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Almost half of women with malignant mesothelioma were exposed to asbestos at home through their husbands or sons

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ABSTRACT

INTRODUCTION: Women often develop malignant mesothelioma (MM) without occupational asbestos exposure. Northern Jutland has a high prevalence of MM due to previously high occupational exposures to asbestos. The aim of this study was to elucidate a possible domestic exposure to asbestos through first-degree relatives in women who develop MM.

MATERIAL AND METHODS: This was a retrospective study in women with MM of the pleura. A total of 30 women were diagnosed with and treated for MM in Northern Jutland from 1996 to 2012. In all, 24 women were included. Demographic data, subtype of MM, time from first hospital contact to diagnosis, survival and information on occupational and domestic exposure to asbestos were obtained from hospital records.

RESULTS: A total of 12.5% of the study population were primarily exposed to asbestos. 46% had domestic exposure to asbestos through their husbands or sons. The median age of the study population was 66.5 years. In all, 75% suffered from the epitheloid subtype, 12.5% from the biphasic and 8.4% from the sarcomatoid subtype. Time from first hospital contact to diagnosis was one month and the median survival time was 12 months. The 1- and 5- year-survival were 58% and 0%, respectively. **CONCLUSION:** Nearly 50% of the women affected by MM have been domestically exposed to asbestos through firstdegree relatives.

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Mesothelioma is a malignant tumour that arises from mesothelial cells. It is an aggressive disease most commonly found in the pleura. Although extensive therapy has prolonged patients' median survival, the prognosis remains poor with a median survival of around nine months [1]. Malignant mesothelioma (MM) can be classified into various subtypes: epitheloid MM (60%) and the non-epitheloid MM including sarcomatoid (10-15%) and biphasic MM (25-30%) [2, 3]. Cases of epithelial tumours have a better survival than cases with other histological types [2]. The incidence rate of MM for men in Denmark is 3.4/100,000 person years and for women 0.53/100,000 person years. In Denmark, the mortality rate is 0.0057% [4]

The majority of cases in industrialised countries are caused by occupational asbestos exposure [5].

One of the main risk factors for people without occupational exposure is living with a high-risk worker [6, 7], referred to as domestic exposure in this study. Although occupational exposure has been shown to carry greater risk than domestic exposure [8], an increased risk for MM in females with domestic exposure to asbestos through first-degree relatives has been demonstrated [9, 10]. Rake et al found that 33.6% of female patients with MM have domestic exposure [11]. These findings are corroborated by other studies [7].

Previously, Northern Jutland had large industries with high levels of occupational exposure to asbestos, and this area is therefore now characterised by a higher prevalence of MM than the rest of Denmark [12].

In Denmark, patients with MM who have been exposed to asbestos through their profession are entitled to financial compensation. Financial compensation is only given to 22.9% of women with MM [13]. Currently, patients who are domestically exposed through their relative's profession receive no compensation. This is also the case in Italy, whereas France has created a special fund which provides financial compensation for the domestically exposed cases [14].

The specific aim of this study was to elucidate the frequency of domestic exposure to asbestos in women suffering from MM in Northern Jutland.

MATERIAL AND METHODS

A retrospective search was performed in the hospital registry for female patients diagnosed with code C45.0, malignant mesothelioma of the pleura, in the International Classification of Diseases (ICD) 10. A total of 30 women residing in Northern Jutland were diagnosed with MM in the period from 1 January 1996 to 31 December 2012 at Aalborg University Hospital. All of the patients were treated at Aalborg University Hospital. The inclusion criteria for MM patients were based on a positive biopsy and cytology test. Six women were ex-

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FIGURE 1

Time from first hospital contact to diagnosis. The median time to diagnosis was one month (1-1.625). In all, 14 of the 24 women were diagnosed after the implementation of national cancer guidelines in the autumn of 2007, 64.3% (9/14) were diagnosed within the stipulated time interval.



cluded. Three due to misclassification and three as the diagnosis had not been verified by biopsy, but only from cytology. The remaining 24 women were all Caucasian and born between 1917 and 1959.

Patients' case records were examined and data on age at the time of diagnosis, subtype of MM, time from first hospital contact to diagnosis, and survival were collected. A working history was sought and primary exposure to asbestos was recorded. We also recorded domestic exposure, which was defined as household contact with direct occupational exposure to asbestos. Most of the women lived with their husbands or sons, and had secondary exposure because they washed their asbestos-contaminated working clothes. In some records, there was only little information to determine whether the source of exposure was primary or secondary through a household contact. Especially patient records from the beginning of the study period were lacking information. Some of the women had died years before the present study was undertaken, and the authors tried to contact relatives to gain more information on the history of their exposure. In a few cases, it was not possible to find any living relatives; others did not want to become involved.

Demographic data are presented as medians and

quartiles. Time from first contact to diagnosis, time from diagnosis to death and 1- and 5-year survival are presented in Kaplan Meier plots. Incidence and prevalence for MM in Denmark and Northern Jutland are discussed.

The study was presented to the local ethical committee, which found no need for further ethical management of the case.

Data were registered and kept according to the provisions of the Danish Data Protection Agency.

Trial registration: none.

RESULTS

A total of 13% (3/24) of the study population had primary exposure to asbestos. In all, 46% (11/24) of the women had domestic exposure to asbestos through their husbands, fathers or sons who worked with asbestos. Previously, the city of Aalborg had large industries with occupational exposure to asbestos. Many men worked at concrete and cement factories, and at shipyards. Furthermore, some men worked in isolation and pluming businesses and as carpenters. In five cases, there were no known exposure to be found, and another five women had no information on asbestos exposure listed in their case records. Hospital records on occupational history showed three cases of employment in industries were asbestos was used, seven women had no information on their occupation and 14 women had occupations where asbestos exposure was very unlikely, e.g. cleaning, health personal, office assistants and childcare.

A total of 75% (18/24) of the women suffered from the epitheloid subtype of MM. The biphasic and sarcomatoid subtypes were found in 12.5% (3/24) and 8.4% (2/24), respectively, and for 4% (1/24) the subtype was uncertain.

The median time from first hospital contact to diagnosis was one month. 66.7% of the women were diagnosed within this time frame (**Figure 1**). The median period from diagnosis to death was 12 months (**Figure 2**).

At the time the data analysis was carried out, 21% (5/24) of the women were still alive. Women diagnosed with MM in Aalborg University Hospital had a one-year survival of 58% and a five-year survival of 0% (**Figure 3**).

In Denmark, a total of 75 new cases of MM were diagnosed in women during the 2007-2011 period [4]. Of those, 11 women were diagnosed in Northern Jutland. Given a total female population in Denmark of 2,823,776, the incidence rate of MM in women is 0.53/100,000 person years. In Northern Jutland, the female population is 288,369, which yields an incidence rate of 0.76/100,000 person years (p = 0.08). Five of the 11 women diagnosed with MM from 2007 to 2011 had a history of domestic exposure.

DISCUSSION

This study has shown a domestic exposure to asbestos in 46% of the 24 women included. A total of 75% suffered from the epitheloid subtype. The share of females with domestic exposure is even higher than the 20% expected by Goldberg et al [15] and the findings of Rake et al, who reported 33.6% of female patients with domestic exposure [11]. Furthermore, the number of domestically exposed women may even be higher in this study, as records of exposure to asbestos were absent in a number of the case records. The high number of patients with domestic exposure may, of course, be explained by the very high degree of occupational exposure that has previously characterised this region. Vianna et al have previously shown that females with first-degree relatives working with asbestos have a relative risk of ten for developing MM [11]. Another explanation could be that the treating physicians in daily clinical practice may underreport domestic exposure, as such registration has no consequence in most countries. France is one of the few countries that offer financial compensation to patients exposed through first-degree relatives.

The female MM incidence in Northern Jutland was higher than the female incidence observed in Denmark in general in recent years, 0.76/100,000 person years and 0.53/100,000 person years, respectively,

(p = 0.08). This was not surprising as the male MM incidence rate in Northern Jutland is significantly higher than anywhere else in Denmark [12]. MM in women is a rare disease and this study has only considered a relatively short time span; thus, the number of cases is limited. In a larger female MM study population from Northern Jutland, significant differences in the female MM incidence rate may have appeared.

It has previously been shown that extensive guestioning for occupational exposure to asbestos in women reveals that 20-30% have an occupational exposure [7]. In the present study, only 12.5% of the women had direct occupational exposure. Although the catchment area of the hospital contains several industries where occupational exposure is likely, these are typically male employed and primary occupational exposure in this female group is therefore as expected. We found that 15 women had a working history that did not include asbestos exposure, but one of them had been in contact with asbestos when renovating her beach house. Seven women lacked information on occupational history and two women worked at an industry site with known asbestos utilisation. There was no information on environmental exposure to asbestos.

The heavy occupational exposure is, however, reflected clearly in the domestic exposure of the women in this study population, given that 46% of the women in-

FIGURE 2

Time from diagnosis to death in the study population. The median survival period was 12 months (6-21.5)



FIGURE 3

Malignant mesothelioma survival at 1-5 years.



cluded had secondary exposure through their father, husband or son. Rake et al previously described that living with a high-risk worker is a potent risk factor for developing MM [11]. This is consistent with our findings.

The epitheloid subtype of MM was found in 75% of the study population. The epitheloid predominance in women is consistent with the previous findings of Wolf



Positron-emission tomography of a 55-year-old woman diagnosed with epitheloid mesothelioma. The patient's father as well as her spouse worked with asbestos.

and Rogli [2, 16] and also consistent with Danish [3] and international findings in general [17].

The median survival time in this study is 12 months, and the one- and five-year survivals were 58% and 0%, respectively. This exceeds the median survival time in Denmark, which is nine months, as well as the one- and five-year survival in Denmark, which are 53% and 4%, respectively [4]. This could be owed to the higher incidence of the epithelial subtype of MM, which is known to be associated with a better survival [2, 17]. The subtypes in women in Denmark in general are not known. Another explanation could be differences in the stages at the time of diagnosis within the country.

According to national Danish cancer guidelines introduced in the autumn of 2007, a patient should be diagnosed within 28 days [18]. 66.7% of the women were diagnosed within a month from their first contact with hospital. In all, 14 of the 24 women were diagnosed after the introduction of the national guidelines; and among these, nine (64.3%) were diagnosed within the stipulated time period. In Denmark, 80.7% of the lung cancers (81.4% in Northern Jutland) were diagnosed within 28 days. No specific national data exist on the time from first hospital contact to diagnosis for MM. Prolonged investigation time may be due to difficulties obtaining the diagnosis; hence, given that MM is a rare disease in women, a doctor's delay in suspecting the diagnosis is a possible explanation.

In this retrospective paper, only 24 women with MM were included, which is a limitation to the study. Using retrospective data, data-collection was challenged as some case records had sparse information on domestic exposure, as this has not been a focus area in previous years. Furthermore, there is no information about the interview strategy of how interviews were performed. More information could probably have been collected if the treating physicians used standardised questionnaires including information on the occupations of husbands and sons. Also, the information available for this study is limited by the fact that some doctors were not specialised pulmonologists and did not bear in mind the relevance of obtaining information on secondary exposure to asbestos. Thus, the hospital records of ten women showed no or uncertain exposure to asbestos. There is no information to be found about the number of women who may have moved to other regions and developed MM previously. If information on this could be obtained, the authors could seek information about the former addresses of the women and include them in the study population.

Both primary and domestic exposure may be underreported as asbestos exposure is not expected in women. Further investigations should therefore be performed in larger populations.

One purpose of this study was to bring attention to the domestic exposure to asbestos among women and to draw attention to the fact that no reimbursement is offered to these women despite the health hazard they have been exposed to – are their premises that different from those of their husbands?

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