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# The influence of the diagnostic technique on the histopathological diagnosis in malignant mesothelioma

**Teun van Gelder[1], Henk C. Hoogsteden[2], Jan P. Vandenbroucke[4], Theo H. van der Kwast[3], and Hans T. Planteydt[5]**

Departments of [1] Internal Medicine I, [2] Pulmonary Medicine and [3] Pathology, Academic Hospital Dijkzigt and Erasmus University, Rotterdam, The Netherlands
[4] Department of Clinical Epidemiology, University of Leiden, Leiden, The Netherlands
[5] Department of Pathology, Streeklaboratorium Zeeland, Middelburg, The Netherlands

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**Summary.** In the histopathology of malignant mesotheliomas three different types (epithelial, connective tissue and mixed type) are distinguished. Some authors believe all tumours to be of mixed type, but consider that due to inadequate sampling or small biopsies this may be missed frequently. In this study the relationship between the histopathological diagnosis and the amount of tissue examined was investigated. In a series of 124 cases of malignant pleural mesothelioma a high percentage of mixed type tumours was found (55%). In cases where the decisive diagnostic procedure had been an Abrams biopsy (the "small-specimen" technique) mixed-type histology was found in 36%. If thoracoscopy, thoracotomy or autopsy (the "large-specimen" techniques) had delivered a definite diagnosis, mixed-type histology was found in 63%. Apparently diagnosing the mixed-type variety depends on the amount of tumour tissue obtained. However, the assumption that all mesotheliomas are of mixed type cannot be confirmed.

**Key words:** Malignant mesothelioma – Diagnostic technique – Histopathology – Biopsy – Pleura

## Introduction

In 1960 Wagner et al. described their observation of a strong relationship between asbestos exposure and the occurrence of malignant pleural mesothelioma in South Africa. We now know that exposure to asbestos may lead to a number of pathological conditions including organs other than lung or pleura (Craighead and Mossman 1982).

The pathological diagnosis of malignant mesothelioma sometimes presents considerable difficulties, partly because of its very variable histological appearance and partly because it is often difficult to distinguish from secondary serosal deposits of carcinoma (Davis 1984; Kwee et al. 1982). The report and recommendations of the Working Group on Asbestos and Cancer, formulated in 1965, still form the basis for the current histopathological criteria (McCaughey et al. 1985). At the histological level epithelial or sarcomatous elements can be recognized; however, mixed types are common (Whitwell and Rawcliffe 1971). In this study we tried to find out whether the size of the specimen of tumour examined was of influence on the histopathological diagnosis. Therefore, we compared the final histopathological diagnosis obtained by "large-specimen" versus "small-specimen" techniques.

*Offprint requests to:* T. van Gelder, Department of Internal Medicine I, Academic Hospital Dijkzigt, Dr. Molewaterplein 40, NL-3015 GD Rotterdam, The Netherlands

## Materials and methods

The medical records of 124 patients presenting with malignant mesothelioma of the pleura were reviewed. All mesotheliomas were diagnosed between 1962 and 1985. For the histopathological diagnosis of diffuse malignant mesothelioma the recommendations of the Commission of the European Community were applied (Jones et al. 1985). All histological specimens were re-evaluated by the Dutch Mesothelioma Panel. For the certainty of the diagnosis the following categories were used:

A. Definite malignant mesothelioma: no doubt as to the histopathological diagnosis.
B. Probable malignant mesothelioma: the reason for the hesitation may be lack of material, poor quality, lack of differentiation, absence of certain histological criteria.
C. Possible malignant mesothelioma: the diagnosis cannot be denied but there is insufficient evidence to come to a positive conclusion.
D. Improbable malignant mesothelioma: probably not a mesothelioma but the diagnosis cannot be absolutely excluded.
E. Definitely not a malignant mesothelioma.

In categories D and E another diagnosis should be made or suggested. Only the histopathological categories A and B were included in the study. The results of the analysis of epidemiological, clinical and diagnostic aspects have already been published (Van Gelder et al. 1989). The chi-squared test was used to compare the numbers of the histopathological diagnosis in the different diagnostic techniques.

## Results

The final histopathological diagnosis was known in all cases. The mixed type was the most prevalent mesothelioma, found in 68 out of 124 patients (55%). In 40 patients (32%) there was a mesothelioma of the epithelial type, while in 16 (13%) it was of the connective tissue type. In 102 cases the diagnosis was considered as "definite", whereas the other 22 were "probable".

The diagnostic procedures used are listed in Table 1. Table 2 shows the distribution of decisive diagnostic procedures among the three histological types. The two patients in which a biopsy of a metastasis had led to the diagnosis were excluded, because the occurrence of metastases is known to be related to the histological type (Law et al. 1982). The seven cases in which the diagnosis was based on cytology were also excluded, since mesotheliomas of the connective tissue type, in contrast to mesotheliomas of epithelial and mixed type, rarely exfoliate and thus would consequently be underestimated in this diagnostic technique (Jones et al. 1985). In three cases it was unknown which diagnostic procedure had given the final diagnosis. When we combine the data for the "single-component" tumours and compare them with the data of the mixed-type tumours, we find the numbers mentioned in Table 3. They clearly show that there is a significantly higher percentage of diagnosis of mixed-type tumours if the investigative diagnostic procedure had been a thoracoscopy, thoracotomy or autopsy ($P<0.05$).

**Table 1.** Diagnostic techniques used in 124 cases of malignant pleural mesothelioma

| Technique | Performed | Positive |
|---|---|---|
| Pleural fluid cytology | 105 | 63 (60%) |
| Abrams biopsy | 85 | 58 (68%) |
| Thoracoscopy | 45 | 39 (87%) |
| Thoracotomy | 21 | 19 (91%) |
| Biopsy of metastasis | 6 | 4 (67%) |
| Bronchoscopy | 3 | 0 (0%) |

**Table 2.** Distribution of decisive diagnostic techniques among the three histological types of malignant pleural mesothelioma ($n=112$)

| | Epithelial | Connective tissue | Mixed |
|---|---|---|---|
| Abrams biopsy | 18 | 5 | 13 |
| Thoracoscopy | 9 | 2 | 19 |
| Thoracotomy | 4 | 4 | 9 |
| Autopsy | 5 | 4 | 20 |

**Table 3.** Distribution of small- and large-specimen techniques among the different tumour types of malignant pleural mesothelioma ($n=112$)

| | Small-specimen technique[a] | Large-specimen technique[b] |
|---|---|---|
| Connective tissue + epithelial type | 23 (64%) | 28 (37%) |
| Mixed type | 13 (36%) | 48 (63%) |
| Total | 36 | 76 |

[a] Abrams biopsy
[b] Thoracoscopy, thoracotomy or autopsy

## Discussion

The histopathological diagnosis of mesothelioma is sometimes complicated by the occurrence of histological variation (Planteydt 1979). Histological subtyping of mesotheliomas is thought to be of importance in prognosis (Adams et al. 1986; Hillerdal 1983; Huncharek and Muscat 1987; Martensson et al. 1984) although others deny this (Chailleux et al. 1988; Solomons 1984). Many pathologists believe that most mesotheliomas are composed of mixed-type histology and that if sufficient numbers of sections were taken most tumours would turn out to be of the mixed type (Becklake 1976). To our knowledge there are no data supporting this point of view.

In this study we found a significantly higher number of mixed-type histology in cases where the decisive diagnostic procedure had been a thoracoscopy, thoracotomy or autopsy. With these "large-specimen techniques" in 63% a mixed-type tumour was found, compared to 36% in the "small-specimen technique" (Abrams biopsy). These findings support the view that diagnosing the mixed variety heavily depends on the extent of histological investigation and on the amount of tissue studied. However, even in cases where an autopsy had been performed the mixed type was found in only 69% (20/29). This latter observation indicates that the statement "all mesotheliomas are of mixed type" is probably overemphatic.

A review of the literature revealed the figures shown in Table 4, which gives the distribution of the histological varieties in different studies. There are considerable differences, with the percentage of mixed-type varying from 0 (McCormack et al. 1982) to 66% (Kwee et al. 1982). These differences could be due to diversity in histopathological criteria for distinction between the three types and since most studies do not give extensive information on applied criteria this cannot be evaluated. It was also only clear occasionally which diagnostic procedure had given the definitive histological diagnosis in these studies. In the study by Huncharek and Muscat (1987) all cases were confirmed histologically after a complete autopsy. We would expect a higher percentage of mixed-type tumours in this "large-specimen" technique.

In conclusion, we report a high percentage of mixed-type malignant pleural mesotheliomas, probably due to the availability of large specimens of tumour for histological examination. We think it is essential that an experienced histopathologist investigates a sufficient number

**Table 4.** Literature review of the proportions of the different tumour types in malignant pleural mesothelioma

| Authors | Year | *n* | Epithelial (%) | Connective tissue (%) | Mixed (%) |
|---|---|---|---|---|---|
| Kwee et al. | 1982 | 32 | 8 (25) | 3 (9) | 21 (66) |
| Law et al. | 1982 | 115 | 60 (52) | 25 (22) | 30 (26) |
| McCormack et al. | 1982 | 149 | 102 (68) | 47 (32) | 0 (0) |
| Solomons | 1984 | 36 | 29 (80) | 2 (5) | 5 (14) |
| Adams et al. | 1986 | 92 | 42 (46) | 21 (23) | 29 (32) |
| Huncharek and Muscat | 1987 | 42 | 20 (48) | 10 (24) | 12 (29) |
| Chailleux et al. | 1988 | 167 | 135 (81) | 7 (4) | 25 (15) |
| Van Gelder et al. | 1989 | 124 | 40 (32) | 16 (13) | 68 (55) |
| Hillerdal | 1983 | 829 | 412 (50) | 134 (16) | 283 (34) |

of sections intensively. If all these conditions had been fulfilled in other studies the percentage of mixed-type histology would probably be higher. Thoracoscopy is thought to be the diagnostic procedure of first choice, allowing visually directed biopsies of large tumour specimens and giving a definite diagnosis of malignant mesothelioma in almost 90%.

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