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CASE REPORT

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Pleural malignant mesothelioma in dental laboratory technicians: A case series

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Asbestos was used in dentistry as a binder in periodontal dressings and as lining material for casting rings and crucible. However, until now, only one case of malignant mesothelioma with occupational exposure to asbestos in dental practice has been reported. We present 4 pleural mesotheliomas out of 5344 cases identified in Lombardy, Italy, in 2000-2014. Three men had been working as dental laboratory technicians, with asbestos exposure for 10, 34, and 4 years, and one woman had been helping her husband for 30 years in manufacturing dental prostheses. The men described the use of asbestos as a lining material for casting rings, while the woman was not able to confirm this use. We confirm the association of malignant mesothelioma with dental technician work. Dental technicians suffering from mesothelioma should be questioned about past occupational asbestos exposure.

KEYWORDS
asbestos, dental technician, dentistry, mesothelioma, occupational exposure

1 | INTRODUCTION

Exposure to asbestos fibers is a risk factor in the development of malignant mesothelioma (MM), a cancer arising from the serous membranes of the pleura and, less frequently, of the peritoneal and pericardial cavities and from the tunica vaginalis testis. Prognosis is severe, and median survival for the pleural form is around 9 months since diagnosis in population-based studies.[1] Many western countries are currently suffering a MM epidemic, considering the extensive use of asbestos between the 1950s and the 1980s in several applications and the long latency period (around 40 years on average) since the beginning of exposure.

Due to the past use of asbestos-made lining material for casting rings since approximately 1930 or as a binder in periodontal dressing since 1967, dental technicians and dentists were potentially exposed to asbestos.[2-9] To our knowledge, only a few cases of pneumoconiosis, small opacities, or pleural plaques have been reported[10-13] and only one case of pleural MM with documented occupational exposure to asbestos[14] has been reported in the literature.

The aim of the manuscript is to describe cases of pleural MM in dental laboratory technicians identified by the Lombardy Mesothelioma Registry (RML), North-West Italy, in 2000-2014.

2 | METHODS

2.1 | The lombardy mesothelioma registry

Since the asbestos ban in 1992 Italy has been one of the most active countries in prevention and control of asbestos-related diseases. A dedicated system of epidemiological surveillance was implemented through the National Mesothelioma Register (ReNaM), active since 1993 (by force of law since 2002) with the remit of estimating MM incidence, investigating occurrences of asbestos exposure, identifying

any possible underrated or unknown source of asbestos contamination and promoting research.[15] Being part of the ReNaM structure of Regional Operating Centers (CORs), the RML, established in 2000, collects all MM cases diagnosed in people living in Lombardy (one of the most populated and industrialized regions in Italy, currently almost 10 million inhabitants), even if admitted to hospitals outside Lombardy [16,17]

The information concerning occupational and extra-occupational history is collected through administration of a standardized questionnaire by trained interviewers to the patient or to his/her next-of-kin. Detailed information on lifetime occupational history (industry, occupation, work environment characteristics) and lifestyle habits are collected, including information on cohabitants (father, mother, spouse, other) with whom the patients have been living, especially whether the cohabitant used to bring dirty working clothes at home to be brushed or washed. Moreover, information about domestic and leisure-time activities involving exposure through asbestos-containing objects and environmental exposures during lifetime residential history, presence of asbestos cement tiles or water-tanks, of industrial plants nearby (ie, asbestos cement, petro-chemical, railroad, or shipbuilding industries) is elicited. A panel of experts classifies lifetime asbestos exposure as occupational, familial (ie, related to the cohabitant), leisure-time (ie, related to activities regarding the house), or environmental.[18]

For the purpose of this paper, we extracted from MM cases diagnosed in the period 2000-2014 records of patients who had been working in a dental laboratory and described their clinical and occupational history

3 | RESULTS

Four patients were found out of 5344 incident MM cases. All pleural MM were histologically diagnosed (Table 1).

3.1 | Patient 1

The first patient was a 72-year-old man, evaluated for dyspnea in May 2004. Chest X-ray revealed a right pleural effusion with pulmonary atelectasis due to a mass obstructing the lower lobe bronchus. After thoracentesis he underwent videothoracoscopy: multiple lung, pleural, and diaphragmatic nodules of neoplastic appearance were present. Histological and immunohistochemical analysis provided the diagnosis of epithelial MM. Extensive surgical treatment was performed by pleuropneumonectomy, excision of the pericardium and of the right hemidiaphragm infiltration, removing the peritoneal apex too. Pericardial and right hemidiaphragm reconstruction was performed. The patient underwent chemoradiotherapy. He died 8.0 months after diagnosis.

3.1.1 | Occupational exposure

From 1953 to 1963 (from 21 to 31 years old) he worked as a dental technician. His activity consisted in preheating one or two cylinders in a dedicated oven for the subsequent metal wax model casting: placing a positive tooth reproduction of wax in the cylinder and then in another small oven heated by means of a platinum electric resistance. Until 1957 the worker used cylinders with inner lining in refractory material and insulated with asbestos; he made five or six castings every week. For 6-8 years he had also been using asbestos gloves (never replaced) when putting the cylinders inside the preheating oven and then into the casting oven. The subject never used to do maintenance and cleaning of the furnace. He used compressed air to clean products. From 1964 to 1988 he worked as freelance dental technician using closed-cycle casting machines.

3.1.2 | Non-occupational exposure

No other sources of asbestos exposure were identified.

3.1.3 | Analysis of asbestos bodies and fibers

Lung samples (from one lobe) were available to be analyzed. Asbestos body and asbestos fiber burden were measured (number per grams of dry weight of lung tissue [gdw]). Lung tissue was digested with hypochlorite and analyzed with optical microscopy at 500 magnification, asbestos fibers (length >1 μm) were counted by means of a Scanning Electron Microscope equipped with X-ray fluorescence microanalyses at 12 000 amplification. The asbestos body burden was 22 000/gdw (95% confidence interval (CI). 16,000-30,000, detection limit 400/gdw). The asbestos fiber burden was below the detection limit of 380,000/gdw

3.2 | Patient 2

The second patient was a 61-year-old woman. The onset of the symptoms was in June 2004, with left chest pain and pneumothorax. After chest drainage, a CT-scan showed effusion and thickening of the middle-lower right pleura. The patient underwent partial left pleural excision aimed at histological sampling. Histological examination of the left parietal and visceral pleura and of lower lobe lung parenchyma showed a biphasic malignant mesothelioma. The patient underwent a second operation with histological re-samples showing infiltrative epithelial MM and then chemotherapy. She survived 4.3 years

3.2.1 | Occupational exposure

From 1959 to 1961 (from 16 to 18 years old) she worked as a clerk in a lawyer's office. From 1961 to 1991 she worked as a housewife, but she used to help her husband in the production of prostheses in his dental laboratory. From 2001 to 2004 she worked as a clerk.

3.2.2 | Non-occupational exposure

The patient reported that at the end of the 1980s she helped her husband in building a sound barrier at the boiler room, in order to insulate a power unit: she held an asbestos-cement slab while her husband drilled holes in it. She had been living from 1946 to 1964 with her father—a dental technician working in his own laboratory

3.3 | Patient 3

A 79-year-old man in 2013 was re-evaluated for transitional papillary carcinoma of the bladder, first diagnosed in 2008. After being

TABLE 1 Characteristics of the four patients

Patient	Age (yrs)	Gender	Year of diagnosis	Morphology	Diagnosis	Immunohistochemical analyses	Occupational history	Asbestos exposure	Survival	Notes
1	72	M	2004	Epithelioid	Certain	Pan-CK++, calretinin +, B72 3 focal+, CEA−	1953-63: dental technician	Definite	8 0 months	Asbestos bodies in lung 22,000/g dry weight of lung tissue
							1964-88: freelance dental technician using closed-cycle casting machines	No		
2	61	F	2004	Epithelioid	Certain	Pan-CK+, calretinin+, HBME-1+, CEA−, Ber-EP4−	1959-61: clerk in a lawyer's office	No	4 3 years	She had been living from 1946 to 1964 with her father − a dental technician working in his own laboratory
							1961-91: housewife, helping her husband in the production of prostheses in his dental laboratory	Possible		
							2001-04· clerk	No		
3	79	M	2013	Epithelioid	Certain	Pan-CK+, calretinin+, WT-1+, TTF-1−, Ber-EP4−	1952-56· dental technician	Possible	11.3 months	2008: transitional papillary carcinoma of the bladder, relapsed in 2013
							1957-59 inspector of radio-set valves	No		
							1959-99: clerk in public administration	No		
4	70	M	2014	Epithelioid	Certain	Calretinin+	1960-64: attended a dental technician laboratory school in Milan	Possible	1.5 years	
							1965-99: freelance technician	Definite		

Pan-CK, pan cytokeratin; CEA, carcino-embryonic antigen, Ber-Ep4, epithelial antigen; WT-1, Wilms tumor protein; TTF-1, thyroid transcription factor-1

evaluated by positron emission tomography for recurrent right pleural effusion, the patient underwent videothoracoscopy Diffuse whitish pleural thickening was observed and the lower right lung lobe visceral pleura, the diaphragmatic pleura, and the anterior and posterior mediastinal pleura were reported as flaking layers of fibrinous and cerebriform tissue. Histological and immunohistochemical analysis provided the diagnosis of epithelioid MM. Nine months later a CT-scan reported vast pleural thickening and peritoneal carcinosis. He survived 11 3 months

3.3.1 | Occupational exposure

From 1952 to 1956 (from 18 to 22 years old) he worked as a dental technician. His activity consisted in the production of crowns, dental bridges and prostheses in a dental laboratory. An electric oven for the metal wax model casting was present From 1957 to 1959 he was inspector of radio-set valves, and from 1959 to 1999 employee in the public administration.

3.3.2 | Non-occupational exposure

No definite asbestos exposures (he did some domestic electrical work) were reported

3.4 | Patient 4

A 70-year-old man was diagnosed in 2013 with hilar fibrosis in a hospital admission for traumatic subarachnoid hemorrhage and underwent resection of prostatic carcinoma, follow-up being regular In the following year he was evaluated for acute respiratory distress: a CT-scan showed effusion of the right hemithorax without contrast enhancement of the pleura As the pleural liquid cytology revealed hyperplastic atypical mesothelial cells suspect of mesothelioma, in 2014 he underwent videothoracoscopy. Ubiquitous pleural thickening with multiple subtle nodules were sampled for histological and immunohistochemical analysis, which revealed an epithelioid MM. He died after 1.5 years.

3.4.1 | Occupational exposure

From 1960 to 1964 (from 16 to 20 years old) he attended a dental technician laboratory school in Milan. He was a freelance dental technician from 1965 to 1999, and stated that asbestos was cut from large rolls kept in the laboratories and used for lining rings in wax model casting prosthesis formation He had been repeating the process twice a week for 10 years

3.4.2 | Non-occupational exposure

No other asbestos exposures were reported.

4 | DISCUSSION

We described four cases of pleural malignant mesothelioma associated with dental technician work who came to the attention of the RML. They had all been exposed or possibly exposed to asbestos while working as (or helping) dental laboratory technicians. For each subject the diagnosis was confirmed by histology and immunohistochemistry.

The first case described asbestos exposure during production of prostheses based on wax model casting. Until 1957 he used casting rings lined with asbestos and also stated that asbestos gloves were used for 6-8 years to insert the cylinders into the oven, and that compressed air was used air to clean products. The fourth case reported cutting asbestos from rolls kept in the laboratories for lining rings in wax model casting

Choudat[19] and Radi et al[12] described the process of prosthesis formation, based on wax model casting: a positive reproduction of the tooth is made in wax; this pattern is placed in a cylinder, which is filled with refractory material. The wax is eliminated by heating, leaving an empty mould chamber. Molten alloy is injected into the mould which is then broken and the prosthesis is polished with a sandblaster and hand finishing tools It is known from ReNaM Guidelines that asbestos had been used, albeit in small quantities, by Italian dental technicians in the lost wax model casting.[18] In the second case we could only document indirect exposure to asbestos while helping her husband for 30 years in dental prosthesis manufacturing.

It is well documented that asbestos has been used in dentistry since approximately 1930 when it was introduced as a lining material for casting rings [2] Paper and powder containing asbestos fibers were used, respectively, in the production of metal prostheses and as a binder in periodontal dressing until the middle of 70's [14] The above mentioned procedures for prosthesis formation were the main production method and therefore they could apply also to the third patient, even if he reported a less detailed history. Since 1976 the Council on Dental Therapeutics[14] reported a hazard of exposure to airborne fibers from asbestos used as binder and to line casting rings or crucibles for casting machines, the fibers being readily released into the air from periodontal dressing powders and from large rolls of asbestos kept in the laboratories.

A simulation of fibers dispersion in the USA showed low concentrations (0.005-0.092 fibers/mL; 0.001-0.006 fibers/mL-time weighted average [TWA]) of chrysotile fibers [20] Another simulation study in Greece found a concentration of 0.008 fibers/cm^3 (chrysotile only) during a 4-h sampling period in a dental laboratory where pleural plaques had been found in three dentists who used to manipulate wet asbestos tape during casting operations.[13] A recent study found asbestos (unspecified type) concentrations of 0.0104-0.0159 fibers/mL in dental laboratories in South Korea [21] To our knowledge, there are no data on asbestos concentrations in dental laboratories in Italy

The hazard from airborne asbestos during various periodontal surgical procedures has been highlighted since 1976. zinc-oxide periodontal dressings consisted of a mixture of a liquid and a powder containing asbestos fibers as a binding agent.[5] Asbestos fibers were indeed used in gingivectomy packs.[3] Use of a resin containing asbestos between 1967 and 1968 at the Royal Dental Hospital, London was reported [8]

Despite the documented use of asbestos in dentistry, only one case of MM arising in workers exposed to asbestos fibers during dental practice had been documented.[14] Another case of MM in a dentist was reported in an obituary but asbestos exposure was not investigated.[22] The British dentist's exposure reported by Reid et al.[14] may have been non-occupational, as only blue asbestos fibers (amphibole)—an

expensive asbestos type not commonly used in dental application—were found in lung tissue. In the United States only white asbestos (chrysotile) has been used in dentistry.[20] Raw materials were similar in the US and UK. Although biopersistence of amphibole fibers is greater than that of chrysotile fibers,[23] clearance of long chrysotile fibers is slow or insignificant; therefore a "clearance effect"[14] does not seem to be an adequate explanation. Also the source of exposure in the case described by Reid et al.[14] remains unclear because that subject may have inhaled blue asbestos used in British gas masks during World War II.[20]

Pleural plaques and pneumoconiosis secondary to manipulating asbestos tapes during casting operations have been reported [10,13,24]

Dental laboratory technicians often start to work early (at the age of about 18 years), are often self-employed, and work alone or in small laboratories Moreover, these workplaces have usually inadequate methods of dust control and self-employed subjects often work more than 8 h per day, with no information about occupational risks.[19 24] Since asbestos was banned in 1992, the possibility that asbestos containing materials are today present in dental laboratories in Italy is remote. Asbestos exposure is currently a possibility in countries where asbestos is still used or was banned only recently.[21]

Asbestos bodies and asbestos fibers in lung tissue have been used for many years as useful markers of cumulative dose and in documenting past exposure to amphiboles.[25] These markers are less useful in the case of chrysotile exposure, because of the low biopersistence of this type of asbestos.[26] In the first patient the asbestos body burden (22,000/gdw) was significantly higher than the limit of 1,000/gdw recommended by the Helsinki Consensus Document, indicating past asbestos exposure with high probability.[27 28] Conversely, fiber concentration was below the laboratory detection limit. This result could be explained by the fact that the patient had probably been using chrysotile and that lung fiber analysis was performed 47 years after last asbestos exposure. On the other hand, asbestos bodies are largely produced by long amphibole fibers, while production from chrysotile is negligible.[29,30] Hence, we can hypothesize that chrysotile materials used by the patient were contaminated by amphibole asbestos. None of the patients described in this paper was aware of the asbestos type used.

Finally, it should be recognized that for patient 1, only one lung lobe was available for asbestos body and asbestos fiber burden. Hence, analysis performance was probably suboptimal To improve sensitivity the recommended procedure is to pool lung samples from all lobes of both lungs.[31]

In conclusion, we have documented two MM cases related to dental technician work with definite asbestos exposure and two with possible occupational asbestos exposure. For all of them we filed claims for compensation to the Italian Workers' Compensation Authority (INAIL). Only the first patient was compensated because the other subjects, being self-employed or not formally employed (the woman), were not covered by work insurance. Availability of a registry focused on MM has provided a fundamental aid in discovering unrecognized or overlooked (due to the long latency of the disease) sources of asbestos exposure. Dental technicians suffering from mesothelioma should be questioned about past occupational asbestos exposure.

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AUTHORS' CONTRIBUTION

Mensi Carolina: conceived the study, collected and evaluated clinical and interview data, and drafted the manuscript. Ciullo Francesco· evaluated clinical and interview data and drafted the manuscript. Barbieri Pietro Gino: collected and evaluated clinical and interview data, contributed to interpretation of findings and discussion, and collaborated to draft the manuscript. Riboldi Luciano· evaluated clinical and interview data and contributed to interpretation of findings and discussion. Somigliana Anna: performed the laboratory tests (fiber and asbestos body count) and contributed to interpretation of findings and discussion. Rasperini Giulio contributed to interpretation of findings and discussion. Pesatori Angela Cecilia contributed to interpretation of findings and discussion. Consonni Dario. collaborated to draft the manuscript and contributed to interpretation of findings and discussion. All authors: revised and approved the manuscript for intellectual content.

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As reporting of malignant mesothelioma to the Registry is compulsory by law, ethics approval is not required.

DISCLOSURE (AUTHORS)

The authors report no conflicts of interest.

DISCLOSURE BY AJIM EDITOR OF RECORD

Rodney Ehrlich declares that he has no conflict of interest in the review and publication decision regarding this article.

DISCLAIMER

None

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