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Etiologic Diagnosis of Pleural Effusion by Punch Biopsy of the Parietal Pleura*

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KAYNE *et al.*[1] STATED THAT 70 TO 80 per cent of pleural effusions in young adults are of tuberculous origin. Tuberculosis was considered to be of significant incidence in older people.[2] However, a recent study in Europe[3] has shown that tuberculosis is the cause only in a minority of cases of pleurisy occurring in the older age group.

The present study was undertaken to investigate the cause of pleural effusion occurring in subjects over 40 years, in the majority of whom the pleural effusion was the principal feature of the illness. Effusions in a younger age group (less than 40) were also studied to compare the relative incidence of the various etiologic factors; the choice of the dividing age period was arbitrary.

Needle biopsy of the pleura in the etiologic diagnosis of pleural effusion was first done in 1955 by the use of the Vim-Silverman needle.[4] A more satisfactory instrument[5] for this purpose has been utilized in the studies reported by Mestitz *et al.*[6] In the present study, except for a few cases in which the Vim-Silverman needle was employed, the Harefield pleural punch biopsy needle has been used. The technique was as described by Abrams[5].

Routine clinical procedures and examination of the pleural fluid for its specific gravity, protein content, cytology, and culture for ordinary pathogens were done. Culture for tubercle bacilli could not be done in most cases. Ancillary investigations such as lymph node biopsy and bronchoscopy were done wherever relevant.

Fifty-eight patients, including five women, have been studied in the older age group and 42, including ten women, in the younger age group; the total number subjected to biopsy was 100. Three subjects in each group had the biopsy repeated since the first biopsy was either a failure or was noncontributory.

The age distribution was as follows:

Younger Age Group		Older Age Group	
Age in Years	No.	Age in Years	No.
15 - 20	8	40 - 45	23
21 - 25	10	46 - 50	9
26 - 30	12	51 - 55	10
31 - 35	10	56 - 60	5
36 - 39	2	61 - 65	8
		66 - 70	2
		76 - 80	1
Total	42	Total	58

Table 1 gives the biopsy results of the 100 cases divided into two groups.

Table 2 shows the correlation between the initial diagnosis based on clinical and pleural fluid findings, and the biopsy result.

The results of this study will be discussed in relation to biopsy findings which could be categorized in the following groups of findings.

I. *Tuberculosis:* The histopathologic diagnosis is easy in the presence of typical epithelioid giant cell tubercle with caseous necrosis. Acid-fast bacilli could be demonstrated in the section in one instance. Granulomatous subpleural cellular nodules

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TABLE 1—RESULTS OF BIOPSY IN THE TWO AGE GROUPS

Group	Total	Tuber-culosis	Malig-nancy	Non-Specific: Thick-ened Pleura, Round cell infiltration etc.	Ame-biasis	Nega-tive*	Malig-nancy
Less than 40	42	15 (35.7%)	2 (4.8%)	21 (50%)	0	3 (7.1%)	1 (2.4%)
40 & above	58	18 (31.1%)	13 (22.4%)	23 (39.7%)	1 (1.7%)	2 (3.4%)	1 (1.7%)
Entire Series	100	33	15	44	1	5	2

*Biopsy not repeated.

composed mostly of epithelioid cells with minimal or no caseation or necrosis (Fig. 1) were found in three instances.

Fifteen cases in the younger age group showed definite evidence of tuberculous infection. Of these, only two had radiologic evidence of parenchymal lesion in the lung, and acid-fast bacilli in the sputum. Of the 18 cases in the older group with tuberculous infiltration of the pleura, only one had parenchymal shadows, though his sputum was negative.

It has been observed that the pathologic change in the pleura being generally widespread, a positive result could be expected in four of five cases of tuberculous effusion as compared with malignant effusions, in which the chances of a positive biopsy are likely to be distinctly less because the lesion is less generalized. However, in our study, it has been observed that nonspecific reactions are more common in patients judged to have tuberculous effusion on clinical grounds than in patients suspected to be suffering from malignancy.

II. *Malignancy:* The diagnosis is obvious when one finds groups or clumps of cells with a pattern and with features of malignancy. An embolus of malignant cells may give the clue (Fig. 2). Often the malignant cells are compressed by dense fibrous tissue.

Bizarre pleural reactive cells mimic malignancy (Fig. 3), and differentiation may be difficult. Under such circumstances a study of serial sections is necessary. Absence of subpleural infiltration aids in differentiating pleural endothelial cells from malignant cells. The differentiation may still be difficult, as in two cases reported "malignancy" by biopsy. One of these cases had a clinical course of nonmalignant effusion; a second biopsy in this patient was, however, not done before the effusion resolved. The other patient could not be traced.

Malignancy accounted for 13 out of 32 positive results (definite histologic diag-

FIGURE 1

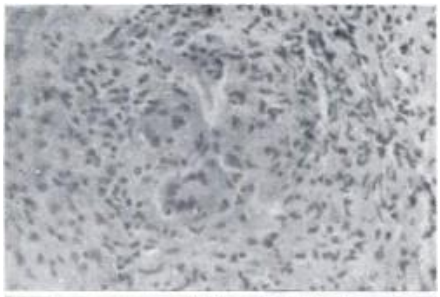

FIGURE 2

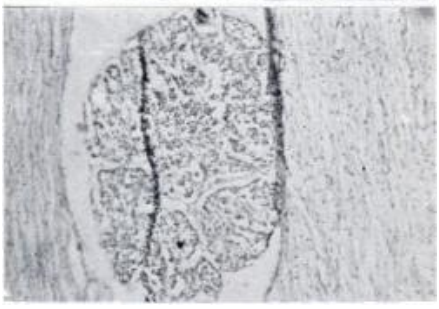

FIGURE 1: Tuberculous granulation tissue composed of mostly epithelioid cells and a few giant cells with minimal caseation. (x 160). FIGURE 2: A tumor embolus seen in the biopsy material. (x 160).

FIGURE 3

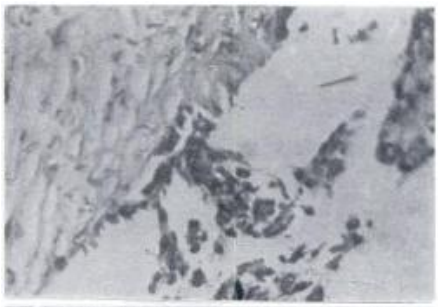

FIGURE 4

FIGURE 3: Bizarre reactive leural cells simulating malignancy. (x320). FIGURE 4: Vascular granulomatous thickening of the pleura with a moderate cellular infiltrate. (x 160).

nosis) in the older age group and two out of 17 in the younger age group. Table 3 shows the association between the pleural biopsy findings and evidence of malignancy other than in the pleura, in cases clinically suspected to have effusions of malignant origin. In two of the cases, suspicion of malignancy was entertained after antituberculosis treatment, given prior to these patients' coming under our care, was ineffective.

From the study of the biopsy material it is seldom possible to be sure of the site of origin of malignancy, unless the deposits are well-differentiated and suggestive of the primary. This would require clinical and ancillary investigations.

III. *Amebiasis:* An interesting case was that of a 58-year-old man with a right sided pleural effusion, with palpable and slightly tender liver. Exploratory thoracentesis revealed chocolate colored material in which *Entamoeba histolytica* (vegetative forms) were found. Biopsy of the pleura done at the same time showed the vegetative forms in the subpleural layer. A report on this case has been accepted for publication in *Diseases of the Chest*. This is probably the first case in which amebae have been demonstrated in the pleural biopsy material. Biopsy in another patient, in the younger age group, with chocolate colored pus in pleural cavity showed only nonspecific reaction.

IV. *Nonspecific Pleural Reaction:* This can show the following features: (a) granulation tissue with varying degrees

TABLE 2—INITIAL DIAGNOSIS OF THE CAUSE OF PLEURAL EFFUSION AND SUBSEQUENT BIOPSY DIAGNOSIS IN THE ENTIRE SERIES

Age Group	Provisional Diagnosis, on clinical and pleural fluid findings	No. of cases	Biopsy Findings					
			Tuberculosis	Malignancy	Nonspecific	Amebiasis	Malignancy	No Pleura in biopsy
Under 40	Tuberculosis	34	15		16		1	2
	Malignancy	3		2	1			
	Empyema	4			3			1
	Amebic Empyema	1			1			
40 & above	Tuberculosis	31	18		11			2
	Malignancy	16		13	3			
	Empyema	3			2		1	
	Amebic Empyema	1				1		
	Postinfarction	1			1			
	Postpneumonic	1			1			
	Nephritis	1			1			
	Congestive heart failure	4			4			

SN.

TABLE 3—ASSOCIATION BETWEEN PLEURAL BIOPSY FINDINGS AND EVIDENCE OF MALIGNANCY AT OTHER SITES

Pleural Biopsy Finding	Evidence of Malignancy at Other Sites										
	Non-Specific	Pleural fluid Suggestive radiologic shadows	Lymph node biopsy	Bronchoscopy & biopsy	Mediastinal adenopathy with pressure effects regressing with deep x-ray therapy	Primary parotid tumor (Oncocytoma)	Liver biopsy	Esophagoscopy	(Esophageal growth)	Subcutaneous nodule	NIL
Malignancy											
13 (over 40)		1	2	1	1	2	1	1			4
2 (under 40)			1	1							
	3 (over 40)			1					1	1	
	1 (under 40)										1

of capillary proliferation (Fig. 4); (b) variable degrees of infiltration with round cells and monocytes, the polymorphs predominating in subacute pyogenic effusions; (c) varying degrees of fibrosis.

Table 2 shows that nonspecific reactions have occurred in effusions of varied etiology. Some observers have also found nonspecific tissue changes either in the form of nonspecific fibrinous pleuritis or fibrous thickening of the pleura, in cases of pleural effusion ultimately concluded to be tuberculous. The point that needs to be mentioned is that proper perspective is necessary relative to the nonspecific pleural biopsy findings because conditions other than tuberculosis, including collagen diseases and pleural counterpart of acute nonspecific pericarditis, probably due to a virus, might cause them.

V. *Incidental Lung Biopsy:* In this series, tiny bits of lung tissue were identified histologically in six cases which included a case of congestive heart failure in which chronic venous congestion was observed in the lung. No untoward effect was noticed in the post-biopsy period, in these cases.

VI. *Negative Biopsy:* Inadequate or no pleural tissue was obtained in the first instance in five cases in either group, three having been attempted with the Vim-Silverman needle.

CONCLUSIONS

In this series, tuberculosis was found to be the etiologic feature in 31.1 per cent of patients, 40 years old and above, and malignancy in 22.4 per cent, in contrast with 35.7 per cent and 4.8 per cent respectively, in the younger group, as proved by biopsy of the pleura. It is difficult to assess the significance of nonspecific pleural biopsy findings. A larger number of cases and a longer follow up, and ancillary studies, like culture of the pleural fluid and of the biopsy material will be necessary for a satisfactory evaluation.

Our experience with needle biopsy of the pleura would suggest that it is only of value as a supplement to the more orthodox investigations and cannot supplant the latter. This is because only 40.5 per cent in the younger age group and 55.2 per cent in the older age group had outright positive reports. We have had no untoward effect due to the biopsy procedure itself.

SUMMARY

Needle biopsy of the pleura using Harefield pleural biopsy punch, has been performed in 100 subjects, 58 of whom were 40 years of age or over, in order to arrive at a histologic diagnosis. Ancillary investigations such as bronchoscopy and lymph node biopsy have been done where necessary and feasible.

In 18 of the 58 in the older age group and in 15 of the 42 in the younger age group, the biopsy showed lesions suggestive of tuberculous infection; 13 in the older age group and two in the other showed evidence of malignancy; 23 in the older and 21 in the younger group showed nonspecific changes. Vegetative forms of *Entamoeba histolytica* were demonstrated in the biopsy material in one case. Biopsy, performed on one occasion only was a failure in five cases.

No untoward effects were noticed as a consequence of the procedure.

Acknowledgment

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Resumen

La biopsia de la pleura por medio de aguja usando el diapositivo de Harefield para biopsia pleural ha sido llevada a cabo en 100 enfermos, 58 de los cuales fueron de 40 años de edad o más, a fin de llegar a un diagnóstico histológico. Las investigaciones auxiliares, tales como la broncoscopía y la biopsia de ganglios linfáticos se han hecho cuando fue necesario y posible.

En 18 de los 58, del grupo de mayor edad, y en 15 de los 42 de la edad más joven la biopsia mostró lesiones sugerentes de infección tuberculosa; 13 en el grupo de mayor edad y 2 en el otro mostraron evidencia de malignidad; 23 en el grupo de mayor edad y 21 en los jóvenes mostraron cambios no específicos. Las formas vegetativas de *Entamoeba histolytica* se mostraron en la biopsia en un caso. Sólo uno de cinco casos de biopsia fue fallido. No hubo efectos desagradables como consecuencia del procedimiento.

Resumé

Une biopsie à l'aiguille avec l'appareil à biopsie pleurale de Harefield a été pratiquée chez 100 sujets, 58 d'entre eux étant âgés de 40 ans ou plus, afin de permettre un diagnostic histologique. Des investigations complémentaires, telles que bronchoscopie, biopsie ganglionnaire ont été faites lorsqu'elles furent nécessaires ou praticables.

Pour 18 des 58 malades du groupe âgé et pour 15 des 42 malades du groupe plus jeune, la biopsie montra des lésions évocatrices d'infection tuberculeuse; 13 malades du groupe âgé et deux de l'autre groupe montrèrent la preuve d'une affection maligne; 23 du groupe âgé et 21 du groupe plus jeune montrèrent des altérations atypiques.

Des formes végétatives *d'entamoeba histolytica* furent mises en évidence sur le matériel biopsique dans un cas. Une biopsie pratiquée à une seule reprise dans cinq cas fut un échec. On ne nota aucun effet nocif à la suite de cette technique.

Zusammenfassung

Es wurde eine Nadel-Biopsie der Pleura unter Verwendung der Pleura-Biopsie-Stanze nach Harefield bei 100 Personen vorgenommen, von denen 58 40 Jahre oder älter waren, um eine histologische Diagnose zu gewinnen. Ergänzende Untersuchungen wie etwa Bronchoskopie, Lymphknotenbiopsie wurden dann ausgeführt, wenn sie erforderlich und durchführbar waren.

Bei 18 der 58 Personen in der älteren Altersklasse und bei 15 der 42 in der jüngeren Altersklasse zeigte die Biopsie Veränderungen, die auf eine tuberkulöse Infektion verdächtig waren; 13 aus der älteren Altersgruppe und 2 in der anderen Gruppe zeigten bösartige Veränderungen; 23 der älteren und 21 der jüngeren Gruppe hatten unspezifische Veränderungen. Eine vegetative Form der Entamöba histolytica wurde im bioptischen Material eines Falles nachgewiesen. Eine nur einmal vorgenommene Biopsie war bei 5 Fällen ein Versager. Als Folge der Methode nota aucun effet nocif à la suite de cette technique.

References

1 Kayne, G. G., Pagel W. and O'Shaughnessy, L.: *Pulmonary Tuberculosis-Pathology, Diagnosis, Management and Prevention*, 3rd Edition, Oxford University Press, London, 1953.

2 Robertson, R. F.: "Primary Tuberculous Pleural Effusion in Older Age Groups," *Brit. Med. J.*, 52:133, 1952.

3 Von Frisch, A.: "Pleurisy in the Aged — Über Greisenpleuritis," *Deutsch. Med. Wochenschr.*, 93:114, 1958.

4 De Francis, N., Kloske, E. and Albano, E.: "Needle Biopsy of the Parietal Pleura—A Preliminary Report", *New Eng. J. Med.*, 252: 948, 1955.

5 Abrams, L. D.: "A Pleural - Biopsy Punch," *Lancet*, 1:30, 1958.

6 Mestitz P., Purves, M. J. and Pollard, A. C.: "Pleural Biopsy in the Diagnosis of Pleural Effusion," *Lancet*, 2:1349, 1958.

7 Richert, J. H., Wier, J. A., Salyer, J. M. and Beyer, J. C.: "The Reliability of Tissue Diagnosis of Pleurisy—A Preliminary Report," *Ann. Int. Med.*, 52:320, 1960.