. Benzpyrene alone was not carcinogenic in these experiments. Although it has been suggested that the incidence of malignant tumors is not increased in those exposed to asbestos who do not smoke, no clear-cut studies are available (12). Smoking is a common habit throughout the general population, including work-

ers in the asbestos industry. Although some investigators believe that the only definite increase in carcinoma of the bronchus occurring in the industry is in patients with asbestosis, cigarette smokers exposed to asbestos are at seven times the risk of development of malignant tumors as workers who do not handle asbestos (13).

There is probably no really safe level of asbestos exposure. The minor exposure experienced by relatives before signs of the disease process develop makes pronouncements of safe or comparatively safe industrial exposure levels for asbestos workers unrealistic and misguided. It is clear that only minor exposure is required for the development of malignant tumors, and this fact serves to stress the importance of regular screening by radiographic examination of the chest of workers and their relatives. The screening of relatives must be routine if full understanding of the dangers of asbestos to the community is to be gained. Furthermore, at present it must be assumed that all forms of asbestos, including chrysotile, remain a serious health hazard because they cause pulmonary fibrosis and induce malignant tumors.

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RESUMEN

Dos casos de mesotelioma maligno después de exposición al asbesto

Se encontró un mesotelioma maligno en dos jóvenes después de estar expuestos al asbesto. En uno de los pacientes las placas pleurales fueron de importancia para el diagnóstico. El paciente estuvo accidentalmente expuesto al asbesto a través de la ropa de su padre, quien era un obrero de asbestos. En el otro paciente, el asbesto crisótilo fue probablemente el carcinógeno.

Se recalca la importancia de la observación clínica y radiográfica en aquellos individuos que están en contacto personal con obreros de la industria de asbestos, y el papel tan importante que desempeña el polvo de asbestos en la producción malignidad.

² MacDonald, A. D., Harper, A., El Attar, O. A., and McDonald, J. C.: Unpublished data, 1969.

RESUME

Deux cas de mésothéliome malin suivant l'exposition à l'amiante

Du mésothéliome malin a été constaté chez deux jeunes hommes après l'exposition à l'amiante. Chez l'un des malades des plaques pleurales étaient de l'importance diagnostique. Ce malade avait été exposé fortuitement à l'amiante dans les vêtements de son père, qui travaillait dans l'industrie de l'amiante. Chez l'autre malade l'asbeste chrysotile paraissait être le carcinogène.

On insiste sur l'importance de l'observation clinique et radiographique des personnes qui sont en contact avec ceux qui travaillent dans l'industrie de l'asbeste, et le rôle important que jouent tous les genres de poussière d'asbeste dans la production des malignités.

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