RESEARCH ARTICLE

Mesotheliomas in Lebanon: Witnessing a Change in Epidemiology

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Abstract

Background: Mesotheliomas are relatively rare tumors in Lebanon. The only previous study goes back to 14 years ago, when we published epidemiological characteristics of mesotheliomas in Lebanon, showing that the pleural location accounted for the vast majority of cases, with clear evidence of asbestos exposure from the Eternit factory of Chekka region. The objective of this current study was to estimate the incidence of mesothelioma in the past decade and to identify its epidemiological, clinical and therapeutic characteristics, making comparisons with our first study published in 2001. Materials and Methods: Between 2002 and 2014, patients diagnosed with malignant mesothelioma at Hôtel-Dieu de France University Hospital were investigated. Epidemiological data focusing on asbestos exposure history were collected from medical records and interviews with the families. Results: A total of 26 patients were diagnosed with mesothelioma, 21 of which were successfully investigated. The mean age of these 21 patients is 62.5 (19-82). Only 3 (14.29%) are women. 18 (85.71%) were smokers. Among the 21 available mesotheliomas, 15 (71.4%) are pleural, while 5 (23.8%) are peritoneal and 1 (4.8%) pericardial. Only 60% of patients with pleural mesothelioma and 50% of those with an obvious exposure to asbestos lived and/or worked in Chekka region. The mean time of asbestos exposure in patients with mesothelioma is 24.5 (1-50) years and the mean latency is 37.4 (4-61) years. Of the 21 patients, 10 (47.6%) underwent surgery during their treatment, 16 (76.2%) received chemotherapy and 3 (14.3%) received best supportive care. Conclusions: Compared to the previous study (1991-2000), substantial changes in the epidemiology of mesothelioma in Lebanon were observed, such as an increase in peritoneal localizations and a lower correlation with Chekka region asbestos contamination.

Keywords: Pleural mesothelioma - peritoneal mesothelioma - Lebanon (capital L) - Chekka (capital C) - asbestos

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Introduction

Mesotheliomas are rare tumors worldwide. In the United States, nearly 3300 cases are diagnosed every year. In France, the figure is 800. According to the National Cancer Registry, around 15 new cases are diagnosed every year in Lebanon (Teta et al., 2008; Le Stang et al, 2010; Lebanese Ministry of public health, 2014).

Mesotheliomas are aggressive tumors arising from serous surfaces: pleura (65%-70%), peritoneum (30%), tunica vaginalis testis and pericardium (1-2%) (Raptopoulos et al., 1985). The characteristics of this type of cancer consist of its close association with exposure to asbestos and its classification as one of the most common occupational diseases. Moreover, mesotheliomas are a major public health problem for the international community, have a bad prognosis and are resistant to standard chemotherapy regimens (Gibbs et al, 1990; Schutte et al, 2003).

Two families of asbestos are described: amphiboles and chrysotiles (Gennaro et al., 2000). Amphiboles are more implicated in the genesis of mesothelioma compared to chrysotiles. Exposure to asbestos is detected in over 80% of pleural mesotheliomas and only in 50% of peritoneal mesotheliomas (Busch et al., 2002). Two types of asbestos exposure are reported: environmental exposure and occupational exposure, the latter consisting of a higher risk of developing mesothelioma. Apart asbestos, many risk factors are associated with the development of mesothelioma, such as a prior irradiation, erionite, Simian Virus 40 and genetic predisposition. There is no proven combination with smoking, but some studies describe that smoking potentiates the effect of asbestos in the development of malignant mesothelioma (Cicala et al., 1993; Antman et al., 2005; Testa et al., 2011).

In the mid 70s, the carcinogenic effect of asbestos was confirmed and many countries started banning its use, production and importation. By 2005, all European

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countries had banned the asbestos (Kazan et al., 2015).

In Lebanon, the whole amount of asbestos is imported. For instance, the import in 1996 is estimated at 235 tons, half of which was used by the factory of Eternit in Chekka. This factory was specialized, since 1962, in producing construction materials and pipelines from the mixture of cement and asbestos. In 1998, a law was passed banning the import of all types of asbestos as raw material, except chrysotiles. Also, in the same period, measures were undertaken to reduce the legally accepted amount of fibers in the factory atmosphere. In 2000, the Eternit factory in Chekka was definitively closed because of financial problems. Only one Lebanese study, conducted by our team and published in 2001, described the epidemiological characteristics of the disease during the decade 1991-2000 and concluded to a narrow and undeniable relationship between asbestos, Chekka region and the development of mesothelioma in Lebanon (Kattan et al., 2001).

Given the paucity of information and research, we aimed in our study to update the epidemiological, clinical and therapeutic characteristics of mesothelioma in Lebanon and to assess occupational and environmental exposure to asbestos in patients with this malignancy.

Materials and Methods

This is a descriptive retrospective study based on computer data collected from the pathology laboratory of Hôtel-Dieu de France of all diagnosed mesothelioma from 2002 to 2014. Hôtel-Dieu de France University Hospital is a tertiary medical center where 20% of the Lebanese cancer patients are estimated to be treated (unpublished data).

Data collection was made from the medical records from the hospital and the patients' records in their physicians' offices. The investigator contacted the patients by telephone calls, or their relatives in case of death of the patient, to complete a predetermined grid on EXCEL, containing all the variables in this study.

Variables studied are age, sex of patients, localization of mesothelioma, histological subtype, type of exposure, route of exposure (occupational and/or environmental), occupation, residence, exposure duration to asbestos, latency for developing mesothelioma, treatment modalities and overall survival. These data were analyzed using SPSS version 20.

Results

26 patients were diagnosed with mesothelioma in our institution, during a period of 12 years. Among them, 21 were successfully investigated, since the critical data lacked in 5 patients. The mean age is 62.48 years, with a minimum of 19 years and a maximum of 82 years. 3 of 21 (14.29%) are women, with a male-female sex ratio of 6.

The location of mesothelioma, among the 21 investigated patients, was in the pleura in 15 cases (71.4%), the peritoneum in 5 (23.8%) patients and the pericardium in 1 (4.8%) case.

8 (53.3%) among the 15 patients with pleural mesothelioma presented dyspnea as the inaugural symptom. For the 5 cases of peritoneal mesothelioma, the most common formats are ascites and abdominal pain, each present in 4 (80%) patients. Patient characteristics concerning age, sex, localization and clinical presentations are summarized in Table 1.

18 (85.71%) among the 21 patients diagnosed with mesothelioma were exposed to asbestos. The mode of exposure includes a single occupational exposure in 9 (42.86%) cases, a single environmental exposure in 5 (23.81%) patients and a mixed occupational and environmental exposure in 4 (19.05%) cases. Consequently, 3 (14.29%) patients were free from any known exposure, of which 2 have developed a peritoneal mesothelioma. Moreover, 18 (85.71%) of the 21 patients were smokers.

Table 1. Characteristics of the 21 Patients: Age, Sex, Localization of Mesothelioma and Presentation Mode

Patient	Age	Sex	Localization	Presentation mode
1	63	M	Peritoneal	Ascites
2	65	M	Pleural	Pleural effusion
3	75	M	Pleural	Pleural effusion and pleural thickening
4	79	M	Pleural	Hilar lymph node
5	42	F	Pleural	Dyspnea
6	55	M	Peritoneal	Abdominal pain and ascites
7	70	M	Peritoneal	Abdominal pain and ascites
8	62	M	Pleural	Dyspnea and hemoptysis
9	57	M	Pleural	Dspnea and pleural effusion
10	73	M	Pleural	Dyspnea, pleural effusion and hemoptysis
11	67	M	Pleural	Dyspnea, cough and pleural effusion
12	72	M	Pleural	Pleural effusion, pleural thickening and cough
13	74	M	Pericardial	Dyspnea and odynophagia
14	19	M	Peritoneal	Abdominal pain
15	53	F	Pleural	Dyspnea and pleural effusion
16	82	M	Pleural	Chest pain
17	59	M	Pleural	Pneumonia
18	75	M	Pleural	Dyspnea and pleural effusion
19	47	M	Pleural	Dyspnea
20	61	F	Pleural	Peripheral facial paralysis
21	62	M	Peritoneal	Abdominal pain and ascites

Table 2. Exposure Mode to Asbestos, Time of Exposure and Latency

Patient	Residence	Occupation	Exposure mode	Asbestos exposure (present +, absent -)	Exposure time (years)	Latency (years)	Tobacco (pack-years)
1	Kuwait/ South of Beirut	Oil station	Occupational	+	12	33	70
2	Kuwait	Swimming pool repair service	Occupational	+	40	40	50
3	Zgharta	Eternit factory	Occupational	+	10	35	0
4	Akkar	Taxi driver	None	-	-	-	150
5	Chekka	Financial expert	Environmental	+	3	23	30
6	Mount Lebanon/ Beqaa	Journalist	None	-	-	-	60
7	Bourj Hammoud	Shoe factory	None	-	-	-	50
8	Chekka	Eternit factory	Occupational and environmental	+	27	27	10
9	Chekka	Eternit factory	Occupational and environmental	+	30	38	120
10	Tripoli / Chekka/ Beirut	Stationery	Environmental	+	10	26	30
11	Chekka	Eternit factory	Occupational and environmental	+	42	42	50
12	Byblos	Air conditioning repair service	Occupational	+	1	47	15
13	Zahle	Agriculture	Occupational	+	15	37	75
14	Sin el Fil	Mechanical industry	Occupational	+	4	4	0
15	Chekka	Housewife	Environmental	+	49	49	50
16	Maghdouche	Builder	Occupational	+	50	50	5
17	Tripoli	Builder	Occupational	+	40	40	60
18	Chekka	Employee in a supermarket	Environmental	+	42	42	60
19	Chekka	Maritime transport	Occupational and environmental	+	N/A	N/A	60
20	Dhour El Choueir	Housewife	Environmental	+	40	61	0
21	Kuwait/ South of Beirut	Asbestos industry	Occupational	+	6	42	30

N/A: Not Available

Table 3. Treatment Modalities, Overall Survival and Histological Subtypes of Mesothelioma

Patient	Treatment modalities	Overall survival (years)	Histological subtypes
1	Surgery and chemotherapy	2	NOS
2	Chemotherapy	3	NOS
3	Chemotherapy	5	Biphasic
4	Chemotherapy	2	Epithelioid
5	Surgery and chemotherapy	1	Biphasic
6	Surgery and chemotherapy	4	NOS
7	Chemotherapy	2	Epithelioid
8	Surgery and chemotherapy	6	Epithelioid
9	Surgery	1	Biphasic
10	Best supportive care	8 months	Biphasic
11	Best supportive care	3*	Desmoplastic
12	Chemotherapy	1	Biphasic
13	Chemotherapy	1	NOS
14	Surgery and chemotherapy	8*	Epithelioid
15	Chemotherapy	8 months	Papillary
16	Best supportive care	3 months*	Desmoplastic
17	Chemotherapy	5 months	Biphasic
18	Surgery and chemotherapy	2*	Epithelioid
19	Surgery	N/A	Epithelioid
20	Surgery and chemotherapy	4	Sarcomatoid
21	Surgery and chemotherapy	1	Biphasic

*Still alive NOS (Not Otherwise Specified)

8 (53.3%) out of the 15 patients with pleural mesothelioma have lived in Chekka region and 4 (26.7%) out of these 15 have worked in the Eternit factory in Chekka. Of these 4 employees in the factory, 3 were also citizens of Chekka region. In total, 9 (60%) of the 15 patients with pleural mesothelioma and 9 (50%) among the 18 patients with obvious asbestos exposure had an occupational and/or environmental contact with the factory. The mean duration of exposure to asbestos in patients who develop mesothelioma is 24.53 [1-50] years, and the mean time of latency is 37.41 [4-61] years (cf. Table 2).

The most common histological subtypes are the biphasic mesothelioma (33.33% or 7 out of 21) and the epithelioid one (28.57% or 6 out of 21). Of the 21 patients, 10 (47.62%) underwent surgery during their treatment, 16 (76.19%) received chemotherapy and 3 (14.29%) received best supportive care. The median overall survival is 2 years, survival ranging from three months to more than 8 years in some (cf. Table 3).

Discussion

The different characteristics of mesotheliomas in our population are comparable to those reported in the literature going from the mesothelioma subtypes, histologic patterns, risk factors and patient's characteristics (Brida et al., 2007).

However, our study, evaluating 21 cases of mesothelioma in Lebanon between 2002 and 2014, has several updates over the last study published in Lebanon in 2001 (Kattan et al., 2001).

The first important finding is the increase in the number of peritoneal mesotheliomas, returning 5 peritoneal cases among 21 mesothelomias in the last decade, compared to only 1 out of 18 in the previous study of 2001. This new percentage (23.8%) reaches the threshold of 20% to 30% reported in the literature (Roptopoulos et al., 1985). Several hypotheses are suggested to explain this variation: first of all, the importation and use of asbestos-containing pipes to irrigate some areas of the Beqaa region, promoting the consumption of asbestos fibers by people who eat food from Beqaa. This is the case of our patient No. 6, who was a journalist and lived in the Beqaa without any obvious exposure to asbestos or other mesothelioma risk factors. Note that asbestos is criminalized only in 50% of peritoneal mesothelioma in the literature, while several other risk factors turned out to be associated with this type of mesothelioma, such as prior radiotherapy, erionite and Familial Mediterranean Fever (Chahinian et al., 1982; Metintas et al., 2002; Antman et al., 2005). Second, Familial Mediterranean Fever or FMF: in the literature, only two cases of pleural mesothelioma were reported associated to FMF, however, several cases of peritoneal mesothelioma were described in these patients, related to chronic inflammation of the serous, without asserting a direct connection between FMF and mesothelioma (Hershcovici et al., 2006; Challita et al., 2015). It is interesting to note that our patient No. 7, who worked in a shoe factory and lived in Beirut suburb, with no known exposure to asbestos, is effectively diagnosed with FMF and suffered from peritoneal mesothelioma. The third reason could be a misdiagnosis of peritoneal mesothelioma in the past, because of the lack of awareness among pathologists and physicians of this rare localization.

The second major finding is that the relationship between the Eternit factory in Chekka and the occurrence of mesothelioma became less intimate in our study. Indeed, only 50% (9 out of 18) of patients exposed to asbestos had an occupational and/or environmental contact with this factory, whereas in 2001, this figure reached 80% (12 out of 15). This means that the plant has lost ground in the process of development of mesothelioma in Lebanon, especially after the emergence of new sources of exposure to asbestos.

Major limitations of this study are the small number of patients, not exceeding 21, being treated in one tertiary teaching hospital, and the inability to present a reliable annual incidence of mesothelioma in Lebanon. This is linked to a lack of census in the country since 1932, for religious and political reasons. Therefore, all figures launched in different areas remain estimates. In addition, the large numbers of Lebanese residents abroad who receive care in their countries of immigration, as well as the considerable number of Palestinian and Syrian refugees in Lebanon, interfere with the true annual incidence of this disease.

The legal issue of asbestos in Lebanon is not yet resolved, despite ministerial decrees and laws passed, and though the Eternit plant in Chekka was closed in 2000. In fact, the ban on the import of asbestos includes the majority but not all fiber types. Contrary to amphiboles (crocidolite, amosite, anthophyllite, actinolite and tremolite), chrysotiles, known as white asbestos and considered to be carcinogenic, are still not prohibited. Also, the factory of Eternit in Chekka has not been closed according to international standards, since asbestos pipes and waste are always exposed to the open air. Moreover, products containing asbestos and imported before the ban are still present, since asbestos can be found in air conditioning ducts, construction sites, car brakes, ironing board covers, etc.

Recently, and during the war of 2006 between Lebanon and Israel, several international reports, published, among others, in "Jordan Times" and "Jerusalem Post", concluded that the war resulted in the destruction of more than 25000 m^2 of Lebanese dwellings (Jernelov et al., 2006). Therefore, tons of asbestos fibers were released and thousands of Lebanese were exposed, since asbestos cement was used as a heat insulator in the construction of these houses. The medical consequences of this disaster must be taken into consideration, especially regarding the development of cancer in general and mesothelioma in particular.

Finally, in addition to strengthening already existing laws, several plans of "asbestos removal" should be designed in collaboration with international professional companies in order to conduct a comprehensive clean-up operation in Chekka and elsewhere in Lebanon, and get rid of the fibers of asbestos previously used and still present, especially in the pipes and homes.

Knowing the long latency required for developing mesothelioma after exposure to asbestos, we estimate that the incidence of mesothelioma will continue to increase in the coming years despite the closure of the Eternit factory in Chekka in 2000. Would other factors, including the war of 2006, delay reaching the peak incidence of mesothelioma in Lebanon?

In conclusion, mesotheliomas in Lebanon remain closely associated with asbestos, but the monopolization by the Chekka region and especially the Eternit factory as risk factors has decreased relatively, as these can no longer be considered the unique sources of exposure to asbestos. In addition, it should be noted that the incidence

of peritoneal mesotheliomas has appreciably increased during the last decade compared to its incidence 20 years ago.

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