

Brief Report

Rarity of Malignant Mesothelioma Prior to the Widespread Commercial Introduction of Asbestos: The Mount Sinai Autopsy Experience 1883–1910

James A. Strauchen, MD*

Background Most malignant mesotheliomas are related to asbestos exposure. Whether malignant mesothelioma occurs in the absence of asbestos exposure remains unsettled. To address this question we reviewed a series of 2,025 autopsies performed at the Mount Sinai Hospital between 1883 and 1910, prior to the widespread commercial introduction of asbestos.

Methods Retrospective autopsy review.

Results No cases of malignant mesothelioma were identified in 2,025 autopsies performed between 1883 and 1910.

Conclusions Malignant mesothelioma was rare prior to the widespread commercial introduction of asbestos. *Am. J. Ind. Med.*

© 2011 Wiley-Liss, Inc.

KEY WORDS: asbestos; mesothelioma; pleura; tumor; autopsy

INTRODUCTION

Asbestos exposure is widely recognized as the leading cause of malignant mesothelioma, accounting for up to 90% of cases (Spirtas et al., 1994). Nevertheless, it has been suggested that some cases of malignant mesothelioma are not caused by asbestos or other proposed causes (therapeutic radiation, chronic irritation, SV40, etc.), but are in fact “idiopathic.” If idiopathic cases of malignant mesothelioma occur, they would have been present in the population prior to the widespread commercial introduction of asbestos in the latter part of the 19th century and early part of the 20th century (Frank, 2006). A review of

all the autopsies performed at the Massachusetts General Hospital starting in 1946, when the first case of malignant mesothelioma was published in the Case Records of the Massachusetts General Hospital and working back to 1896, when the first autopsy was performed, identified no cases of malignant mesothelioma prior to 1946 (Mark and Yokoi, 1991). The authors comment: “One must conclude that the background level of diffuse malignant mesothelioma in Europe and in the United States prior to 1930 was extremely low. No case was detected at the Massachusetts General Hospital until 1946.”

The Mount Sinai Hospital in New York City is a 1,000 bed tertiary care hospital and medical center founded in 1852 as the Jews’ Hospital in New York (Hirsh and Doherty, 1952). It is coincidentally where Irving J. Selikoff, M.D. did his pioneering studies on asbestos-related disease. The first recognized case of malignant mesothelioma at the Mount Sinai Hospital was reported in 1931. The authors reported 5 cases of primary pleural tumors (2 at surgery, 3 at autopsy; Klemperer and Rabin, 1931, 1992). Three of the tumors consisted of a bulky

Department of Pathology, Mount Sinai School of Medicine, New York, New York

*Correspondence to: Dr. James A. Strauchen, MD, Box 1194, 1 Gustave Levy Place, New York, NY 10029. E-mail: james.strauch@msm.edu

Accepted 4 March 2011

DOI 10.1002/ajim.20951. Published online in Wiley Online Library (wileyonlinelibrary.com).

solitary mass attached to the visceral pleura and would now be considered solitary fibrous tumors, one was a giant lipoma, and another was a biphasic diffuse malignant mesothelioma. The latter case occurred in a 26-year-old woman admitted to the Mount Sinai Hospital in August, 1929, complaining of pain in the left side of chest from which she had suffered for a period of 11 months. Following an "exploratory puncture" no fluid was obtained and her course rapidly deteriorated. At autopsy she was found to have "complete encasement and infiltration of the lung by tumor" which on histologic examination had the characteristic biphasic pattern of a diffuse malignant mesothelioma with epithelial and sarcomatous portions. No occupational history survives.

To determine if malignant mesotheliomas occurred with any frequency prior to the widespread commercial introduction of asbestos, we reviewed the earliest autopsies performed at the Mount Sinai Hospital from February 1883 to December 1910, for which there was a continuous record. These cases represent a 28-year period prior to the widespread commercial introduction of asbestos and prior to sufficient latency for the development of asbestos-related malignant mesothelioma.

MATERIALS AND METHODS

The record of 2,025 autopsies performed at the Mount Sinai between February 2, 1883 and December 31, 1910 were reviewed. The material reviewed consisted of age and gender, date of admission, sometimes a brief clinical summary, detailed description of the autopsy findings, and final diagnoses. Autopsy descriptions were limited to the gross findings in early cases; microscopic findings were provided as early as 1887, but were not provided in all cases. Unfortunately, no slides from these autopsies survive. The criteria used to identify cases of mesothelioma were those used by other authors (Mark and Yokoi, 1991): tumor involves the pleura and no other tumor is identified. Tumor spreads upon the serosa.

RESULTS

Among the 2,025 cases autopsied, malignant tumors were identified in 281 (13.9%). Understandably, most deaths in the pre-antibiotic era were from infectious diseases, including pneumonia, tuberculosis, mastoiditis, and appendicitis. Table I indicates the distribution of the 281 malignant tumors identified at autopsy and the surprising sophistication with which these tumors were recognized and classified, considering the limited techniques of the time and lack of histology in many cases. A wide range of tumors were recognized, including 17 sarcomas of bone or soft tissue, 25 primary tumors of the central nervous system, 20 lymphomas, and 13 leukemias and myeloma.

TABLE I. Malignant Neoplasms in 2,025 Cases Autopsied at the Mount Sinai Hospital 1883–1910

Tumor	Cases	Percent
Sarcoma of soft tissue or bone	17	6.0
Primary central nervous system	25	8.9
Lung	6	2.1
Mediastinum	2	0.7
Stomach and esophagus	73	26.0
Colon and rectum	43	15.3
Pancreaticobiliary and liver	20	7.1
Other gastrointestinal	18	6.4
Breast	5	1.8
Uterus and ovary	10	3.6
Lymphoma	20	7.1
Leukemia/myeloma	13	4.6
Genitourinary and testis	18	6.4
Miscellaneous (head and neck, adrenal, skin)	8	2.8
Unknown primary	3	1.0
Total	281	

Carcinomas of the gastrointestinal tract were by far the most common accounting for almost 55% of the cases. Carcinoma of the stomach or esophagus was the single most common tumor (73 cases, 26.0%) followed by carcinoma of the colon and rectum (43 cases, 15.3%). Lung cancer was infrequent (6 cases, 2.1%). No definite cases of malignant mesothelioma were identified. One case of an "endothelioma primary in the pleura (?) metastases" was recorded at autopsy in 1903. The patient, E.S., was a 47-year old female who at autopsy was found to have her pleura "studded with verrucous small white firm nodules." Since she also had widespread metastases in the liver, omentum, pericardium, ribs, lungs, and uterine serosa, a diagnosis of metastatic carcinoma of unknown primary site was considered more likely.

DISCUSSION

The results of this study confirm previous studies that the background level of diffuse mesothelioma prior to 1930 was extremely low (Mark and Yokoi, 1991). In a retrospective review of autopsy records collected from eight cities in the United States and Europe from 1910 to 1946, the rate of primary pleural tumors was 0.07%; in a comparable series from 1950 to 1970, the rate of primary pleural tumors was 0.24% (McDonald and McDonald, 1987).

The use of retrospective autopsy review to assess the occurrence of malignant mesothelioma has limitations. Although the term "mesothelioma" was not well established in the literature until 1931 (Klemperer and Rabin, 1931, 1992), these tumors were previously recognized

under other terms such as “endothelioma of the pleura” (Hochberg et al., 1947). Malignant mesothelioma prior to modern thoracic surgery, radiotherapy, and chemotherapy, was, and unfortunately in most cases still is, a fatal disease, often not diagnosed with certainty until autopsy. The absence of histology in early autopsy series is limiting. Nevertheless, the characteristic clinicopathologic features and anatomic distribution of mesothelioma at autopsy permit recognition in most cases (Mark and Yokoi, 1991). Distinction of mesothelioma from pleural metastases of adenocarcinoma of thoracic or extrathoracic site remains problematic to the present day, however, an autopsy series affords the opportunity to assess an extrathoracic primary tumor and lung cancer itself was uncommon at this time (Table I).

Selection biases include the population studied. Only patients who died in the hospital and had an autopsy performed were studied. In that era, hospitals served a predominantly indigent and immigrant population; wealthier patients preferring to receive medical care at home (Hirsh and Doherty, 1952). Patients were predominantly from the indigent and immigrant areas of Manhattan, what would now be referred to as the “inner city”; no specialized chest hospital yet existed, however, several hospitals for the care of patients with tuberculosis were in operation by 1900 (Drolet and Lowell, 1952). Infectious diseases were rife and the leading causes of death, particularly tuberculosis (Hirsh and Doherty, 1952). Although mesothelioma could be confused clinically with tuberculosis (Marchand, 1991) and could be missed if tuberculosis cases were not autopsied, tuberculosis cases were autopsied and accounted for 9% of the autopsies in this series, comparable to the 13% of deaths in New York City attributed to tuberculosis in the period from 1900 to 1904 (Drolet and Lowell, 1952).

The early literature on mesothelioma is clouded by confusion regarding the origin of the tumor, the use of confusing, and misleading terms (e.g., pleural endothelioma), the failure to distinguish between diffuse and localized tumors, and doubt as to the very existence of the tumor as a distinct entity (Hochberg et al., 1947). Distinction between localized and diffuse tumors of the pleura was emphasized by Klemperer and Rabin (1931, 1992), noting the subpleural connective tissue origin of the former and the surface lining cell origin of the latter. They made the recommendation, now generally accepted, that diffuse tumors of the pleura be designated as “mesothelioma,” which “may present the characteristics of epithelium, connective tissue, or both” (Klemperer and Rabin, 1931, 1992); the localized tumors, in contrast, would today be considered solitary fibrous tumors of the pleura.

The high ratio of localized to diffuse tumors (3:1) observed by Klemperer and Rabin (1931, 1992) also supports the rarity of diffuse malignant mesothelioma in that era, since it is the reverse of the 1:3 ratio of solitary fibrous tumor to diffuse malignant mesothelioma observed today (Thorgeirsson et al., 2010).

In summary, in a series of 2,025 patients autopsied at the Mount Sinai Hospital in New York City between February 2, 1883 and December 31, 1910, no definite cases of malignant mesothelioma were observed. The results indicate that the incidence of malignant mesothelioma prior to the widespread commercial introduction of asbestos was very low.

ACKNOWLEDGMENTS

I am indebted to Barbara Niss, Archivist, L. Gustave, and Janet W. Levy Library, Mount Sinai School of Medicine, for granting me access to the Mount Sinai Archive.

REFERENCES

- Drolet GJ, Lowell AM. 1952. A half century's progress against tuberculosis in New York City 1900–1950. New York: New York Tuberculosis and Health Association, p. i–xxv.
- Frank AL. 2006. The history of the extraction and uses of asbestos. In: Dodson RF, Hammar SP, editors. Asbestos risk assessment, epidemiology, and health effects. Boca Raton: Taylor & Francis, p. 1–7.
- Hirsh J, Doherty B. 1952. The first hundred years of the Mount Sinai Hospital of New York 1852–1952. New York: Random House, p. 3–13.
- Hochberg LA, Epstein IG, Pernikoff M. 1947. Endothelioma (mesothelioma) of the pleura. Presentation of a case treated surgically. *Chest* 13:621–626.
- Klemperer P, Rabin CB. 1931. Primary neoplasms of the pleura. A report of five cases. *Arch Pathol* 11:385–412.
- Klemperer P, Rabin CB. 1992. Primary neoplasms of the pleura. A report of five cases. *Am J Ind Med* 22:1–31.
- Marchand PE. 1991. The discovery of mesothelioma in the north-western Cape Province in the Republic of South Africa. *Am J Ind Med* 19:241–246.
- Mark EJ, Yokoi T. 1991. Absence of evidence for a significant background incidence of diffuse malignant mesothelioma apart from asbestos exposure. *Ann NY Acad Sci* 643:196–204.
- McDonald AD, McDonald JC. 1987. Epidemiology of malignant mesothelioma. In: Antman K, Aisner J, editors. Asbestos related malignancy. New York: Grune and Stratton, p. 31–55.
- Spirtas R, Heineman EF, Bernstein L, Beebe GW, Keehn RJ, Stark A, Harlow BL, Benichou J. 1994. Malignant mesothelioma: attributable risk of asbestos exposure. *Occup Environ Med* 51:804–811.
- Thorgeirsson T, Isaksson HJ, Hardardottir H, Alfredsson H, Gudbjartsson T. 2010. Solitary fibrous tumor of the pleura: an estimate of population incidence. *Chest* 137:1005–1006.