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Association of Asbestos Exposure With Malignant Mesothelioma Incidence in Eastern China

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The reported incidence of malignant mesothelioma (MM) in China is 1.5 cases per million population, much lower than in other countries.¹ In China, the prevalence of MM in different regions is unknown,¹ and only 15% of MMs have been associated with asbestos exposure^{1,2} compared with more than 70% in most of the world.^{3,4}

Methods

We reviewed all pleural and peritoneal malignant tumors diagnosed as MM from January 1, 2002, through December 31, 2015, in the Zhejiang Cancer Hospital (ZJCH), which is the largest cancer hospital in Hangzhou, China, and where there is no asbestos industry, and in

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the nearby (112 km) Yuyao People's Hospital, Yuyao, China, located in the Chinese textile asbestos industrial area, where most patients are exposed to asbestos. We reviewed a total of 92 MMs: 34 in the pleura, 56 in the peritoneum, and 2 in the tunica vaginalis.

Asbestos exposure was determined by a trained oncologist (W.M., Z. Guo, or Z. Gao) who interviewed patients for occupational and family histories. Individuals who worked in trades in which asbestos exposure was likely or who grew up or lived in families in which others were employed in the textile industry or trades associated with asbestos were identified as being exposed to asbestos. This retrospective study was approved by the Zhejiang Cancer Hospital Ethical Committee and the Zhejiang Academy of Medical Sciences Ethical Committee. We obtained formalin-fixed, paraffin-embedded tissues from blocks kept in Department of Pathology, Zhejiang Cancer Hospital, and Yuyao Hospital. Patient information was obtained through medical records and patient and family interview. All patients provided verbal informed consent, and data were not deidentified.

Results

Reviewing histologic findings with the aid of a large immunohistochemical panel, we confirmed the diagnosis of MM in 28 patients from ZJCH and 24 from Yuyao People's Hospital (52 of 92 cases [57%]). The male to female ratio was approximately 1:4 (19%; 95% CI, 10%–32%) compared with 4:1 (80%) in the United States ($z = 11.0$, $P < .001$). The pleural to peritoneal MM ratio was approximately 1:3 (24%; 95% CI, 13%–38%) compared with 5:1 (83%) in the United States ($z = 11.2$, $P < .001$). The mean (SD) age at diagnosis was 50.6 (7.9) years (95% CI, 48.4–52.7 years) compared with 72 (9.5) years in the United States ($t_{51} = 19.3$, $P < .001$). Twenty of the 52 MMs (5 in the pleura, 14 in the peritoneum, and 1 in the tunica vaginalis) occurred in asbestos-exposed individuals (38%; 95% CI, 25%–53%): 2 of 28 (7%; 95% CI, 1%–23%) at the ZJCH and 18 of 24 (75%; 95% CI, 53%–90%) at Yuyao People's Hospital. Computed tomograms available for 16 of 28 MMs found at the ZJCH supported asbestos exposure in 2 of 16 cases (13%; 95% CI, 2%–38%). Asbestos-related MMs occurred in 19 women and 1 man. Nine of 52 MMs (17%; 95% CI, 8%–30%) occurred in individuals 40 years or younger compared with less than 1% in the same age group in the United States³ (Table 1 and Table 2).

Discussion

The higher prevalence of peritoneal vs pleural MMs in China, especially among nonexposed young women, is unique.^{3,4,6} Initially we thought that asbestos was the main cause because 13 of 18 peritoneal MMs (72%; 95% CI, 46%–90%) from Yuyao People's Hospital occurred in women exposed to asbestos. However, only 1 of 14 peritoneal MMs (7%; 95% CI, 0%–34%) from the ZJCH was associated with asbestos. Except for asbestos exposure, no significant demographic differences were observed between the ZJCH and Yuyao People's Hospital (Table 1 and Table 2), suggesting that asbestos may not be the main cause of MM in these women. These findings point to a unique opportunity to investigate other causes of peritoneal MMs in this population, aside from asbestos. In the United States and Europe, an increasing number of peritoneal MMs do not seem to be associated with asbestos,⁵ leading

some authors to speculate that a subgroup of peritoneal MMs may have a different pathogenesis.^{3,6}

In most industrialized countries, pleural MMs characteristically occur in a setting of asbestos exposure.^{3,6} Because men are most often involved in asbestos trades, the incidence of pleural MMs is higher in men, with a male to female ratio of approximately 4:1.^{3,6} Instead, among Chinese patients with 12 pleural MMs, 10 of 12 were women (83%; 95% CI, 52%–99%) and only 5 of 12 (42%; 95% CI, 15%–72%) had been exposed to asbestos, underscoring the unusual prevalence of MM in Chinese women (Table 1).

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Table 1

Demographic Characteristics of the Study Participants

Characteristic	ZJCH/Yuyao Hospital Patients		
	Total No. of Patients	No. of Patients With Asbestos Exposure	Exposure Time, Mean (SD), y
Pleural MM			
Sex			
Male	2/0	0/0	NA
Female	10/6	5/5	8.8 (1.6)/8.8 (1.6)
Age at diagnosis, y			
50	6/3	2/2	9.0 (1.4)/9.0 (1.4)
>50	6/3	3/3	8.6 (2.1)/8.2 (2.1)
Asbestos exposure			
Not exposed	7/1		NA
Exposed	5/5		NA
Histologic type			
Epithelioid	8/5	4/4	9.3 (1.5)/9.3 (1.5)
Biphasic	2/1	1/1	7.0 (0)/7.0 (0)
Sarcomatoid	2/0	0/0	NA
Peritoneal MM			
Sex			
Male	6/0	0/0	7.7 (3.6)/8.1 (3.1)
Female	32/18	14/13	NA
Age at diagnosis, y			
50	22/11	6/6	5.7 (2.7)/5.7 (2.7)
>50	16/11	8/7	9.4 (3.7)/10.1 (1.7)
Asbestos exposure			
Not exposed	24/5		NA
Exposed	14/13		NA
Necrosis			
Absent	24/13	10/9	8.0 (3.6)/8.7 (3.0)
Present	14/5	4/4	6.8 (3.5)/6.8 (3.5)
Stroma			
No inflammation	15/7	6/5	7.5 (5.3)/8.6 (4.2)
Inflammation	23/11	8/8	7.8 (2.5)/7.8 (2.5)
Depth of invasion ^a			
0	1/1	0/0	NA
1	1/1	1/1	7.0 (0)/7.0 (0)
2	4/1	0/0	NA
3	32/15	13/12	7.7 (3.6)/8.2 (3.2)

ZJCH/Yuyao Hospital Patients			
Characteristic	Total No. of Patients	No. of Patients With Asbestos Exposure	Exposure Time, Mean (SD), y
Histologic Type			
Epithelioid			
Tubulopapillary	20/9	8/7	6.3 (3.5)/7.0 (3.2)
Solid or deciduoid	8/3	1/1	10.0 (0)/10.0 (0)
Biphasic	7/4	3/3	11.3 (1.2)/11.3 (1.2)
Sarcomatoid	3/2	2/2	6.0 (1.0)/6.0 (1.0)

Abbreviations: MM, malignant mesothelioma; NA, not applicable; ZJCH, Zhejiang Cancer Hospital.

^aDepth of invasion according to Lee et al⁵; 0, noninvasive; 1, invasion into the stroma; 2, invasion into the fat; and 3, invasion into nearby tissue or organs. Note that the study sample size was small and the results were not adjusted for any confounding variables.

Table 2

Association of Age, Asbestos Exposure, and Sex With Malignant Mesothelioma in 52 Patients

ZJCH/Yuyao People's Hospital Patients				
Variable	Total No. of Patients	No. of Patients by Age Group, y		Mean Age at Diagnosis, y
		50	40	
Total	52/24	29/14	9/1	50.6/52.6
Site				
Pleura	12/6	6/3	3/1	49.5/53.2
Peritoneum	38/18	22/11	6/0	50.8/52.4
Tunica vaginalis	2/0	1/0	0/0	52.0/0
Sex				
Male	10/0	5/0	3/0	47.8/0
Female	42/24	24/14	6/1	51.2/52.6
Asbestos exposure				
Not exposed	32/6	20/6	9/1	47.3/45.2
Exposed	20/18	9/8	0	55.2/55.1

Abbreviation: ZJCH, Zhejiang Cancer Hospital.