

## HISTOLOGICAL FEATURES IN DIAGNOSTIC PLEURAL BIOPSY

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In 1966 Chew and Tan reported on the results and clinical aspects of 72 consecutive pleural biopsies obtained by the Harefield needle. The present communication is to elaborate on the histological aspects of these biopsies.

Out of the 72 cases, one was an empyema, which histology being non-specific, would not be discussed here. There were 51 tuberculous cases and 48 of these showed a specific histology for tuberculosis whilst one biopsy was inadequate. Out of the 20 malignant cases, 13 showed undoubted histology for malignancy, 3 had inadequate tissues and 4 were non-specific. On review of the latter 4 non-specific cases, 2 cases were shown to be suggestive of malignancy.

### MATERIAL AND METHOD

All the pleural biopsies were immediately fixed in 10% formal-saline solution. After 24 hours of fixation, the whole bottle was poured into the processing metal basket. When the tissue was processed and blocked, serial sections were cut and stained with Haematoxylin and Eosin. A Ziel-Nielsen stain was made on one representative slide on each case. After scrutinising all the serial sections, the slide with the most pathological tissue was chosen for closer study. Each slide usually had 3 to 5 sections on it. Owing to previous experience when acid-fast bacilli were not easily identified from pleural biopsies, we were contented with examining only one Z.N. slide of each case. This was especially so as we required the remaining slides to study the histological features. Consequently we were able to see acid-fast bacilli in only 3 out of the 48 biopsies that were diagnostic of tuberculosis.

### HISTOLOGICAL FEATURES OF TUBERCULOUS PLEURAL BIOPSIES

The case with an inadequate biopsy showed only striated muscle, whilst the 2 non-specific cases revealed only granulation tissue and fibrosis with a sprinkling of mononuclears. The 48

cases with tuberculous histology varied from the classical granulomatous tubercle with caseation (Fig. 1) to cases where only epithelioid histiocytes were seen in the process of forming early granulomas (Fig. 2).

**Histiocytes** were seen in every biopsy of these 48 tuberculous cases. They varied from the thin spindle cell to the characteristic polygonal epithelioid cell. Their numbers were gauged into 3 categories:—(a) +, (b) ++ (Figs. 3 & 4), and (c) +++ (Figs. 2 & 5). Out of the 48 cases, 29 were profuse (+++) and 19 showed moderate (++) numbers. Not a single biopsy could be classified into the "few" (+) category. These histiocytes invariably palisaded themselves (Figs. 3 & 4) whether they were surrounding foci of caseation or not. These same epithelioid histiocytes could be seen conglomerating themselves into giant cells (Figs. 3 & 5).

**Giant cells.** There was no attempt in this study to separate them into the Langhan and foreign body giant cells. Except for descriptive purposes, the distinction had not the slightest pathological significance. However, they were again segregated into "+", "++" and "+++" in increasing numbers, and in 14 cases, no giant cell was seen. In 3 cases they were scarce (+) (Figs. 4 & 6), in 18 cases moderate numbers (++) (Figs. 1 & 2) were present, whilst in 13 cases they were numerous (+++) (Fig. 5). They were invariably associated with histiocytes (Figs. 3 & 5).

**Caseation.** Out of the 48 cases, only 25 biopsies revealed caseation. When classifying the amount of caseation into 3 categories, 6 biopsies showed minimal (+) amount (Fig. 2), 13 had moderate (++) quantities (Fig. 6) and 6 presented with extensive (+++) areas of caseation (Figs. 1 & 4). In some cases, the early areas of caseation could be seen to be purely of a coagulative type of necrosis superimposed on previous collagen (Figs. 6 & 7). At this stage, when the granular texture had not set in, the glossy ropy background of previous collagen could still be discerned, and the lack of nuclear,

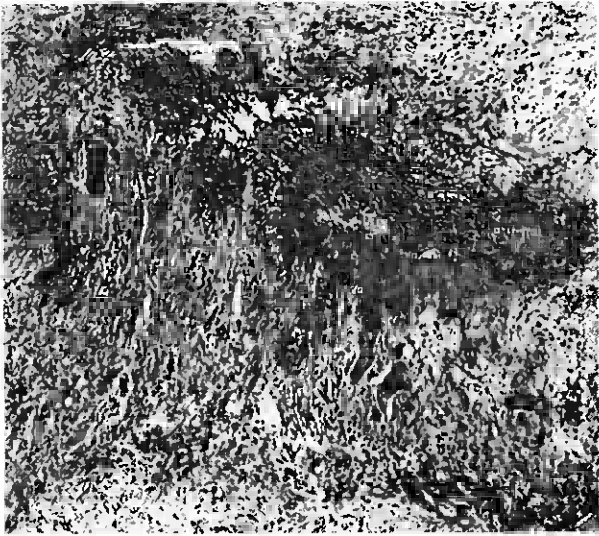


Fig. 1. Note massive caseation in a thickened fibrotic pleura with moderate numbers of giant cells and scanty lymphocytes. (H&E x 75).

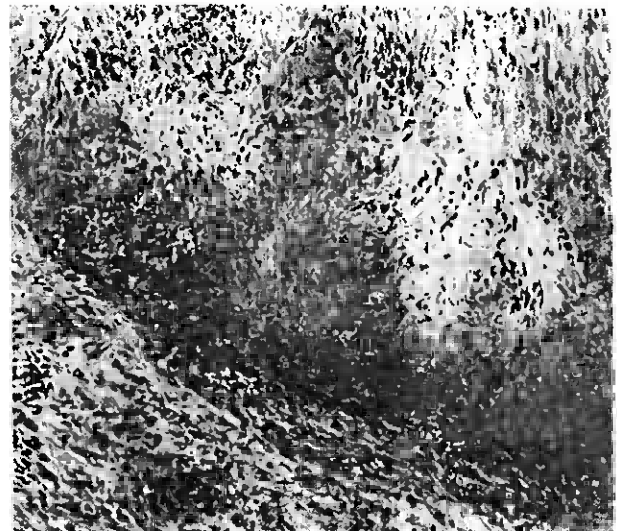


Fig. 4. Massive area of caseation with a poor palisade of histocytes. (H&E x 150).

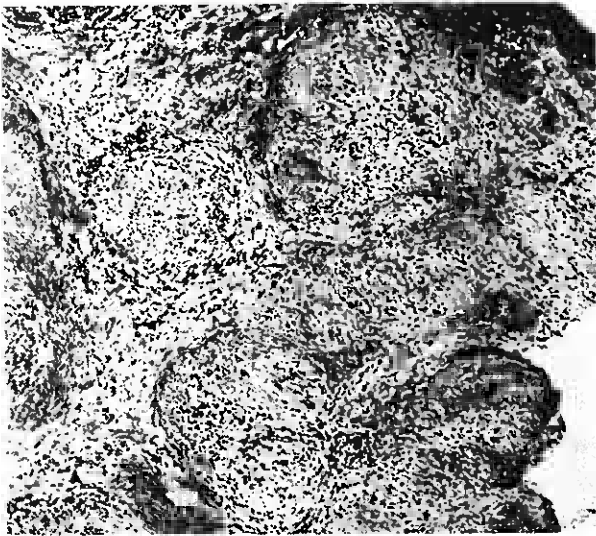


Fig. 2. Numerous tuberculoid granulomas with several Langhan giant cell formations. The fibrotic background is prominent and no caseation can be discerned. (H&E x 75).

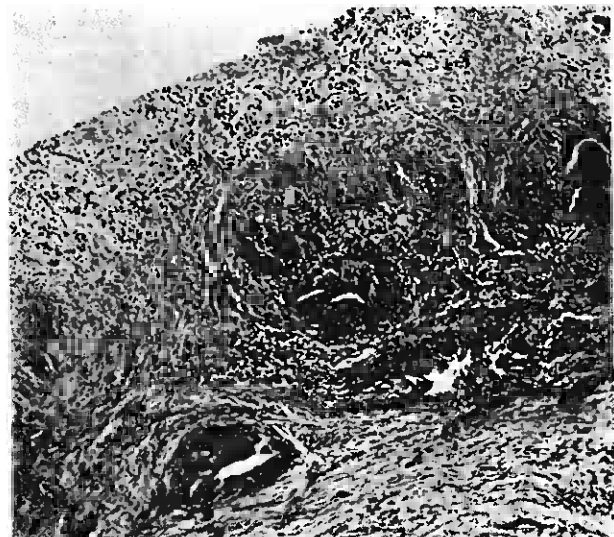


Fig. 5. Many tuberculoid granulomas with numerous (---) foreign body type giant cells (H&E x 75).

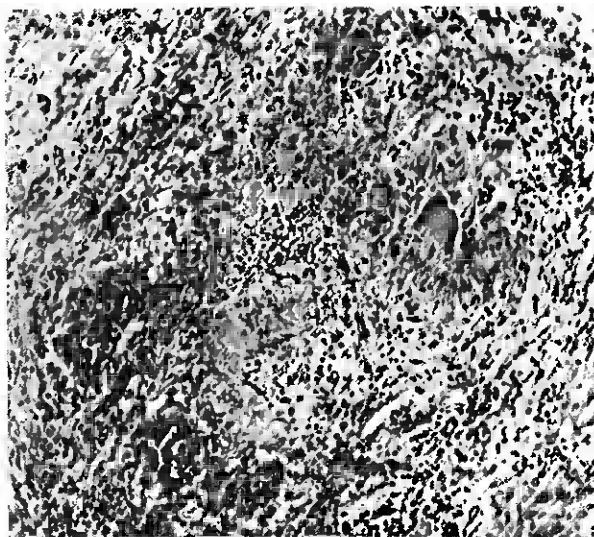


Fig. 3. Tiny granuloma composed of a central Langhan giant cell surrounded by a broad rim of histocytes. This microphotograph depicts the area with the most numerous lymphocytes out of the 48 cases. (H&E x 150).

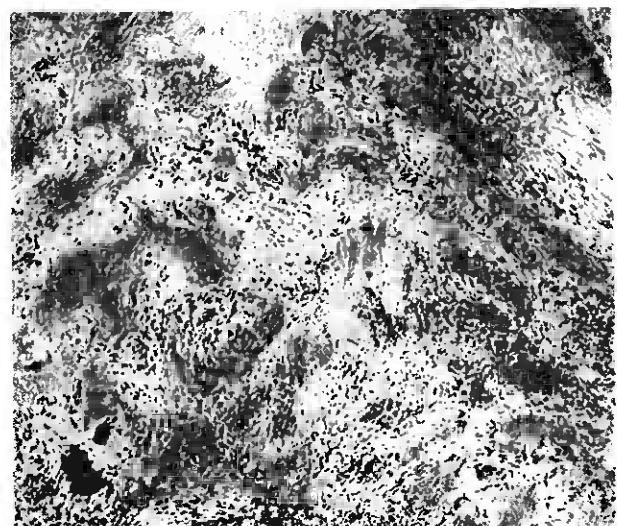


Fig. 6. Early caseating process with scanty accompaniment by histocytes, giant cells and lymphocytes (H&E x 75).

chromatinic debris (Fig. 7) differs sharply with the early caseating areas in lymph nodes. Early caseation in the lymph nodes usually showed numerous chromatinic dots.

**Lymphocytes.** Although they were present, their numbers were never as numerous as in other situations (*e.g.* lungs and brain). Only 8 cases showed moderate numbers (++) (Fig. 3), whilst the rest of the biopsies were rather scanty in lymphocytes (Figs. 1, 6 & 7). An occasional plasma cell could be seen in most cases.

**Fibrosis.** Utilising the number of granulomatous lesions as an index of activity, the accompanying fibrosis encountered was more than expected compared to other sites (Figs. 1, 4 & 6). This was probably due to the peculiar situation of the pleura. The amount of fibrosis, therefore, could not be used as a linear measure of the process of healing.

TABLE I

HISTOLOGY OF 48 CASES OF TUBERCULOUS PLEURAL BIOPSIES

	+++	++	+	—
Histiocytes	29	19	0	0
Giant Cells	13	18	3	14
Caseation	6	13	6	23
Lymphocytes	0	8	40	0

HISTOLOGICAL FEATURES OF MALIGNANT PLEURAL BIOPSIES

Out of the 20 cases of primary carcinoma of the lung, 13 biopsies were diagnostic of malignancy, and 3 biopsies did not prove enough tissue for diagnosis. On review of the remaining 4 non-specific cases, 2 of them could be classified as suggestive of malignancy, but the number of malignant cells present were so small that it was not possible to categorise them into any histological type. As actively proliferating mesothelial cells could very well mimick carcinomatous cells, it was their infiltrative quality (Fig. 12) that prompted us to label them as truly malignant.

The 13 indentifiable malignant biopsies showed 6 adenocarcinomas (Figs. 8 & 9), 5 undifferentiated carcinomas (Fig. 10) and 2 squamous cell carcinomas (Fig. 11). The 2 squamous variety were moderately to poorly differentiated (Fig. 11). The adenocarcinomas were distinct and unmistakable and were easiest to identify. The 5 undifferentiated carcinomas

included 2 biopsies which showed unmistakable carcinoma of poor differentiation and could possibly be pidgeon-holed into one of the 2 former categories if more malignant tissue were available for study. The remaining 3 undifferentiated carcinomas (Fig. 10) had enough malignant tissue for study, and included the oat-cell type and those that had no tendency to differentiate into any other type. Fibrosis was very prominent in all the 15 malignant biopsies (Figs. 10 & 12) and inflammatory infiltrate was very scanty.

Therefore, on review of the histological slides the previous figure of 65% had now improved to 75% showing features "suggestive or diagnostic of malignancy." Table II summarises the histological findings.

TABLE II

PLEURAL HISTOLOGY OF 20 CASES OF LUNG CARCINOMA

Adenocarcinoma	-	-	6
Undifferentiated	-	-	5
Squamous cell	-	-	2
Suggestive of Malignancy	-	-	2
Non-specific	-	-	2
Inadequate	-	-	3

DISCUSSION

As far as the tuberculous cases are concerned the histopathology is no different to tuberculosis in other situations except that there is less lymphocytic infiltration and more fibrosis, and early caseation is distinctively coagulative in nature. Acid-fast bacilli were disappointingly difficult to find in the sections. All the 48 cases were diagnostic of tuberculosis and no case could be put in the category of "Suggestive of tuberculosis".

However in the malignant group, 2 cases are put in the "Suggestive of malignancy" category after review. It was originally put in the non-specific group because of the paucity of the pathological tissue. It is the infiltrative quality of the cells that gave away their malignant nature. Although the figure of "75% positive" biopsies is good, it certainly can be improved by repeated biopsies. The same improvement would also apply to the tuberculous group. The repeated biopsy in the malignant group would also provide more material for a more exact identification of the histological type. As it is, 4

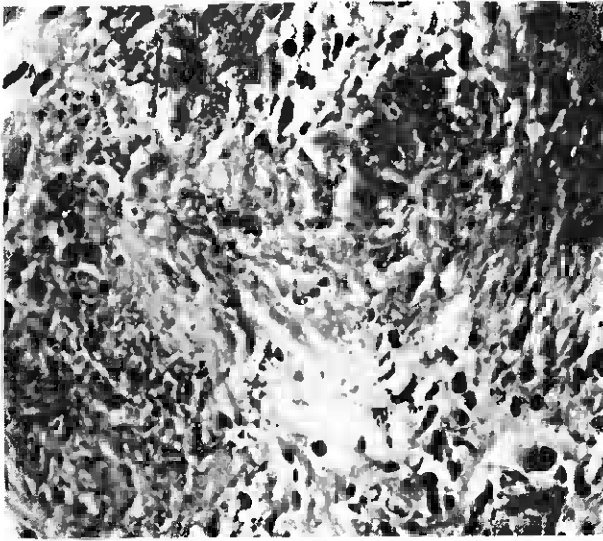


Fig. 7. High power view of one of the early caseating areas depicted in Fig. 6. It shows the acellular, ropy type of coagulation necrosis. There are no chromatinic debris in this early caseation. (H&E x 500).

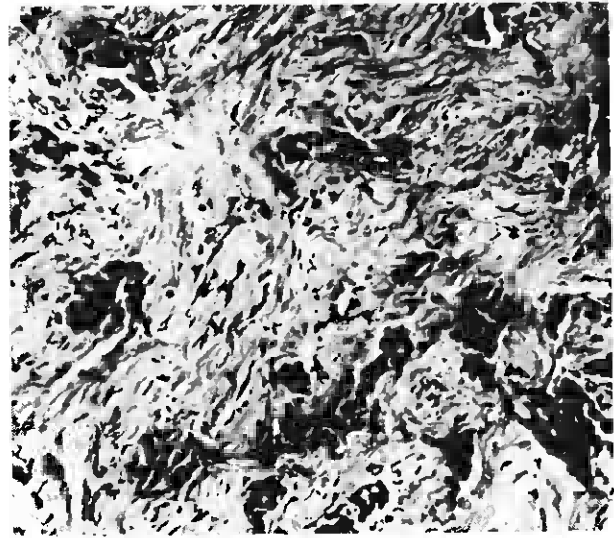


Fig. 10. Undifferentiated carcinoma in a scirrhous background. Anaplasia and pleomorphism with no attempt at differentiation are the features. (H&E x 150).

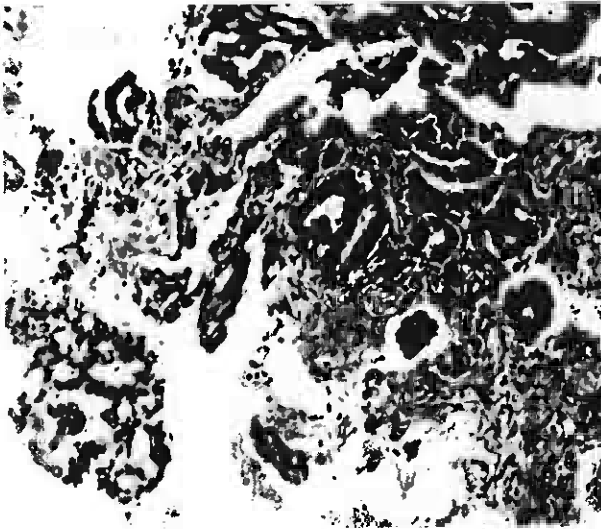


Fig. 8. Well differentiated adenocarcinoma of the lung shown in this pleural biopsy by well formed acini. (H&E x 150).

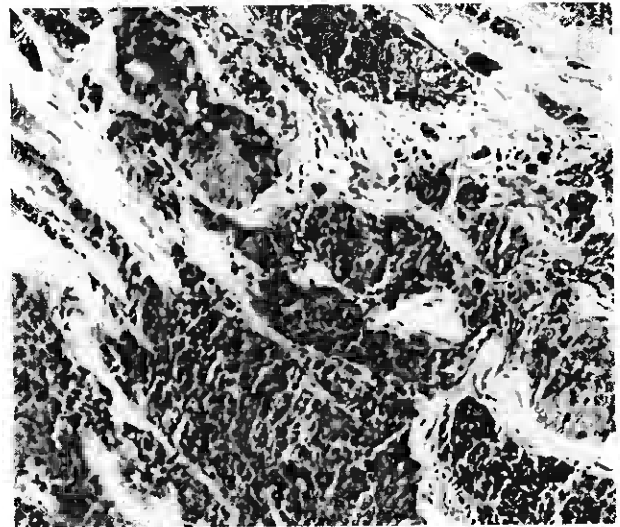


Fig. 11. Poorly differentiated squamous cell carcinoma. Sheets and columns of carcinomatous cells with foci of squamous differentiation. (H&E x 150).

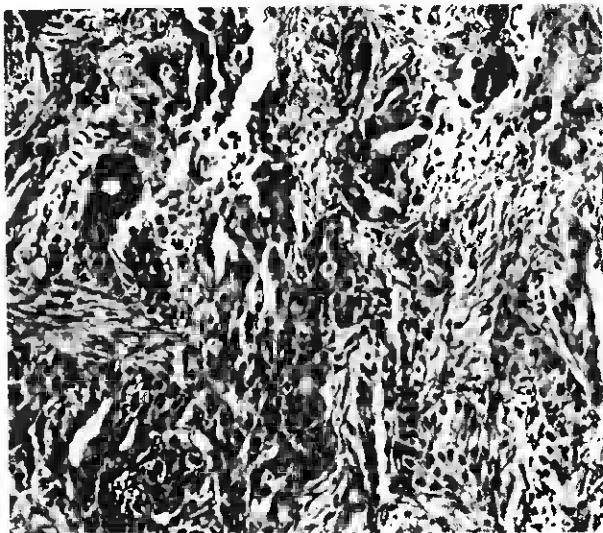


Fig. 9. Moderately differentiated adenocarcinoma in a fibrotic background. The tubular nature can be discerned with closer scrutiny. (H&E x 150).

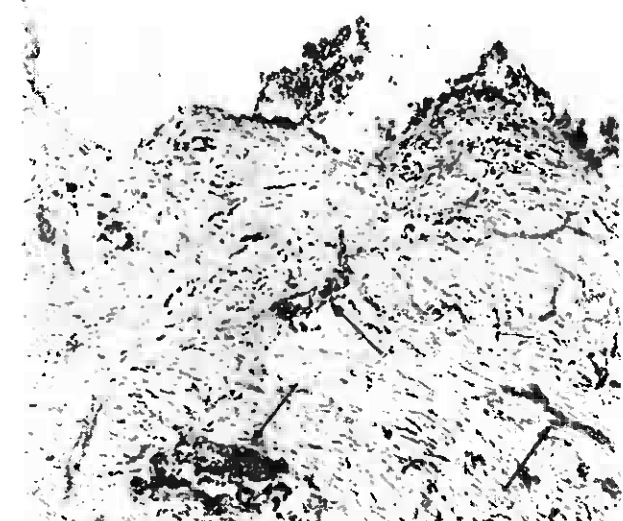


Fig. 12. Thick expanse of fibrotic pleura lined by malignant epithelium. These same malignant cells can be seen infiltrating the deeper reaches of the hyalinised pleura (arrows). (H&E x 75).

out of 15 cases defied classification owing to the paucity of the malignant tissue. It is interesting to note that although squamous cell carcinoma of the bronchus is the most prevalent tumour, yet the adenocarcinoma appears to manifest itself in the pleura more frequently than the other histological types. This phenomenon is almost certainly due to the peripheral location of the adenocarcinomatous primary in the lung. The undifferentiated variety cannot rightly claim second place, because 4 cases are not classifiable owing to the inadequacy of the malignant material.

With regard to the pathogenesis of tuberculous pleural effusion, Patterson in 1917, showed that live or dead tubercle bacilli when introduced into the pleural space of a guinea pig could produce an effusion only if the animal had already been rendered hypersensitive to tuberculosis by a previous infection. Other workers have since extended this study which suggested that tuberculous pleural effusion was essentially the result of an allergic response to a small number of bacilli in the pleural cavity. However, it is shown that a positive histological diagnosis can be obtained in more than 90% of patients with tuberculous pleural effusion with a single needle biopsy. Furthermore, some of the pleural biopsies may show extensive areas of caseation as shown in our figures 1 and 4. This clearly suggests that the infection of the pleura is by no means minimal and although the role of hypersensitivity cannot be denied, tuberculous pleurisy is mainly the result of actual infective dissemination of tubercle bacilli. If the concept of hypersensitivity is to be justified, the tuberculin reaction should invariably be strongly positive. This, however, is often not the case (Chew, 1965). Furthermore, Stead et al (1955) usually found widespread tuberculosis of the pleura at thoracotomy in patients with pleural effusion who otherwise had no radiological evidence of parenchymal disease. Confronted with this pathological picture, it seems clear that tuberculous pleural effusion should be regarded as seriously

as other forms of tuberculosis and for which chemotherapy should be the mainstay of therapy.

#### SUMMARY

A histological survey of 72 pleural biopsies from 72 patients is reported. Out of the 51 tuberculous cases, 48 pleural biopsies (94%) were diagnostic, 2 were non-specific, and one was inadequate for diagnosis. The histological features of tuberculosis in pleural biopsies are no different from those seen in other organs. Out of the 20 malignant cases, 13 pleural biopsies were diagnostic and 2 were suggestive of malignancy. Two were non-specific and three yielded inadequate material. The adenocarcinoma is the most frequent histological type seen in this survey. This gives a figure of 75% positive.

In our opinion, this safe and simple diagnostic tool of pleural biopsy has yielded the highest positive result compared to any other diagnostic measure. These results could be further improved with repeated biopsies.

The pathogenesis of tuberculous pleural effusion is briefly discussed and it is emphasized that tuberculous pleural effusion is primarily the result of widespread infection of the pleura while the role of hypersensitivity should be regarded as only of secondary importance.

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