

The incidence of intrathoracic tumours in Manchester, 1868-1926

Incidenza dei tumori intratoracici a Manchester, Regno Unito, 1868-1926

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Summary

Dr J. B. Duguid published a paper in 1927 entitled "The incidence of intrathoracic tumours in Manchester". It was based on autopsies conducted at the Manchester Royal Infirmary between 1868 and 1926. While the majority of intrathoracic tumours had been diagnosed as bronchogenic carcinomas, there remained a small number affecting the pleura about which there had been uncertainty. Lancashire had been the cradle of Britain's asbestos industry: Turner Brothers Asbestos had converted a cotton mill to asbestos in Rochdale in 1880, and had built another factory in Manchester in 1913, so that there would have been time enough for the development of asbestos associated malignancies. When in 1991 hindsight prompted a review of the Manchester clinical and autopsy materials, it was discovered that they had all been disposed of recently. The published descriptions of histopathological appearances in the uncertain cases were reviewed and it was concluded that, while it was impossible categorically to identify these lesions as mesothelial in phenotype, the anatomical site and the description offered the possibility. It is a matter of conjecture whether the identification of malignant mesothelioma in association with exposure to asbestos in 1926, would have prompted effective action to avert a major international public health disaster. Eur. J. Oncol., 12 (1), 5-8, 2007

Key words: malignant mesothelioma, history of medicine

Riassunto

Nel 1927 il Dottor J. B. Duguid pubblicò un lavoro intitolato "L'incidenza dei tumori intratoracici a Manchester". Esso si basava su autopsie eseguite al Manchester Royal Infirmary tra il 1868 e il 1926. Mentre la maggioranza dei tumori intratoracici era stata diagnosticata come carcinoma broncogeno, rimase un piccolo numero di tumori interessanti la pleura sui quali c'era stata incertezza. La contea di Lancashire era la culla dell'industria britannica dell'amianto: nel 1880, a Rochdale, la Turner Brothers Asbestos aveva convertito un cotonificio in una fabbrica per la tessitura di filati in amianto, e nel 1913 aveva costruito un'altra fabbrica a Manchester, cosicché ci sarebbe stato un tempo sufficiente per lo sviluppo di tumori maligni dovuti all'amianto. Quando nel 1991 il senno di poi suggerì una revisione del materiale clinico ed autoptico di Manchester, si scoprì che esso era stato recentemente eliminato. Furono esaminate le descrizioni pubblicate sui quadri istopatologici dei casi incerti e si concluse che, mentre era impossibile identificare con certezza queste lesioni come fenotipicamente mesoteliali, la sede anatomica e la descrizione deponevano per questa possibilità. È oggetto di dibattito se l'identificazione del mesotelioma maligno correlato all'esposizione ad amianto nel 1926 avesse potuto promuovere azioni efficaci per evitare un disastro internazionale di sanità pubblica. Eur. J. Oncol., 12 (1), 5-8, 2007

Parole chiave: mesotelioma maligno, storia della medicina

Received/Pervenuto 15.9.2006 - Accepted/Accettato 6.10.2006

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Introduction

Some 65 years ago, an article in *The Lancet* reported on the incidence of intrathoracic tumours at post mortem, in the years 1868-1926¹. Its author, a lecturer in Morbid Anatomy in the Victoria University of Manchester, had formed the impression, shared by others who had conducted post mortems at the Manchester Royal Infirmary, that the incidence of intrathoracic tumours was high. As reports from other centres in America and in Europe indicated a similar increase, Duguid decided to analyse the hospital's autopsy data to look for a trend, and to investigate the occupations of cases. Registers of all autopsies performed at the Infirmary since the year 1868, apart from 1910, had been preserved and were available to him.

Numbers of intrathoracic tumours diagnosed at Manchester Royal Infirmary

Out of a total of 10,780 autopsies, 175 intrathoracic tumours had been diagnosed, the first in 1871. The percentage of intrathoracic tumours increased from 0.24 up to the end of 1885, to 2.57 in the period 1921-1925, though not monotonically. Present day physicians may not appreciate how uncommon carcinoma of the bronchus was before the Second World War, and how brief were the lives of members of the lower social classes. For example, in 1921, for men in Social Classes IV (partially-skilled occupations) and V (unskilled occupations) combined, the mean age at death was 52.2 years, and their cumulative death rate per cent from lung cancer was 0.15².

Duguid was careful not to overinterpret the available information, conscious of the effects of missing data, the small number of cases, and of the biases introduced by the policies for admitting patients to the Infirmary, and for pursuing permission for autopsies. Hospitals were supported by local authorities and charity, and not being over-endowed, required to economize, so that selection for admission to hospital involved triage, with priority being given to cases most likely to benefit. In the matter of autopsies, then, as now, more effort was used to obtain permission in "interesting" cases.

Histological characteristics of Manchester Royal Infirmary intrathoracic tumours

In the event, Duguid was able to find and review histological material from only 78 of the intrathoracic tumour

cases. The majority he placed in either of two groups, the first included a large-celled alveolar type and a squamous celled type, the second included an oat-cell type and small round-celled exceptions. He differentiated a further group.

"These are tumours composed of spindle cells arranged in intertwining bundles. They are as a rule devoid of cellular tissue and the cells are of somewhat epithelioid type: some of them showing a slight resemblance to squamous cells, but the fact that the blood vessels are very numerous and thin-walled prevents their being classified as epitheliomata. Their structure is one which is associated with growths of the pleura and, by some, they are considered to be of endothelial origin".

He described several cases in the group where the pleura was especially mentioned as being affected.

"Case 1... Reported September 1922, as 'an endothelioma of both pleurae'. The tumour is composed of large closely-packed spindle cells, some of which are irregular, branching, and almost syncytial".

"Case 3... Reported May 1915, as 'endothelioma of both lungs'. A tumour composed of rather loosely arranged large spindle cells".

"Case 4... Reported June 1914, as 'a tumour of possibly thymic origin, involving the pleura and lung and invading pericardium'. It is composed of large spindle cells amongst which are a few polymorphic giant cells".

"Case 7... Reported May 1909, as 'a malignant growth of the pleura'. It is composed of rather irregular, large, loosely arranged spindle cells. Some of them appear to have branching processes, so that there is a fine reticular appearance. The vessels are numerous and thin walled. A tumour of very uncertain type".

"Case 8... Reported September 1903, as 'endothelioma of left pleura with secondary nodules in liver and peritoneum'. It is composed of large spindle cells arranged in whorl formation".

Eight photomicrographs were included in the paper, but none came from the special pleural cases.

Selikoff takes an interest

Dr Irving J. Selikoff wondered whether asbestos-associated pleural malignant mesothelioma cases might be identified in the Manchester archival material, and suggested to the author (Greenberg) that he might investigate. This was not a fanciful conjecture, as Turner Brothers had converted a cotton mill to produce asbestos

textiles in Rochdale in 1880, and had built an asbestos factory in Manchester in 1913, a time when dust exposures were largely uncontrolled. The adverse respiratory effects of asbestos had made themselves noticed in Britain within 20 years of the start up of the industry³, and not much later in France⁴, where deaths occurring within 5 years of starting work suggest extremely high exposure levels. Further, it is commonly understood that the awareness of malignant mesothelioma being associated with exposure to asbestos came from South Africa⁵, whereas the condition had been recognized earlier in European asbestos workers⁶.

A factor that might have militated against finding malignant mesotheliomas in asbestos workers, but did not rule the possibility out entirely, would have been the short life expectation for working class males in the UK in 1900. While this was only 45 years, a school leaving age of 12 provided time for the tumour to evolve.

At the time that Duguid was writing, there was in Britain an influential opinion sceptical of diagnoses of malignant pleural mesothelioma. Nevertheless, his contemporary Professor Matthew Stewart records having given a tutorial on mesothelioma, and his eponymous collection of stained sections included eight primary tumours of the pleura, one bovine and 7 human, described by him variously as sarcoma, endothelioma or mesothelioma⁷. Stewart's catchment area included large asbestos factories to which he acted as a consultant.

Occupations reported for males with intrathoracic tumours

Duguid found occupational details for 143 of the males with intrathoracic tumours. He observed that the largest number in any single occupation was for "labourers" not otherwise described (28), the next largest was for carters (9) followed by clerks (8). Impressed by the number of carters, he aggregated those he deemed to be in closely related occupations under "transport workers", listing them as: carters (9), van drivers (2), lorrymen (1), coachmen (1), teamsters (1), horse keepers (2), ostlers (1), stablemen (1), tram drivers (3), engine drivers (2), tram guards (1) and railway guards (1), totalling 25. With 18 engaged with horses, and 7 with mechanical traction, a common agent is not immediately apparent. This group he calculated to constitute 16.55% of all male cases, which compared with 12.34% that the census reported for transport workers as a proportion of the total male population.

He concluded that the numbers involved were too small to allow useful comparisons to be made. With hind-

sight, it is conceivable that some of the 28 workers classified as "labourers" might have, as a result of occupational disease, gravitated to physically less demanding work. It is unlikely that disabled ex-asbestos workers will have been found among the transport jobs, as generally these required special skills, experience and physical fitness for loading and unloading, with single handed carters being expected to load, unload and carry minimally 112 pound sacks.

Histological confirmation

It was hoped to review the registers of autopsies and to submit the relevant histological sections, which had been identified by their case numbers in the Manchester University pathology department's day books, to an expert panel of pathologists for a further opinion. Historic pathology material from Leeds University, in the way of Post Mortem Record Books, is preserved in the Brotherton Library's Special Collection, and the Matthew Stewart collection of sections and the blocks from which they had been derived, has, despite pressures on space, been preserved at the initiative of members of the university pathology department⁷. Disappointingly, it was learnt that the historic Manchester pathology collection had been disposed of (Professor D.L. Gardner, personal communication).

Duguid's description of the appearances in the cases presented above were reviewed (Trott) for their compatibility with malignant pleural mesothelioma. The histological diagnosis of malignant mesothelioma is fraught with difficulty⁸, and the appearances have to be differentiated both from benign mesothelial proliferative lesions and malignancies arising from other sites, notably the bronchus. The commonest histological pattern is epithelioid but sarcomatoid features can exist, both mixed with epithelioid and in pure form, and there is a desmoplastic tumour where the cells appear compressed and diffused between dense sheets of hyalinised collagen so that the examination of small biopsies renders the diagnosis difficult. Desmoplastic tumours form about 5% of mesothelioma and are notoriously malignant despite their comparatively banal appearances.

The problem is compounded by the fact that the epithelioid type can have many patterns including tubular, papillary, solid and deciduioid. Immunohistochemistry is essential for the modern pathologist to deploy, but even the advent of modern monoclonal antibodies has not produced a reagent that is always positive, nor can a panel of antibodies provide the characteristic features in all cases. Pathologists nowadays use a panel of antibodies

that include a pan-cytokeratin (AE1-AE3 CAM5.2), cytokeratin 5/6, calretinin, carcinoembryonic antigen and thyroid transcription factor for pleural tumours or Ber-EP4 for peritoneal tumours. Ultimately the diagnosis relies on a combination of clinical and radiological data as well as histological features.

So with this background what conclusion can be drawn from Duguid's descriptions of the 5 tumours? Firstly, it is important to note that in all cases the pleura is mentioned as being primarily affected. Secondly, although a variety of histological features is described, they mostly are referred to as endothelioma which may well be the epithelioid appearances described by modern pathologists. Whereas it is impossible to identify these lesions categorically as mesothelial in phenotype, the anatomical site and the description, such as it is, certainly offers the possibility.

Conclusion

Had some or all of the 5 rare pleural tumours singled out by Duguid been malignant mesotheliomas, and had a causal association been established with asbestos exposure, would today's worldwide public health problem have been averted?

The history of occupational health provides a number of instances where small clusters of rare and even common tumours have led to the recognition of a causal association, but it is far from invariable that this has led to effective and prompt intervention. Selikoff repeatedly looked on such early reports as missed opportunities for prompt intervention to prevent disability and death.

In the case of asbestos, a number of "early warnings" were sounded between 1898 and 1960, none of which was promptly and effectively acted on⁹. There is no reason to believe that had Manchester's pleural cancers

been identified as causally associated with occupational exposure to asbestos in 1926, today's asbestos disease epidemic would have been averted.

Declaration of interests

Neither author has received payment for preparing this paper nor expects interests to derive benefit from its publication.

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