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Asbestos Exposure in Cases of Pleural Mesothelioma in the Argentine Republic

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Abstract

Introduction: Pleural mesothelioma is a rare tumor with a high degree of malignancy. It is considered an occupational disease that has developed in parallel with the industrial use of asbestos. In Argentina, the asbestos was prohibited in 2003. The objective of this study is to know the clinical and diagnostic characteristics and treatment of pleural mesothelioma and to determine the characteristics of asbestos exposure in 40 cases of mesothelioma in different regions of the Argentine Republic.

Materials and Methods: It is a descriptive, multicenter study. Hospitals from Buenos Aires, Tucumán, Córdoba and Rosario participated in this study from January 2013 until January 2015. Clinical data were recorded in a Medical Form, and history of environmental, domestic and occupational exposure was recorded in an Exposure Form. Each participant was classified as: exposed, not exposed or unknown. The patient was considered as "exposed" if he/she identified at least one of the three types of exposure: occupational, environmental or domestic.

Results: 40 cases of pleural mesothelioma were analyzed, 55% of which were male. We found reference of at least one exposure to asbestos in 75% of the cases; 7.5% denied every possible type of exposure and in 17.5% exposure was unknown. The probability of exposure was: 57.5% environmental, 60% domestic and 37% occupational. There was a greater statistically significant proportion of men with occupational exposure.

Conclusion: The contribution of this work relies on the information about the different types of asbestos exposure in cases of pleural mesothelioma in the Argentine Republic.

Key words: Asbestos; Mesothelioma; Occupational disease; Argentine Republic

Introduction

Mesothelioma, a rare neoplasia difficult to diagnose and highly aggressive, is mainly originated in the mesothelial cells of the pleura, peritoneum and, less frequently, the pericardium or tunica vaginalis of testicles.[1] It is considered an occupational disease that developed in parallel with the industrial use of asbestos, a genotoxic agent that may induce damage to DNA mediated at least in part by liberation of free radicals.[2] The asbestos fibers are iron, sodium and magnesium hydrated silicates disposed in

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fine fibers. The industries have used it a lot for its physical characteristics: fire-resistant, insoluble and indestructible. Occupational exposure is recognized as the main risk factor for mesothelioma. The incidence rate of mesothelioma in men with work-related occupational respiratory disease in Great Britain is 5.4 (4.8-6.0) (95% CI [Confidence Interval] by 100,000 per year.[3] However, currently worries focus on exposure to low doses of asbestos and the effect of environmental or domestic pollution.[4]

In Argentina, all forms of asbestos were prohibited in 2003.[5] Despite that prohibition, the frequency of mesothelioma is expected to remain high until mid XXI century, due to a prolonged latency period of up to 40 years between exposure and disease but also due to the possibility that the asbestos has remained in a poor state of conservation in different working environments or that it has been removed without the appropriate preventive measures.[6] The objective of this study is to describe the characteristics of asbestos exposure in patients diagnosed with pleural mesothelioma in hospitals of different regions of the Argentine Republic.

Materials and Methods

We conducted a descriptive, multicenter study. Participant centers were: Hospital General de Agudos Dr. Enrique Tornú and Hospital del Tórax Dr. Antonio Centrángolo of the city of Buenos Aires; Hospital Ángel C. Padilla of the city of Tucumán and different public and private healthcare providers of the city of Rosario and Córdoba. Patients with pleural mesothelioma diagnosed between January 1 2013 and January 1 2015 were included in the study in a prospective way. All the individuals gave informed consent to participate in the study before filling out the medical form with clinical data and the questionnaires with their history of asbestos exposure. The interview was held at the patient's home or at the reference hospital. The medical form included information on smoking history, and the disease's clinical characteristics, diagnosis, pathologic anatomy with immunohistochemistry and treatment. No there was no case follow-up, only detection and notification at the moment of the diagnosis by the centers. The exposure form included demographic data, chronological information of the patient's occupational background and current and previous place of residence. Regarding the place of residence, data was collected in relation to the characteristics of the home, the environment and the neighborhood. Regarding the occupational background, information was gathered on a specific list of activities or industries considered as probable exposure to asbestos according to products containing asbestos fibers of the chrysotile variety **(Table 1)**.

TABLE 1. List of explored types of occupational exposure

Chemical industry Plastic Petroleum Iron and steel Asbestos removal Construction/demolition Construction with fiber cement (tiles, water tanks, fluted metal sheets)	extile manufacturing with asbestos (rope, fabric, cardboard) Sound isolation (cinemas, theatres, recording studios) Concrete slab Ceiling tiles Walls	Thermal insulation (boiler, chimneys, heating, radiators) Fire suppression system Friction elements (brake system, clutch plate) Shipyards Railroad Mining with asbestos extraction

Participants were classified into three categories of asbestos exposure (exposed, not exposed, unknown). We considered there was environmental exposure to asbestos if the patient answered affirmatively to at least one of the following: presence of industries that have used asbestos at a distance of up to 2000 meters from the patient's home (Table 1), neighborhoods with deteriorated fiber cement ceilings or demolition areas. We considered there was positive domestic exposure if there was suspicion of the presence of asbestos-containing material at the patient's home after the patient answered affirmatively to at least one of the following: the habit to take home work clothes that could possibly be contaminated with asbestos dust and presence of asbestos-containing material at his/her home (ceilings, water tanks or fiber cement piping, thermal insulation for heaters or boilers of domestic use). We considered

there was occupational exposure when the patient answered in his/her occupational background that at least one of his/her jobs had been developed in industries using asbestos or that he/she had been in the presence of materials containing some of the asbestos fibers.

In general, the patient was considered as exposed to asbestos if at least one of the three types of exposure (occupational, environmental or domestic) could be identified. We considered a case as "unknown exposure" whenever there wasn't enough information to know whether there had been exposure or not.

Patients with detected occupational exposure to asbestos were interrogated about the period of exposure and the period of latency. The period of exposure was defined as the time (in years) since the person began his/her tasks in areas exposed to asbestos until the moment he/she abandoned such workplace. The latency period was calculated as the time passed since the first exposure until the diagnosis of mesothelioma.

The results are shown as mean and standard deviation for numerical variables and as percentages in categorical variables. In order to compare proportions we used the Fisher Exact Test, and to compare numerical variables, we used the Mann-Whitney Test. A value of $p < 0.05$ was considered as significant.

Results

We analyzed the data of 40 cases of pleural mesothelioma. The description of the sample is shown in **Table 2**. Confirmation by immunohistochemistry was made at 95% (n = 38); classified as epithelioid variety at 86.8% (n = 33). Two patients showed peritoneal extension.

TABLE 2. Description of demographic and clinical characteristics of samples

Characteristics	Cases of pleural mesothelioma (n = 40)
Demographic	
Age (years)	66,1 ± 11
Mean ± standard deviation	
Masculine gende *n (%)*	22 (55)
History	
Smoking *n (%)*	21(52,5)
Form of presentation	
Pleural effusion *n (%)*	34 (80)
Thoracic pain *n (%)*	21(52,5)
Diagnosis*	
Pleural biopsy *n (%)*	18 (45)
Video-assisted thoracic surgery (VATS) *n (%)*	20 (51,2)
Minimal thoracotomy *n (%)*	5 (12,5)
Histologic findings	
Epithelioid variety *n (%)*	33 (86,8%)
Treatment*	
Chemotherapy *n (%)*	33 (86,8)
Surgery *n (%)*	3 (7,5)
Radiotherapy *n (%)*	3 (7,5)
Treatment combination including palliative therapy *n (%)*	7 (38,9)

* There may have been more than one method of diagnosis and type of treatment per individual, thus percentage addition is not 100%.
Values expressed as number of diagnosed cases in percentage between January 2013 and 2015.

Table 3 shows the situation of the 40 interviewed individuals regarding asbestos exposure, according to the type of exposure. We found reference of at least one type of asbestos exposure in 75% (n = 30) of the cases; 7.5% (n = 3) denied every possible exposure, and 17.5% (n = 7) were cases of unknown exposure.

TABLE 3. Situation of asbestos exposure according to the type of exposure (environmental, domestic or occupational) in 40 patients with pleural mesothelioma

Type of asbestos exposure *n (%)*	Exposed	Not Exposed	Unknown exposure	Total
Occupational*	15 (37)	21 (52,5)	4 (10)	40 (100)
Environmental*	23 (57,5)	9 (22,5)	8 (20)	40 (100)
Domestic*	24 (60)	1 (37,5)	1 (2,5)	40 (100)
At least one type of exposure*	30 (75)	3 (7,5)	7 (17,5)	40 (100)

*Values expressed as number of exposed cases (percentage of every type) between January 2013 and 2015.

22.5% (n = 9) of patients made reference to the three types of exposure (environmental, domestic and occupational). 10 of 21 cases without occupational exposure showed domestic and environmental exposure, 2 showed environmental exposure only and 1 showed only domestic exposure. There were 4 cases without domestic and occupational exposure but with unknown environmental exposure.

Of the 30 exposed patients, only 6 said they were aware of their situation regarding asbestos exposure.

Of the 10 patients with occupational exposure who remembered the moment the exposure began, 5 had an exposure period of more than 10 years, and 5 had a period between 1 and 10 years. The period of latency of the disease was longer than 30 years in 7 cases, between twenty and thirty years in 7 cases, between 10 and 20 years in 3 cases and less than 10 years in 3 cases. Twelve patients don't remember the latency period. This data were collected in 32 of 40 cases of pleural mesothelioma. **Table 4** shows case comparison between women and men.

TABLE 4. Comparison of exposure types between men and women

	Women (n = 18)	Men (n = 22)	p value
Age (years) *Mean ± standard deviation*	69,8±9	63±11	0,055
Occupational exposure*			
Yes	3	12	
No	14	7	0,012
Unknown	1	1	
Environmental exposure*			
Yes	12	11	
No	3	6	0,622
Unknown	3	5	
Domestic exposure*			
Yes	12	12	
No	6	9	0,858
Unknown	0	1	

*Values expressed as number of cases

There was a greater statistically significant proportion of men with occupational exposure. 2 of 7 male subjects with no occupational exposure had environmental and domestic exposure, 1 had environmental exposure only, 1 only domestic and 3 unknown exposure. 8 of 14 female subjects with no occupational exposure had environmental and domestic exposure, 1 had environmental exposure only, 1 only domestic exposure, 3 had no asbestos exposure at all and 1 unknown exposure. Of the 21 cases with no history of occupational exposure, we registered environmental or domestic exposure in 10 women (of 14) and in 4 men (of 7) (p = 0.428).

Discussion

According to the International Agency for Research on Cancer, there are 70,000 chemical agents present in the industry, and most of them haven't been studied,[7] but the asbestos is recognized as one of Group I carcinogenic agents and is related to mesothelioma in humans. After Wagner et al[8] showed the relationship between mesothelioma and crocidolite asbestos within South African miners in 1960, the erionite and tremolite mineral fibers or asbestos fibers were described as related to the disease.[9] Despite the fact that criteria attributable to asbestos, apart from clinical results and compatible images, are necessary for the diagnosis of lung diseases by inhalation, in the case of mesothelioma, the SEPAR (Spanish Society of Pulmonology and Thoracic Surgery) rules suggest not to look into any other true causal factor of the disease other than asbestos exposure, even if its minimal.[10]

The incidence of mesothelioma varies in the different countries around the world when there are no specific records of the disease, and exposure to the mineral is usually unknown. In countries of the European Union, there is approximately 1.5 case per 100,000 inhabitants every 5 years, where the disease manifestation peak is found in individuals between 50 and 70 years.[11]

Argentina and other countries don't have mesothelioma records. There is only national mortality data where the disease is coded since 1997 as pleural disease with the CIE-10 international classification.[12] Just like the rest of the world, when coding and advising about a disease, the mortality rate increases. Trotta[13] reported an increase in the raw mesothelioma mortality rate (MMR), which was 2.27 million in 1997 and 5.63 in 2013.

The National Cancer Institute[14] of our country provides data collected in each province about this disease. It is worth mentioning that there is an important difference among the provinces that used asbestos until 2003. In Jujuy or Santa Cruz no cases have been detected, whereas most cases of mesothelioma are found in Córdoba, Santa Fe and Buenos Aires. Differences are also observed between industrialized and rural areas.

This series of 40 cases of pleural mesothelioma diagnosed in a period of two years (2013 and 2014) showed clinical characteristics similar to those already reported by other authors. The mean age of 66 years was consistent with the description of frequent manifestation between 6th and 7th decade of life[1]. 55% of the cases were male, and the literature describes the masculine gender as more frequent, even sometimes with a 4:1 ratio (male/female).[15] The form of clinical presentation described as the most common one is pleural effusion, and was shown in 80% of the series. One of the most common symptoms is pleuritic chest pain, present in 52.5% of patients, concurrent with the findings of the literature.[16] The invasive diagnosis method by means of a pleural biopsy was high (45%). VATS was used without previous pleural biopsy in 51.2% of cases. It is well-known that thoracoscopy is the gold standard of diagnosis.[17] Confirmation was required through immunohistochemistry techniques for the histologic diagnosis. The epithelioid variety was found in 86.5%. This variety has a better prognosis than sarcomatoid and biphasic.[18]

The population of workers who perform asbestos production, exploitation or manufacture tasks is the one with occupational exposure to asbestos, and the most recognized type of exposure. Currently, the importance of environmental exposure, related to mesothelioma[19, 20, 21] is widely accepted at a global level. There are some geographical areas in countries such as Turkey, Cyprus, Corsica and Greece with high levels of erionite and tremolite air fibers that report cases of mesothelioma associated with environmental exposure. Urban population residing between 500 and 2000 meters from an industrial area that uses the fiber or nearby an asbestos mine would be at a higher risk due to environmental exposure.[22] However, we can't discard domestic exposure to asbestos in people who normally share their home with a worker who is exposed at his workplace, for example, when the worker brings home his work clothes for his wife to clean or mend. Individuals sharing home with those workers may be exposed to contamination even inside the house.

The main limitation of this study is the number of cases that can't be considered as representative of the situation throughout the country. However, the main contribution of this work relies on the information about the different types of exposure to asbestos in cases of mesothelioma in Argentina. A

thorough questionnaire about environmental, domestic and occupational exposure completed by the individuals the moment the disease was diagnosed, and rigurous medical records of asbestos exposure resulted in an exposure probability of 57.5% for environmental exposure; 60% for domestic and 37% for occupational. Occupational exposure was found in more than half of male cases.

Taking gender into consideration, occupational exposure is significantly higher in men. This fact was expected, since mostly men are part of industrial activities. Greater occupational exposure was found in the iron and steel, chemical, construction and plastic industries, respectively. Environmental and domestic exposure are not statistically significant, yet more common in women. Especially when there is a negative history of occupational exposure.

7.5% of the series denied all three types of asbestos exposure explored. In these cases, we can't discard the presence of some of the factors related to pleural mesothelioma other than asbestos, such as ionising radiation in patients with lymphoma, chest or breast cancer[23] or, controversially and without enough evidence, the SV40 virus.[1 2] Harvey Pass said that asbestos is placed in the first nine out of ten main causes of mesothelioma, and the SV 40 virus could be number ten.

Harding et al[25] analyze mortality among British workers exposed to asbestos who underwent regular medical tests between 1971 and 2005, and emphasize the high mortality rate of workers who perform asbestos removal tasks. They also emphasize the importance of workers surveillance as a strategy to help regulate the control of sources of occupational exposure. In our country there are health monitoring programs for populations exposed to asbestos. However, it would be advisable to have more strict Public Health Policies to regulate the control of occupational, domestic and environmental exposure to asbestos, to have specific records and evaluate the tendency of mortality by pleural mesothelioma.

We presented a series of 40 patients diagnosed with pleural mesothelioma in different Argentinian centers. Even though only 35% had history of occupational exposure to asbestos, 75% claimed they had been exposed to at least one type of exposure (occupational, domestic and environmental). In cases without any records of mesothelioma or without any other way of getting to know each situation, it wouldn't be right to present the disease as lacking history of asbestos exposure, it should be expressed as "mesothelioma with unknown exposure".

Declaration of Conflicts of Interest: The authors declare they have no conflict of interest directly or indirectly related to the contents of the original text.

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References

1. Rudd RM. Malignant mesothelioma. British Medical Bulletin. 2010; 93: 105-23.
2. Carbone M, Ly BH, Dodson RF, et al. Malignant Mesothelioma: Facts, myths and hypotheses. J Cell Physiol. 2012; 227: 44-58.
3. Carder M, Darnton A, Gittins M, et al**.** Chest physician-reported, work-related, long-latency respiratory disease in Great Britain. Eur Respir J. 2017; 50: 170096 [consulted 01- 10-2018]: Available at: https://doi.org/10.1183/13993003.00961-2017
4. Agudo Trigueros A., Mesotelioma pleural y exposición ambiental al amianto. (Tesis Doctoral). 2003. [consulted on 10- 07-2017]: Available at: https://www.researchgate.net/publication/242623948_Mesotelioma_Pleural_y_Exposicion_Ambiental_al_Amianto
5. Rodríguez, Eduardo J. Prohibición del Asbesto en Argentina. Int J Occup Environ Health. 2004; 10: 202-8.
6. Zurbriggen R, Capone L. Enfermedad pulmonar por amianto en trabajadores de acería. MEDICINA (Buenos Aires). 2013; 73: 224-30.
7. International Agency for Research on Cancer (IARC); World Health Organization; [consulted on 10- 21-2017]: Available at: http://www.iarc.fr

8. Wagner JC, Sleggs CA, Marchand P. Diffuse pleural mesothelioma and asbestos exposure in the north western cape province . Brit. J Industr. Med. 1960; 17: 260-71.
9. Roushdy-Hanmady I, Siegel J, Emri S, Testa JR, Carbone M. Genetic-susceptibility factor and malignant mesothelioma in the Cappadocian region of Turkey. Lancet. 2001; 357: 444-5.
10. Normativa SEPAR. Recomendaciones sobre el diagnóstico y el manejo de la patología pleural y pulmonar por asbestos. 2017. [consulted on 12- 07-2017]: Available at: https://www.separ.es
11. Isidro Montes I, Abu Shamsb K, Alday E, et al. Normativa sobre el asbesto y sus enfermedades pleuro-pulmonares. Arch Bronconeumol .2005; 41: 153-68.
12. Organización Panamericana de la Salud. OMS. Clasificación Internacional de Enfermedades para Oncología.CIE-0. 3ª ed. Washington DC: OPS. 2003;586:1-246.
13. Trotta A, Santana VS, Alazraqui M. Mortalidad por mesotelioma en la Argentina, 1980-2013. Salud Colectiva. 2017; 13: 35-44.
14. Instituto Nacional del Cáncer, Ministerio de Salud de la Nación. Atlas de mortalidad por cáncer en Argentina, 2007-2011. Buenos Aires: Nation's Ministry of Health; 2013.
15. Ferrer J, Martínez C. El diagnóstico de las enfermedades respiratorias causadas por el asbesto. Arch Bronconeumol. 2008; 44: 177-9.
16. Moore A, Parker R, Wiggins J. Review. Malignant mesothelioma. Orphanet Journal of Rare Diseases. 2008; 3:4.
17. Scherpereel A, Astoul P, Baas P, et al. Guidelines of the European Respiratory Society and the European Society of Thoracic Surgeons for the management of malignant pleural mesothelioma. Eur Respir J. 2010; 35: 479-95.
18. Husain A, Colby T, Ordonez N, et al. Guidelines for Pathologic Diagnosis of Malignant Mesothelioma. 2012 Update of the Consensus Statement from the International Mesothelioma Interest Group. Arch Pathol Lab Med. 2013; 137: 647-67.
19. Norio Kurumatani, Shinji Kumagai. Mapping the Risk of Mesothelioma Due to Neighborhood Asbestos Exposure. Am J Respir Crit Care Med .2008; 178: 624-29.
20. Tarrés J, Albertí C, Orriols R, et al. Patología ambiental por amianto en una población cercana a una fábrica de fibrocemento. Influencia de la proximidad y su situación respecto al foco emisor. SEPAR 2010 Congress.
21. Maule M, Magnani C, Dalmasso P, et al. Modeling Mesothelioma Risk Associated with Environmental Asbestos Exposure. Environ Health Perspect. 2007; 115: 1066–71.
22. Tarres J, Abós-Herràndizb R, Albertíc C, et al. Enfermedad por amianto en una población próxima a una fábrica de fibrocemento. Arch Bronconeumol. 2009; 45: 429-34.
23. Cugell D, Kamp D. Asbestos and the Pleura. Chest. 2004; 125: 1103–17.
24. Pass Harvey I, Vogelzang N, Carbone M, editors. Malignant Mesothelioma. Pathogenesis, Diagnosis, and Translational Therapies. New York: Springer; 2005.
25. Harding AH, Darnton A, Wegerdt J, et al. Mortality among British asbestos workers undergoing regular medical examinations (1971-2005). Occup Environ Med. 2009; 66: 487-95.