Acta Medica Okayama

Volume 14, *Issue* 3 1960 *Article* 4

SEPTEMBER 1960

Report of results of pleural biopsy (Needle biopsy and open biopsy) in 108 cases and 245 biopsies

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Abstract

1. The results of 245 pleural biopsies perfomed in 108 patients including 219 pleural needle biopsies and 26 pleural open biopsies were reported. The method of pleural biopsy seems to be superior to any other currently available diagnostic procedures for the etiological diagnosis of pleurisy. 2. When the pleural needle biopsy is compared with the pleural open biopsy, the former method has definite advantages over the open biopsy. The pleural needle biopsy is simple, repeatable and has almost no complication. The method of pleural needle biopsy is the initial method of choice as Donohoe correctly stated and should be employed in every cases of the pleurisy to confirm the etiological diagnosis. The open biopsy should be reserved only for those cases in whom the needle biopsy had not proved satisfactory. 3. Utilizing the method of needle biopsy, the pathological diagnosis was made in 86 per cent of our cases at the initial biopsy. By repeated needle biopsies, the results have improved to 91-92 per cent. 4. Most of the failures of the pleural needle biopsy were noted at the early stage of the study due to the unfamiliarity of the biopsy technique and later due to the incooperation of the patients. 5. The presence of the free pleural fluid serves as a convenient guide for the performance of the needle biopsy but successful needle biopsy was easily done without presence of pleural fluid when there is adequate pleural thickening. 6. 63-75 per cent of our diagnosed cases were proved to have granulomatous pleuritis, 13-31 per cent non-specific pleuritis and 5.4-5.8 per cent eosinophilic pleuritis due to paragonomiasis. The distribution of this pathological diagnosis seems to reflect quite well the actual picture of incidences of pleurisy of various different etiology in young adults in Korea. 7. The relationship of the success in obtaining adequate tissue by needle biopsy and interval between onset of symptom and biopsy was discussed. It was found that the interval has no significant effect on the production of adequate tissue by needle biopsy if the time elapsed is 4 weeks or more from the onset of symptom. 8. The significance of the pathological findings of ranulomatous pleuritis at one biopsy and non-specific pleuritis at another biopsy in the same patient was discussed. It is concluded that the single finding of nonspecific pleuritis at one needle biopsy cannot rule out the presence of granulomatous pleuritis and it is recommended that pleural biopsy be repeated whenever necessary. 9. The diagnostic significance of the chemical analysis of the pleural fluid was discussed in correlation with the results of the pleural needle biopsies. It is concluded that the number of examinations are not quite sufficient to draw any definite conclusion at the present stage of our study. 10. The finding of sanguinous pleural fluid in the patient of granulomatous pleuritis is

quite high (72.7 %) and it was found that the sanguinous pleural fluid was most frequently found in the patients with granulomatous pleuritis in non-cancerous age. 11. Two groups of pleurisy patients with or without parenchymal lung lesion on chest X-ray were discussed in correlation with the results of the needle biopsy. It was found that the incidence of the pathological evidence of granulomatous inflammation on the biopsy specimens in these two groups is almost the same regardless of the presence of the demonstrable parenchymal lung lesion. 12. Histopathological finding of granulomatous pleuritis was discussed in conjunction with the significance of two types of tubercles, the soft tubercles and hard tubercles. In all specimens diagnosed as granulomatous pleuritis granulomas were demonstrated ranging from large, conglomerate tubercles with central caseation or giant cells to small granulomas without central caseation or Langhans' giant cells. 13. Histopathological significance of the finding of non-specific pleuritis on the biopsy specimens was discussed and the existence of a specific entity of "non-specific pleuritis" which is equivalent to the non-specific inflammation of the pericardium. 14. Cases of pleurisy due to paragonomiasis were discussed and the need of specific attention for search of new cases was emphasized.

Acta Med. Okayama 14, 185—213 (1960).

REPORT OF RESULTS OF PLEURAL BIOPSY (NEEDLE BIOPSY AND OPEN BIOPSY) IN 108 CASES AND 245 BIOPSIES

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Received for publication, June 9, 1960

The entity of pleurisy presents many diagnostic problems in Korea. It is generally stated that from 80 to 90 per cent of the otherwise unexplained cases of exudative pleurisy in young persons are of tuberculous origin. However, it is rather difficult to obtain the mycobacterium tuberculosa in the pleural fluid and gastric washing in tuberculous pleuritis in the ordinary hospital facilities. The data of the chemical analysis of the pleural fluid are not quite sufficient to yield definitive diagnostic evidence. The practice of the gastric washing in the patients of pleurisy for the detection of the acid-fast bacilli was discarded at our hospital due to the poor result and the dislike of the patients. The isolation of the etiological organism from the pleural fluid is time-consuming and the results have been extremely poor at our hospital. The physicians are, most of the time, forced to establish the diagnosis in the earliest time possible and it is not uncommon to have to institute the antituberculous treatment before the diagnosis is confirmed. For long a suitable procedure has been sought for the early establishment of the etiological diagnosis of the pleural effusion. The needle biopsy of the parietal pleura is quite simple and appears to be most useful for this purpose. Since Nicholas De Francis and associates[1] first in 1955 published an article on the needle biopsy of the parietal pleura in the patients of pleural effusion, considerable number of articles regarding the usefulness of this procedure as a diagnostic aid in the presence of pleural effusion have accumulated in the medical literature[2,3,4]. Recently R. F. Donohoe[5,6] was successful in establishing diagnosis in 73 per cent of 45 cases of pleural effusion and according to Mestitz needle biopsy established the diagnosis in 80 per cent of the patients with tuberculous effusion and in 60 per cent of those with malignant effusions.

In view of the fact that the Army has considerable number of pleurisy cases and the control of the tuberculous infections is one of the major pro-

The outline of this study was presented at the Annual Session of The Korean Medical Association, Pusan, Korea, October 11, 1959.

jects the Korean Army is confronted with, the study of the needle biopsy was undertaken for the purpose of early establishment of the etiological diagnosis and prompt institution of proper treatment in the presence of pleurisy. The major objectives of this study were (1) to establish the significance of the needle biopsy and open biopsy of the parietal pleura as the diagnostic procedure in the patients of pleurisy, (2) to evaluate the diagnostic significance of the study of pleural fluid in correlation with the results of pleural biopsy(3), to study and discuss the pathology and pathogenesis of idiopathic pleural effusion, eosinophilic plseuritis, and tuberculous pleuritis (4) to perform repeated needle biopsy for the study of pathological changes of the pleural lesions during the course of the illness and(5) to study the influence of the chemotherapy on the pleural lesion in the idiopathic pleuritis and tuberculous pleuritis. This report concerns the data accumulated from July 1958 to November 1959 at the Capital Army Hospital in Korea.

METHOD AND MATERIAL

The method of needle biopsy is that which has been described by De Francis and associates in 1955. An ordinary thoracentesis tray with the addition of a Vim-Silverman biopsy needle and two Kelly Clamps was used as the pleural biopsy set[7]. Ordinarily the premedication is not required in most of the patients. The biopsy site is prepared with Mercurochrome solution and alcohol. Thoracentesis was done in the usual manner after two per cent procaine solution is used for local anesthesia. When the pleural effusion is profuse to produce the respiratory difficulty, sufficient amount of the effusion is evacuated in addition to the amount of fluid required for the chemical and bacteriological study. After the aspiration of fluid the needle is withdrawn gradually until no fluid can be aspirated. The needle is withdrawn a centimeter and a Kelly Clamp is applied on the needle at the skin surface. The distance between the tip of the needle and the Kelly Clamp is then marked on the Vim-Silverman biopsy needle using another Kelly Clamp. The biopsy needle so marked with Kelly Clamp is inserted and advanced to the level of the clamp. Then the obturator is removed and the cutting needle of the Vim-Silverman needle is inserted to its full length. The outer needle is advanced a centimeter while the cutting needle is held in place. The entire needle is rotated 360 degrees and then removed. The specimen is found between two blades of the cutting needle.

When the free pleural fluid is not aspirated and there appears to be present a pleural thickening, the aspirating needle is carefully pushed

forward until the resistance becomes least and then withdrawn a centimeter. A Kelly Clamp is applied on the needle at the skin surface. This procedure is called blind needle biopsy since it ia done without the guidance of free pleural fluid.

The open surgical biopsy in this study was done according to the method described by Small and his associates in 1955[8]. The thoracic cavity was entered through the sixth, seventh or eighth intercostal space on the appropriate side. The size of the incision was held to a minimum, 6 or 8 inches, but all cases allowed the introduction of the examining hands and a small retractor. The entire thoracic cavity could be explored with ease, and adequate biopsy specimen of the involved portion could be taken. Thus, in many cases, exposure was sufficient to establish a diagnosis and yet produce a minimum of postoperative distress[9,10].

There are 108 patients in this study, of whom 106 were males and 2 females. All patients except two were military personnels. The youngest patient was 19, the oldest 45 and the average age was 24. Out of 108 patients 7 patients had open biopsy only without needle biopsy and 101 patients underwent needle biopsy. 19 out of 101 patients had both needle biopsy and open biopsy. In this study the open biopsy was done only for the comparative study of diagnostic significance of needle biopsy and open biopsy. Total 245 biopsies were performed in 108 patients including 26 open biopsies and 219 needle biopsies. In a group of patients needle biopsies were repeated with an interval of one month after anti-tuberculous medication was started to study the pathological changes of the pleural lesion during the course of illness and the influence of the chemotherapy on the pleural lesion. 52 patients had only one needle biopsy, 49 patients two or more needle biopsies, 36 patients three biopsies (Table 2).

In all patients the chest X-ray, erythrocyte sedimentation rate, tuberculin skin test, complete blood count, urinalysis, sputum examination for acid-fast bacilli and paragonimus Westermani, stool examination for parasites and examination of pleural fluid for organism and chemical analysis at initial needle biopsy on admission. Chest X-ray, erythrocyte sedimentation rate and study of pleural fluid were repeated at each time when the repeated biopsy was performed at monthly interval. In patients whose history and/or pathological examination of the biopsy specimen suggested the paragonomiasis, paragonimus antigen skin test was done. According to Tominaga, the reliability of paragonimus antigen skin test is very high as 98.3 per cent.

In chest X-ray pleurisy was found in the right side of chest in 55 cases, in the left side in 44 cases, in both sides in 6 cases, in right side

with mediastinum in 2 cases and in left side with mediastinum in 1 case. 14 cases revealed parenchymal lung lesion in chest X-ray and in 94 cases the parenchymal lung fields were free. Positive tuberculin skin test was noted in all patients and paragonimus antigen skin test was positive in 6 cases. There are some possibilities that paragonimus antigen skin test may turn out to be positive in more patients, since this test was limited only in strongly suspected patients.

Bacteriological study of sputum proved to be positive for acid-fast bacilli in 2 cases and for paragonimus Westermani in 4 cases. Smear and culture of pleural fluid for acid-fast bacilli were studied in all patients who yielded free pleural fluid and the results were extremely poor. Among 219 thoracentesis pleural fluid was obtained in 101 biopsies. The character of the pleural fluid was serous in 90 thoracentesis and sanguinous in 11. Clinical data and laboratory studies were summarized in Table 1.

RESULTS

Needle biopsy : 101 cases had initial needle biopsy on admission and adequate pleural tissue for the pathological diagnosis was obtained in 87 cases (86%). In 14 patients (13.9%) the tissue was inadequate for the pathological examination (Table 3). Of the 87 cases (Table 4), pathological evidence of granulomatous pleuritis, with or without caseation, was demonstrated in 55 (63.2%), eosinophilic infiltration in 5 (5.8%), normal pleural tissue in 1 (1.1%) and non-specific pleuritis was found in the remaining 26 (29.9%). One of the 55 cases, whose pleural biopsy specimen showed granulomatous pleuritis, had past history of paragonimiasis and positive skin test for paragonimus infection. One case in 26 non-specific pleuritis group underwent the supra-clavicular lymphnode biopsy to have the pathological diagnosis of tuberculous lymphadenitis. Of 14 cases, whose initial biopsy specimen were inadequate for the pathological diagnosis, the second needle biopsy showed respectively granulomatous pleuritis and non-specific pleuritis in 2 patients. The second biopsy yielded also inadequate tissue for diagnosis but the third biopsy proved to be granulomatous pleuritis in one. Open biopsy was performed in 3 cases. Evidence of granulomatous pleuritis was obtained in 2 and non-specific pleuritis in one. In 5 cases only one needle biopsy was performed and no further investigation was followed (Table 5). Out of 101 cases, 52 cases had only one needle biopsy. 49 cases, however, had second needle biopsy approximately one month after the initial one. When the results of both initial and second biopsies are considered together, 92 cases (91.1%) produced adequate pleural

Table 1

Clinical Data and Laboratory Studies on Pleural Fluid.

	Number of cases
TOTAL CASES	108
TOTAL BIOPSIES	245
AGE :	
Range	19—45
Mean	24
SEX :	
Male	106
Female	2
X-RAY FINDING :	
Pleurisy in Right Side	55
Pleurisy in Left Side	44
Both Sides	6
Right Side with Mediastinum	2
Left Side with Mediastinum	1
With Parenchymal Lung Lesion	14
Negative Lung Lesion	94
CLINICAL AND LABORATORY EXAMINATION :	
Positive Skin Tests	
Tuberculin	11 Cases
P. W.	6
Bacteriology	
AFB in Sputum	2
P. W. in Sputum	4
AFB in Pleural Fluid	
Smear	0
Culture	Not Satisfactory
AFB in Pleural Tissue	Not Satisfactory
Pleural Fluid	
Fluid was Obtained by Thoracentesis	101
No Fluid	118
Total	219
Total Thoracentesis	101
Serous Fluid	90
Sanguinous Fluid	11
Protein	83
Maximum	11.2 gm %
Minimum	1.1 gm %
Average	3.9 gm %
Chloride	58
Maximum	130 m Eq
Minimum	99 m Eq
Average	109 m Eq
Sugar	64
Maximum	133 mg %
Minimum	14 mg %
Average	76.5 mg %
Cell Count	88
Predominantly Lymphocytes	86
Eosinophils in Fluid	2

Table 2

	Number of cases
TOTAL CASES	108
Needle Biopsy	101
Open Biopsy	26
Open Biopsy Only	7
Needle Biopsy Plus Open Biopsy	19
TOTAL BIOPSIES	245
Open Biopsies	26
Needle Biopsies	219
One Needle Biopsy Only	52
Two Neeele Biopsies or More	49
Three Needle Biopsies or More	36
Four Needle Biopsies or More	26
Five Needle Biopsies or More	7

Table 3 Results of Initial Biopsy of the Parietal Pleura in 101 Cases

Results	Number of Cases	Percentage
Diagnosed by Needle Biopsy	87	86.1
Tissue was Inadequate for Diagnosis	14	13.9
Total	101	100.0%

Table 4 Pathological Results of Needle Biopsy of 87 Cases in which Adequate Tissue was obtained at Initial Biopsy

Pathological Diagnosis	Number of Cases	Percentage
Granulomatous Pleuritis*	55	63.2
Eosinophilic Pleuritis	5	5.8
Non-Specific Pleritis △	26	29.9
Normal Pleura	1	1.1
Total	87	100.0%

* Lee, Hyun-Kyun has Past History of Paragonomiasis and Positive Skin Test.

△ Kim, Tai-Shik was proved to be Tuberculous by Supraclavicular Lymphnode Biopsy.

tissue for the pathological diagnosis and in 9 cases (8.9%) the tissue was inadequate for the pathological examination (Table 6). Thus, by doing second needle biopsy adequate tissue for the pathological diagnosis was obtained in 5 more cases, in which previously the initial needle biopsy was unsuccessful to obtain the adequate tissue. The pathological diagnosis of needle biopsy of 92 cases, in which adequate tissue was obtained at initial

Table 5

Results obtained in 14 Cases in Which Tissue was Inadequate for Diagnosis Initially.

	Number of cases
2nd Needle Biopsy Proved as Follows :	
Granulomatous Pleuritis	4
Non-Specific Chronic Pleuritis	1
2nd Needle Biopsy yielded also Inadequate Tissue for Diagnosis, but 3rd Biopsy was proved to be Granulomatous Pleuritis	1
Open Biopsy yielded Following Results.	
Granulomatous Pleuritis	2
Non-Specific Pleuritis	1
Only one Needle Biopsy was Performed Without any Further Investigation	5

Table 6 Results of Initial and 2nd Needle Biopsies of the Parietal Pleura in 101 Cases.

Results	Number of cases	Percentage
Diagnosed by Needle Biopsy	92	91.1
Tissue was Inadequate for Diagnosis	9	8.9
Total	101	100.0%

or second biopsy or both biopsies, diagnosis of granulomatous pleuritis were made in 67 cases (72.8%), eosinophilic pleuritis in 5 cases (5.4%), non-specific pleuritis in 19 cases (20.7%) and normal pleural tissue was found in 1 case (1.1%) (Table 7). Among 49 cases, who had second needle biopsy, 36 cases had third needle biopsy approximately one month after the second biopsy. When the results of all three needle biopsies are summarized together, adequate pleural tissue for the pathological diagnosis was obtained in 93 cases (92.1%) and 8 cases remained undiagnosed

Table 7 Pathological Diagnosis of Needle Biopsy of 92 cases in Which Adequate Tissue was Obtained at Initial or 2nd Biopsy or Both Biopsies

Pathological Diagnosis	No. of cases	%
Granulomatous Pleuritis	67	72.8
Eosinophilic Pleuritis	5	5.4
Non-Specific Pleuritis	19	20.7
Normal	1	1.1
Total	92	100.0%

Table 8 Results of Initial, 2nd and 3rd Needle Biopsies of the Parietal Pleura in 101 Cases

Results	No. of Cases	%
Diagnosed by Needle Biopsy	93	92.1
Tissue was Inadequate for Diagnosis	8*	7.9
Total	101	100.0

* Three cases out of 8 proved to have granulomatous pleuritis in two and non-specific pleuritis in one case by open biopsy. Remaining five cases had only one needle biopsy without any further investigation.

by needle biopsy (Table 8). Of these 8 cases 5 cases had only one needle biopsy without any further repeated trial. When the overall results of all the three biopsies are compared with the results of the initial and the second biopsies, we find that the results are very similar. There are only one per cent increase in the percentage of success in obtaining adequate tissue by doing third biopsy. There were, however, 5 per cent increase by doing second biopsy when the result of initial biopsy and those of both initial and second biopsies are compared. The pathological diagnosis of needle biopsy of 93 cases, in which adequate tissue was obtained at the initial, second and third biopsies revealed granulomatous pleuritis in 70 cases (75.2%), eosinophilic pleuritis in 5 (5.4%), non-specific pleuritis in 17 (18.3%) and normal in 1 (1.1%) (Table 9). Approximately one

Table 9 Pathological Diagnosis of Needle Biopsy of 93 Cases in Which Adequate Tissue was obtained at Initial, 2nd and 3rd Biopsies.

Pathological Diagnosis	No. of cases	%
Granulomatous Pleuritis	70	75.2
Eosinophilic Pleuritis	5	5.4
Non-Specific Pleuritis	17	18.3
Normal	1	1.1
Total	93	100.0

month after the third biopsy 26 cases had the fourth needle biopsy and 7 cases fifth biopsy one month following the fourth biopsy. There were altogether 219 needle biopsies performed in 101 cases. Out of 219 biopsies, 193 biopsies (88.1%) produced adequate tissue for the pathological diagnosis and the tissue was inadequate for the pathological examination in 26 biopsies (11.9%) (Table 10). In five biopsies needle biopsy produced

Table 10 Results of Needle Biopsy of the Parietal Pleura in 219 Needle Biopsies

Results	No. of cases	%
Diagnosed by Needle Biopsy *	193	88.1
Tissue was Inadequate for Diagnosis △	26	11.9
Total	219	100.0

* One Cases with Spieen Tissue.
△ Liver Tissue in Five Biopsies.

liver tissue instead of pleural tissue. The pathological results of 193 needle biopsies, in which adequate tissue was obtained, revealed granulomatous pleuritis in 121 biopsies (62.7%), non-specific pleuritis 60 (31.1%), eosinophilic pleuritis 11 (5.7%) and normal pleural tissue in 1 (0.5%) (Table 11).

Table 11 Pathological Results of 193 Needle Biopsies in Which Adequate Tissue was Obtained.

Results	No. of cases	%
Granulomatous Pleuritis	121	62.7
Non-Specific Pleuritis	60	31.1
Eosinophilic Pleuritis	11	5.7
Normal	1	0.5
Total	193	100.0

The comparison of the results of the needle biopsy in four groups (group of initial needle biopsy, group of initial and 2nd needle biopsies, group of initial, 2nd and 3rd biopsies and group of total biopsies) is shown in Fig. 1. According to this study the results of the initial needle biopsy and that of total needle biopsies are relatively similar, being successful in obtaining adequate tissue in 86.1 per cent of the cases in the former group and 88.1 per cent in the latter group. When these results are compared with the Donohoe's results, adequate tissues were obtained in more cases in our series. The pathological diagnosis of the needle biopsy in four groups are illustrated in Fig. 2. 63—75 per cent of our cases proved to have granulomatous pleuritis, 18—31 per cent non-specific pleuritis, and 5.4—5.8 per cent eosinophilic pleuritis. There was no malignancy. These results are quite understandable when we consider the age of the cases under study. The distribution of the pathological diagnosis shown in Fig. 2 seems to reflect quite well the actual picture of incidences of pleurisy

FIG. 1 Results of Needle and Open Biopsy

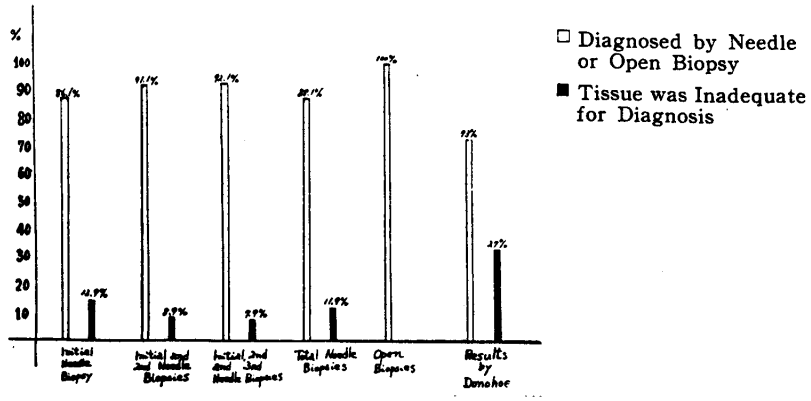
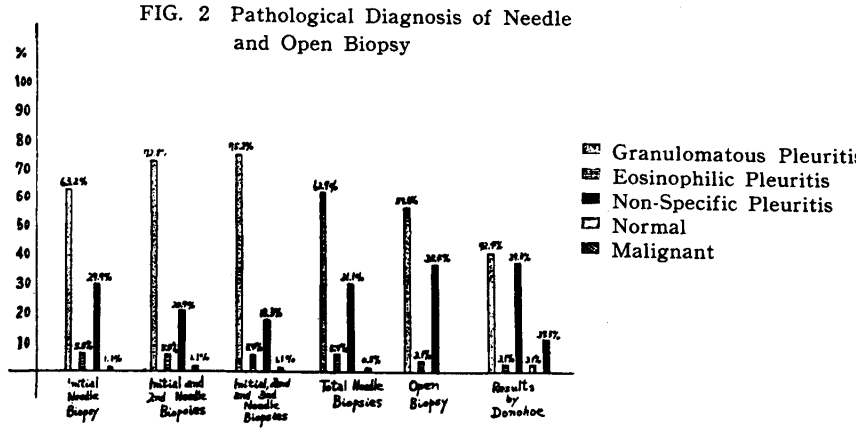


FIG. 2 Pathological Diagnosis of Needle and Open Biopsy



of various different etiology in young adults in Korea.

Open Biopsy, Comparison of Open Biopsy and Needle Biopsy : Open biopsy of the parietal pleura in pleural effusion or pleural adhesion by means of small thoracotomy[11,12], which was described previously, was performed in 26 cases. These 26 cases were selected arbitrarily among pleurisy patients for the purpose of the comparative study of the results obtained by these two methods. In all the 26 cases it was successful to obtain adequate pleural tissue for the pathological diagnosis as shown in Table 12. Granulomatous pleuritis was diagnosed in 15 cases (57.7%), eosinophilic pleuritis in 1 (3.8%), and non-specific pleuritis in 10 (38.5%). The incidence of granulomatous pleuritis is lower in this open biopsy group compared with the needle biopsy group possibly due to the fact that the former

Table 12 Results of Open Biopsy in 26 Cases. All Cases of Open Biopsy Yielded Adequate Tissue for Diagnosis

Pathological Diagnosis	No. of cases	%
Granulomatous Pleuritis	15	57.7
Eosinophilic Pleuritis	1	3.8
Non-Specific Pleuritis	10	38.5
Total	26	100.0

included the cases of pleural adhesion. Among 26 cases who had open biopsy, 19 cases had both needle biopsy and open biopsy. The comparison between the pathological results of these two groups are shown in Table 13. The evidence of granulomatous pleuritis was demonstrated in almost the same number of cases; in 10 cases (53%) in the former group and in 11 cases (58%) in the latter group. Non-specific pleuritis was found in 3 cases (16%) in the former group and in 7 cases (37%) in the latter group. Inadequate tissue was obtained in 5 cases (26%) in the former and all the biopsies were successful in the latter. Thus, it is found that the results of the patholgical diagnosis are almost equal in both methods indicating that the method of needle biopsy is as satisfactory as the methods of open biopsy for the diagnostic purpose of pleural effusion.

Table 13 Comparison of Results Obtained in 19 Cases by Needle Biopsy and Open Biopsy

Biopsy / Diagnosis	Needle Biopsy		Open Biopsy	
	Number	%	Number	%
Granulomatous Pleuritis	10	53%	11	58%
Eosinophilic Pleuritis	1	5%	1	5%
Non-Specific Pleuritis	3	16%	7	37%
Inadequate Tissue for Diagnosis	5	26%	0	0%
Total	19	100%	19	100%

Of 26 cases of open biopsy group, 3 cases developed hemoptysis immediately following the biopsy. The hemoptysis persisted for one week to 10 days and then disappeared spontaneously. The incidence of hemoptysis appears to occur more often when there is thick adhesion between the parietal and visceral pleura and the adhered visceral pleura is resected at the time of biopsy. There was, however, no incidence of

broncho-pleural fistula. Subcutaneous emphysema was noted in one case following the biopsy and one case developed empyema after the thoracotomy. This last case, who doveloped empyema, turned out to have pleurisy due to the paragonomiasis. It is generally believed that the pleurisy due to the paragonimus Westermani infection is more prone to develop secondary infection after the surgical intervention. There was no single significant complication among the group of needle biopsy (Table 14). In view of the fact that the results obtained by needle biopsy is as satisfactory as the results of open biopsy, that there is no complication following the needle biopsy and that the needle biopsy is quite simple to perform, the pleural needle biopsy would be the first choice as the diagnostic procedure in the presence of pleurisy.

Table 14 Complication Following Needle and Open Biopsy

Conplication / Biopsy	Total Biopsies	Hemoptysis		Sobcutaneous Emphysema		Empyema	
		No.	%	No.	%	No.	%
Neeble Biopsy	219	0	0	0	0	0	0
Open Biopsy	26	3	11%	1	3%	1	3%

Interval between onset of symptom and biopsy : The initial needle biopsy was performed as soon as the patient was admitted to the hospital. Some patients, however, were transferred from the evacuation hospital or other medical units in the combat zone and the patients had repeated needle biopsies at one month's interval. Of 219 total needle biopsies, 19 needle biopsies were performed upon 4 weeks after onset of symptoms; 47 8 weeks after the onset; 31 12 weeks after the onset; 35 16 weeks after the onset and 23 each 20 and 24 weeks after the onset of symptoms. In 9 biopsies, more than 40 weeks elapsed between the time of onset of symptoms and biopsies. Fig. 3 illustrates the numerical incidence of pathological diagnosis of granulomatous pleuritis, non-specific pleuritis, and inadequate tissue obtained in each group of biopsies with appropriate intervals. Fig. 4 shows the incidence of pathological diagnosis in percentage according to the interval between the onset of symptom and biopsies. It is evident from these illustrations that no significant difference can be found to obtain adequate pleural tissue for diagnosis regardless of interval if it takes 4 weeks or more between the onset of symptoms and biopsies.

The incidence of pathological diagnosis of granulomatous pleuritis,

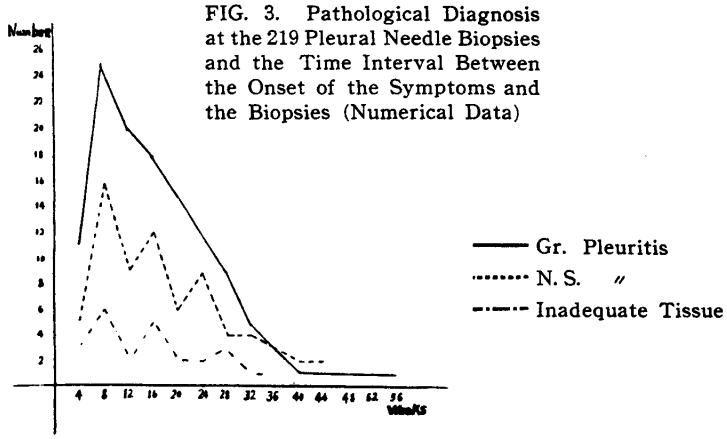


FIG. 3. Pathological Diagnosis at the 219 Pleural Needle Biopsies and the Time Interval Between the Onset of the Symptoms and the Biopsies (Numerical Data)

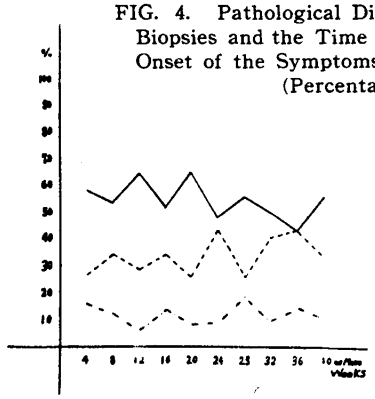


FIG. 4. Pathological Diagnosis of 219 Needle Biopsies and the Time Interval Between the Onset of the Symptoms and the Biopsies. (Percentage)

non-specific pleuritis and inadequate tissue are almost the same at each 4-week interval, granulomatous pleuritis being around 50—70 per cent, non-specific pleuritis 25—35 per cent and inadequate tissue 10—18 per cent. After lapse of 24 weeks however, the incidence of non-specific pleuritis shows increase and the granulomatous pleuritis decrease.

Table 15 shows the pathological diagnosis of repeated needle biopsies at 4 weeks' interval in 36 cases who had more than three needle biopsies. Granulomatous pleuritis was demonstrated in 20 cases at the first biopsy, in 19 cases at the second and in 21 cases at the third biopsy. Non-specific pleuritis was demonstrated in 10 cases at the initial biopsy, in 9 cases at the second and in 14 cases at the third biopsy. Inadequate tissue was obtained at the first biopsy in 6 cases, at the second biopsy in 8 cases and in only 1 case at the third biopsy. In only one case the needle biopsy failed repeatedly to produce adequate tissue at the first and second needle

biopsy. The third biopsy, however, was succcessful to obtain adequate tissue to prove granulomatous pleuritis. In remaining 5 cases, who failed to produce adequate tissue at the initial biopsy, the second biopsy produced adequate tissue to be diagnosed as granulomatous pleuritis or non-specific pleuritis. The failures to produce adequate tissue at the second biopsy were noted in patients who had been already diagnosed successfully at the first biopsy. Thus, it is clear from these reslts the interval between the onset of symptoms and biopsy has little to do on the failure of obtaining adequate pleural tissue for pathological diagnosis. According to the Table 15, most of the cases were constantly found to have pathological diagnosis

Table 15 Pathological Diagnosis of Repeated Needle Biopsies in 36 cases who Had More than Three Needle Biopsies.

case No.	1st Biopsy	2nd Biopsy	3rd Biopsy	4th Biopsy	5th Biopsy
1	Gr.	Gr.	Gr.	Gr.	Gr.
3	Gr.	Inad.	Gr.	N. S.	
4	Gr.	Inad.	Gr.	Gr.	Gr.
5	N. S.	N. S.	Gr.	Gr.	Gr.
6	Inad.	Gr.	Gr.	Gr.	Gr.
7	N. S.	Gr.	Gr.	N. S.	
8	Gr.	N. S.	N. S.	N. S.	
9	Inad.	Gr.	Gr.	Gr.	
10	Gr.	N. S.	N. S.	N. S.	
11	Inad.	Inad.	Gr.	Gr.	
12	Gr.	Gr.	Gr.	Gr.	Gr.
13	Gr.	N. S.	Gr.	N. S.	
14	Gr.	Gr.	N. S.		
15	Gr.	Gr.	Gr.		
26	Gr.	Gr.	Gr.		
27	Gr.	Inad.	N. S.	N. S.	
28	Gr.	Gr.	Gr.		
29	N. S.	N. S.	N. S.	Gr.	
31	Inad.	N. S.	N. S.	N. S.	
32	Inad.	Gr.	N. S.		
33	Gr.	Gr.	Gr.	Gr.	
35	N. S.	N. S.	N. S.	N. S.	
63	Gr.	Inad.	N. S.		
64	N. S.	N. S.	Gr.	N. S.	
65	N. S.	Gr.	N. S.	Gr.	
66	N. S.	Gr.	Inad.	Inad.	
68	Gr.	Gr.	Gr.	Gr.	
69	Gr.	Inad.	Gr.		
70	N. S.	Inad.	N. S.	Inad.	N. S.
72	Gr.	Gr.	Gr.	Gr.	N. S.
73	N. S.	Inad.	N. S.	N. S.	
76	Gr.	Gr.	Gr.	Gr.	
80	Inad.	Gr.	N. S.		
101	Gr.	Gr.	Gr.	Gr.	
105	N. S.	N. S.	N. S.	N. S.	
106	Gr.	Gr.	Gr.		

Gr. .....Granulomatous Pleuritis
N. S. .....Non-Specific Pleuritis
Inad. .....Inadequate Tissue.

of granulomatous pleuritis or non-specific pleuritis at the repeated serial needle biopsies. A few cases, however, were found to have granulomatous pleuritis at one biopsy and non-specific pleuritis at the other biopsy. Since the specimen obtained by needle biopsy is very small, it would be quite possible that the needle misses the site of typical granulomatous changes

and yielded only the area of non-specific changes at one occasion and at the next biopsy the needle hits the exact site of typical pathological changes to produce the diagnosis of granulomatous pleuritis. When the pleural lesion of granulomatous involvement is extensive as well as intensive, the needle biopsy will easily yield the typical picture of granulomatous pleuritis. However, when the pleural lesion is not quite intensive, it is quite possible to reveal only the non-specific changes unless the site of granulomatous inflammation is hit by biopsy needle.

Pleural Fluid : Pleural free effusion was present in the early stage of the pleurisy in all cases who had pleural needle biopsy. As the disease progresses or takes the course of healing under chemotherapy, there is gradual disappearance of the free fluid in the pleural cavity leaving only thickened pleura. In 101 needle biopsies (Table 16) pleural fluid was present at biopsy. Of these 101 biopsies, 13 biopsies (12.9 %) were unsuccessful to produce adequate tissue. No pleural fluid was noted at biopsy in 118 biopsies. 13 (11.1 %) out of 118 biopsies yielded inadequate tissue for pathological diagnosis. The presence of free effusion in the pleural cavity serves as a convenient guide to locate the level of parietal pleura and thus to obtain adequate pleural tissue at the early stage of the illness. However, once there appears sufficient thickness of the pleura as the disease progresses, adequate pleural tissue could be easily obtained without the guidance of the presence of free pleural effusion. The pleural needle biopsy could be performed in the presence of either free pleural fluid or a thickened pleura with equal success.

Table 16 Presence of Pleural Fluid and Inadequate Tissue Obtained for Diagnosis by Needle Biopsy

Biopsy / Presence of Pleural Fluid	Number of Biopsy	Inadequate Tissue for Diagnosis	
		Number	Percentage
Pleural Fluid was Present at Biopsy	101	13	12.9%
No Pleural Fluid at Biopsy (Blind Biopsy)	118	13	11.1%
Total	219	26	11.9%

Of the 101 thoracentesis 90 thoracentesis yielded serous fluid and sanguinous fluid was noted in 11 thoracentesis. Table 17 shows the relationship of needle biopsy of the parietal pleura and character of pleural fluid, 44 (48.9 %) revealed granulomatous pleurisy, 33 (36.7 %) non-specific

Table 17 Pathological Diagnosis of Needle Biopsy of Parietal Pleura and Character of Pleural Fluid

Pleural Fluid \ Path. Diag.	Total Number	Gran.	N. S.	Inad.
Serous Fluid	90	44 (48.9%)	33 (36.7%)	13 (14.4%)
Sanguinous Fluid	11	8 (72.7%)	2 (18.2%)	1 (9.1%)

pleuritis and inadequate tissue was obtained in 13 (14.4%). Of 11 biopsies, which were performed with the presence of sanguinous fluid, 8 (72.7%) showed granulomatous pleuritis, 2 (18.2%) non-specific pleuritis and inadequate tissue was obtained in 1 (9.1%). It is clear from these results that the sanguinous pleural fluid in non-cancerous age is most frequently associated with granulomatous (presumably tuberculous) pleurisy.

Examination of the protein content in pleural fluid was done 83 times. The maximum protein content was 11.2 mg%, minimum 1.1 mg% and the average was 3.9 mg %. There were 68 biopsies which had more than 3.0 mg % protein content in pleural fluid. Of the 68, 34 (50%) were diagnosed as granulomatous pleuritis, 24 (35.2%) non-specific pleuritis. 15 biopsies had 2.9 mg% or less protein contents in pleural fluid. Of these 15, 7 (46.6%) were granulomatous pleuritis and 4 (26.7%) non-specific pleuritis. Most of the cases of granulomatous pleuritis and non-specific pleuritis had more than 3.0 mg % of protein content in pleural fluid. (Table 18).

Table 18 Pathological Diagnosis of Needle Biopsy of Parietal Pleura and Protein Content of Pleural Fluid

Total Number of Examination 83
Maximum ..... 11.2 mg %
Minimum ..... 1.1 mg %
Average ..... 3.9 mg %

Protein Content \ Path Diag.	Total Number	Gran.	N. S.	Inad.
3.0 mg % or More	68	34 (50%)	24 (35.2%)	10 (14.8%)
2.9 mg % or Less	15	7 (46.6%)	4 (26.7%)	4 (26.7%)

Chloride was examined in 58 cases. Maximum chloride content in pleural fluid was 130 m Eq., minimum 99 m Eq. and average was 109 m Eq. It was difficult to find any definitive correlation between the patho-

logical diagnosis and the chloride content in pleural fluid. Sugar content in pleural fluid was examined in 64 cases. Maximum content was 133 mg%, minimum 14 mg% and average was 76.5 mg%. No definite conclusion can be drawn at this time concerning the diagnostic value of the sugar content in pleural effusion.

Pathology and Pathogenesis : The details of pathology and an assessment of the pathogenesis will be discussed in a separate paper in conjunction with the pathological changes of the pleural lesion during the course of the illness under chemotherapy. In this paper only brief statement will be made on the pathological findings of the biopsy specimens[13,14].

The patients were classified into three groups according to the chest X-ray and clinical impression (Table 19). Group 1 represents those patients in whom tuberculosis was thought to be the most probable cause of the pleurisy and the chest X-ray revealed the parenchymal lung lesion. There were 13 cases in group 1, in whom 20 needle biopsies were performed (Table 20). Of 20 biopsies, granulomatous pleuritis was demonstrated in 12 biopsies (60%), non-specific pleuritis in 6 (30%), eosinophilic pleuritis in 1 (5%). The biopsy was unsuccessful in 1 (5%). In about 60 per cent of the needle biopsies performed in the patients of pleurisy with the

Table 19 Classification of the Patients According to the Chest X-Ray and Clinical Impression.

Group I. Patients in whom tuberculosis was thought to be the most probable cause and the chest X-ray revealed the parenchymal lung lesion.

Group II. Patients in whom tuberculosis was thought to be the most probable cause but the chest X-ray was free of any parenchymal lung lesion.

Group III. Indeterminate group of patients in whom no etiology was readily apparent.

Table 20 Results of Needle Biopsy in Patients with Parenchymal Lung Lesion and in Patients without Lung Lesion

	Patients with Parenchymal Lung Lesion (13 Cases)	Patients without Lung Lesion (88 Cases)
Gran.	12 (60%)	109 (54.7%)
N. S.	6 (30%)	53 (26.6%)
Eos.	1 (5%)	11 (5.5%)
Norm.	0 (0%)	1 (0.6%)
Inad.	1 (5%)	25 (12.6)
Total Biopsies	20 (100%)	199 (100%)

demonstrable parenchymal lung lesion in chest X-ray, the pathological diagnosis of granulomatous pleuritis which were compatible with the tuberculous pleuritis could be confirmed. Interesting enough in one case eosinophilic pleuritis was demonstrated on needle biopsy specimen and subsequently the patient was found to have paragonimiasis with positive sputum examination for paragonimus Westermani and positive paragonimus antigen skin test. Group II includes those patients in whom tuberculosis was thought to be the most probable cause and the chest X-ray was free of any parenchymal lung lesion. Group III indicates indeterminate group of patients no etiology was readily apparent. There were 87 cases in group II and 1 case in group III. In both group II and group III the chest X-ray was free of any parenchymal lung lesion. There were 88 cases in total and 199 biopsies were performed (Table 20). Needle biopsy specimens of 109 biopsies (54.7%) demonstrated granulomatous pleuritis, 53 biopsies (26.6%) revealed non-specific pleuritis, 11 biopsies (5.5%) showed eosinophilic pleuritis. In 25 biopsies (12.6%) the tissue was inadequate for pathological examination. In comparison of the pathological diagnosis of the needle biopsy specimens in patients with parenchymal lung lesion with those of patients without parenchymal lung lesion, the incidence of granulomatous pleuritis and non-specific pleuritis is slightly higher in the former group and on the contrary the failure of obtaining adequate tissue was much higher in the latter group.

Among 193 needle biopsies, which produced adequate tissue for pathological diagnosis, 121 biopsies were diagnosed as granulomatous pleuritis (Table 21). In these 121 biopsy specimens of granulomatous pleuritis, gra-

Table 21 Pathology of the Granulomatous Pleuritis by Needle Biopsy in 121 Needle Biopsies.

	Number of Biopsies	Percentage
Tubercle Only	61	50.4%
Tubercle with Giant Cell	50	41.3%
Tubercle with Caseation	60	49.7%
Tubercle with Pleural Thickening	54	46.3%

nulomas were demonstrated ranging from large, conglomerate tubercles with central caseation and Langhans' giant cells, to small granulomas without central caseation or giant cells. 61 of the 121 needle biopsy specimens showed only tubercles consisted of epitheloid cells without any evidence of central caseation. In the remaining 60 biopsy specimens, the

tubercles demonstrated central zones of caseation necrosis and 50 out of these 60 biopsy specimens showed Langhans' giant cells in addition to the central caseation necrosis. Thus, there are two main group of granulomatous pleuritis according to the characteristics of the pathological findings of the biopsy specimens. In the first group, the main pathological structure is composed of hard tubercles without any evidence of central caseation or presence of giant cells. In the second group, the lesion is composed of fairly typical soft tubercles with central zones of caseation necrosis in the granuloma. The number of biopsy specimens of the first group and the second group are equal occupying the half of the total biopsy specimens. Histopathologically, granulomatous pleuritis can be demonstrated in many disease processes including tuberculosis, sarcoidosis, various fungus diseases, leprosy and syphilis. However, utilizing specific skin tests and laboratory tests in conjunction with the clinical course, the granulomatous pleuritis is compatible with the manifestation of tuberculous origin both clinically and pathologically. In about half of the biopsy specimens, anilin-fuchsin acid-fast stains were made, but no specific organisms were demonstrated. Among 121 needle biopsy specimens, there were 54 specimens which showed moderately advanced pleural thickening (pleural fibrosis) of the pleura.

Sixty needle biopsy specimens in 193 needle biopsies, which produced adequate pleural tissue, showed non-specific pleuritis. A consistent feature of the non-specific pleuritis was an inflammatory reaction, predominantly lymphocytic in nature. This reaction was characteristically diffuse, but often was accompainied by focal infiltration associated with focal necrosis. This type of non-specific inflammation is observed in miscellaneous systemic diseases. In some instances, the same patient yields non-specific pleuritis at one needle biopsy and granulomatous pleuritis at another needle biopsy or open biopsy. According to Table 15, which illustrates the pathological results obtained in 36 cases by repeated needle biopsies, 5 cases yielded constant findings of non-specific pleuritis in all biopsy specimens whenever adequate tissue was obtained. The precise implications of this finding remain to be elucidated and to be discussed later.

In 11 needle biopsy specimens of 5 patients, the main pathological finding was an inflammatory reaction with eosinophilic infiltration (Table 22). Three of these 5 patients had history of hemoptysis. The chest X-ray revealed a parenchymal lesion in one patient, paragonimus antigen skin test was positive in all 5 patients and sputum examination for paragonimus Westermani was positive in all but one. The WBC count revealed elevated eosinophils in all patients. 3 patients yielded pleural fluid by thoracentesis and no fluid was obtained in 2 patients. The character of the pleural fluid

Table 22 Summary of Five Cases of Eosinophilic Pleuritis

Name of Paitent	Hemo-ptysis	Chest X-Ray	P.W. in Sputum	P. W. Skin Test	Eosino-phils in WBC(%)	Pleural Fluid
Yoo, I.	+	−	++	+	10~24	No Fluid
Chai, R.	−	−	−	+	20	Lymphocytes 100%
Sohng, H.	−	−	+	+	11~18	Eosinophils 94% Lymphocytes 6%
Lee, Y. S.	+	−	++	+	12	Eosinophils 18% Lymphocytes 82%
Lee, Y. K.	+	+	+	+	8	No Fluid

One Case had History of Paragonimiasis and Positive Skin Test, but Pleural Biopsy Showed Granulomatous Pleuritis.

in 3 patients was serous. In one case the cell count of the pleural fluid revealed 94 per cent eosinophils and 6 per cent lymphocytes. In the second case the eosinophils were 18 per cent and the lymphocytes were 82 per cent. In the third case the entire cells were composed of lymphocytes.

DISCUSSION

We have performed 245 pleural biopsies in 108 patients including 219 pleural needle biopsies and 26 pleural open biopsies. The method of pleural needle biopsy seems to offer a useful, safe and early diagnostic aid in the presence of pleurisy with or without effusion. Since papers on the pleural open biopsy by Sutliff and his associates in 1954[15] and on the pleural needle biopsy by De Francis and his associates in 1955 were published, there have appeared quite many articles concerning the pleural biopsy in the medical literature. Sutliff performed surgical biopsy with exploration in 21 patients and obtained tissue diagnosis of granulomatous pleuritis in 17 patients, malignancy in 2 and non-specific pleuritis in 1 patient. De Francis introduced the method of pleural needle biopsy utilizing the Vim-Silverman needle for the etiological diagnosis of idiopathic pleural effusion in 6 patients. He was successful in obtaining adequate tissue in 2 patients, who were proved to have granulomatous pleuritis by this pleural needle biopsy method. Small and his associates introduced the method of surgical pleural biopsy without exploration and applied this method in 5 patients. The biopsy specimens of all 5 patients showed the clear evidence of granulomatous pleuritis and they stressed the clinical significance of this open pleural biopsy for the diagnostic confirmation of the pleural effusion. Breckler and his associates[16] reported on 16 consecutive cases of open pleural biopsy and found that this method had definite

advantages over the needle biopsy and quickly abandoned the latter. Heller and his associates[17], on the contrary, proposed the wide use of the pleural needle biopsy from their experiences with both open and needle biopsies in 25 cases. 132 biopsies were performed in 111 patients by Donohoe and his associates and the surgical and aspiration methods were compared. From this study they concluded that needle biopsy was the initial method of choice and should be employed early in the course of effusion. According to them surgical biopsy, with or without total exploration, should be reserved for those in whom needle biopsy had not proved rewarding. Recently Landsden and his associates advocated the advantage of small thoracotomy as the diagnostic procedure in idiopathic pleural effusion.

Our first aim of this study was to establish the diagnostic significance of the pleural needle and open biopsies and we found that the method of pleural needle biopsy is quite satisfactory, safe and far superior to any currently available diagnostic procedure in the presence of dry or exudative pleurisy. The diagnosis of pleural effusion was made in 86 per cent of our patients at the initial needle biopsy, which was far better than Donohoe's result of 73 per cent and Mestitz's 80 per cent. When the needle biopsy was repeated, the results became even better showing 91-92 per cent of success of obtaining the adequate tissue for the pathological diagnosis. The needle biopsy has the advantage of repeatability and reproductibility and by doing repeated needle biopsy the results could be much improved as shown in our study. When we compare the two needle and open pleural biopsy methods, we noticed that there is no significant advantage in doing open biopsy for the production of specific diagnostic tissue. The percentages of granulomatous pleuritis and non-specific pleuritis were almost the same. The incidence of inadequate tissue obtained were higher in cases of needle biopsy, but this could be improved by doing repeated needle biopsy. There were almost no complication in needle biopsy, whereas several complications could be found in pleural open biopsy. From the results of this study it is quite evident that the pleural needle biopsy is quite satisfactory, safe and early diagnostic procedure of the choice in the presence of pleurisy. As Donohoe and his associates stated, the needle biopsy has proved to be unsuccessful even after the repeated trial.

Most of the failures of the pleural needle biopsy were noted at the early stage of the study or due to the incooperation of the patients. The presence of the free pleural fluid serves as a convenient guide for the performance of the needle biopsy but successful needle biopsy was easily done without presence of pleural fluid when there is adequate pleural thicken-

ing.

The interval between onset of symptom and biopsy seems to have no significant effect on the production of adequate tissue by needle biopsy if the time elapsed is 4 weeks or more between the onset of the symptoms and biopsy. According to the study of 36 cases by repeated needle biopsy with the interval of 4 weeks, the distribution of number of cases and incidence of percentage of granulomatous pleuritis, non specific pleuritis and inadequate tissue at each time of biopsy was found to be quite similar. However, after 24 weeks have elapsed, the incidence of non-specific pleuritis shows increase and the granulomatous pleuritis decreases. It seems that it indicates the increase of the healing process due to the chemotherapy around 24 weeks after the onset of the symptoms. According to the results of present study, 63-75 per cent of our diagnosed cases were proved to have granulomatous pleuritis, 13—31 per cent non-specific pleuritis and 5.4—5.8 per cent eosinophilic pleuritis. The eosinophilic pleuritis was due to the paragonimus Westermani infestations. The distribution of this pathological diagnosis seems to reflect quite well the actual picture of incidences of pleurisy of various different etiology in young adults in Korea.

The 36 patients in whom more than 3 repeated needle biopsies were performed require special attention in this study. According to Table 15 the same patient may be found to have granulomatous pleuritis on one biopsy specimen, whereas the specimen showed non-specific pleuritis at the next needle biopsy. In such cases of pleurisy, the small biopsy specimen in the Vim-Silverman needle may not always represent the actual picture of the diseased pleura. At one biopsy the biopsy needle may hit the exact site of the diseased, granulomatous to yield correct diagnosis. However, the next biopsy may miss the typical, granulomatous lesion only to produce non-specific inflammatory changes. When the pleural lesion of granulomatous involvement is extensive as well as intensive, the needle biopsy will easily produce the typical picture of granulomatous pleuritis at each time of repeated biopsies. However, when the granulomatous involvement of the pleura is not quite extensive or intensive (in early or healing stage of the disease process), the needle biopsy may produce only the non-specific changes unless the site of the granulomatous inflammation is hit by the needle. Thus, only one needle biopsy of non-specific pleuritis cannot rule out the presence of granulomatous pleuritis and it is recommended that pleural biopsy be repeated whenever necessary.

The presence of free pleural fluid in the pleural cavity serves as a convenient guide for the pleural needle biopsy as De Francis originally described. However, when the biopsy technique is improved and diseased

pleura shows some evidence of thickening, the pleural needle biopsy can be done with the same success and ease as at the presence of free pleural fluid. In our study 101 biopsies were done with the aid of presence of free pleural fluid and there were 13 failures (12.9%) of obtaining adequate pleural tissue. Blind needle biopsy was done in 118 biopsies and 13 biopsies (11.1%) were unsuccessful in producing adequate tissue. Thus, the pleural needle biopsy could be performed in the presence of either free pleural fluid or a thickened pleura with equal success.

Numerous attempts have been made to correlate the data of the chemical analysis of pleural fluid with the diagnosis of the pleural lesion in the past[18,19,20,21,22]. Protein and sugar contents in the pleural fluid were most extensively studied. In our present study protein, sugar and chloride contents in the pleural fluid were studied in accordance with the pleural lesions diagnosed by needle biopsy. The number of cases studied are not quite sufficient to draw any definitive conclusion at the present stage of our study.

In the past, the sanguinous pleural fluid was thought to be most frequently associated with malignancy and rare in the tuberculous pleuritis. In our series of 101 biopsies, which yielded free fluid in the pleural cavity, 90 were serous and sanguinous fluid were found in 11. Of these 11 biopsies, 8 (72.7%) showed granulomatous pleuritis on pleural biopsy specimens. Thut, it is evident that the presence of the sanguinous pleural fluid does not always indicate the malignancy and it is most frequently associated with granulomatous (presumably tuberculous) pleuritis in non-cancerous age.

Strandgaard found that the patients whose chest X-ray demonstrated parenchymal lung lesion subsequently developed pulmonary tuberculosis in 33 per cent, whereas the patients, in whom no such lesion was demonstrated, the tuberculous morbidity was only 10 per cent. Jacoboeus found no difference in appearance of the pleura by thoracoscopic examination in idiopathic exudative pleurisy and tuberculous pleuritis secondary to pre-existing pulmonary tuberculosis. In our series, there were 20 biopsies performed in 13 patients, whose chest X-ray revealed the parenchymal lung lesion. In 60 per cent of 20 biopsies the biopsy specimens showed granulomatous pleuritis and in 30 per cent non-specific pleuritis. In 88 patients, whose chest X-ray was free of any parenchymal lung lesion, 199 needle biopsies were performed. There were 109 biopsies (54.7%) which demonstrated granulomatous pleuritis and 53 biopsies (26.6%) demonstrated non-specific pleuritis.

It is a general agreement among physicians that the prognosis of a

tuberculous patient who develops a pleurisy is rather serious, whereas the prognosis of a previously well patient who develops idiopathic pleural effusion is considerably better. The distinction of these two groups were usually made by the presence of a parenchymal lung lesion in the chest X-ray. According to our study of comparison of the results of pathological diagnosis in two groups of patients in whom the chest X-ray demonstrated parenchymal lung lesions in one and no lesion in the other, the incidence of granulomatous pleuritis and non-specific pleuritis is only slightly higher in the former group.

The granulomatous pleuritis presumably due to the tuberculous infection is a manifestation of tuberculosis itself and we found that the incidence of the pathological evidence of granulomatous inflammation in these two groups is almost the same regardless of the presence of the demonstrable parenchymal lung lesion. The demonstrable parenchymal lung lesion seems to indicate that in these patients the lung is more intensively involved by tuberculous infection than in those without demonstrable parenchymal lung lesion in X-ray.

In all 121 biopsy specimens histopathologically diagnosed as granulomatous pleuritis granulomas were demonstrated ranging from large, conglomerate tubercles with central caseation or giant cells to small granulomas without central caseation or Langhans' giant cell. Histopathologically, granulomas can be demonstrated in many deseases other than tuberculosis. However, utilizing specific skin tests and laboratory tests in conjunction with the clinical course, the etiology could be determined without much difficulty. The granulomatous pleuritis in this study is quite compatible with the manifestations of tuberculous origin both clinically and pathologically.

The tubercle may have arisen from the emigration to the area of an epitheloid cell (monocyte) with a phagocytosed tubercle bacillus according to Medlar. It may be that tubercles can be formed without the presence of bacilli in animal experiments, but this would be impossible to prove in a study of human tissue. According to Medlar, it would appear that the tubercle represents a lesion in which there is an even balance between the tubercle bacillus and the host and there would be no formation of the tubercles in human body without the presence of tubercle bacillus. It is not seldom that quite a number of tubercles could be demonstrated in those small area of specimens obtained by needle biopsy and this seems to mean that the tuberculous pleuritis is a result of actual tuberculous infection and the hypersensitivity plays only the secondary role.

In about half of the granulomatous pleuritis the lesion was composed

of fairly typical soft tubercles with central zones of caseation necrosis with or without Langhans' giant cells. Caseation necrosis and hypersensitivity have an intimate relationship and hypersensitivity is essential to the development of caseation. The degree of the caseous necrosis depends on the doses of the invading tubercle bacilli and the hypersensitivity on the side of pleural tissue. Early caseation is the result of large doses of invading tubercle bacilli in a highly allergic individual. Thus, it could be said that in about half of the patients with granulomatous pleuritis in our series, the pleurisy was a combined results of large doses of invading tubercle bacilli and the state of hypersensitivity.

In about one third of the 193 needle biopsies, which produced adequate pleural tissue for pathological diagnosis, there was evidence of moderately advanced pleural thickening. The pleural thickening indicates the advanced stage of pleurisy with healing process and the finding of the pleural thickening was noted in the biopsy specimens obtained at the biopsies which were performed when considerable time has elapsed after the onset of the symptoms.

Non-specific pleuritis was found in 60 needle biopsies. The finding of non-specific pleuritis could be observed in many miscellaneous systemic diseases but the following observation draws special attention in the series of our study. In the same patients, it is not seldom to find the granulomatous pleuritis in one biopsy specimen, and non-specific pleuritis at the next biopsy, or vise versa. In such instances, the non-specific inflammation seems to represent the surrounding tissue reaction of the pleural lesion when the exact site of the granulomatous lesion was missed by biopsy needle or the lesion under healing process of the pre-existing granulomatous lesion. Thus, even if non-specific pleuritis is noted on the biopsy specimen at one biopsy, the presence of granulomatous pleuritis cannot be ruled out.

There were several cases in whom the repeated biopsies produced the finding of non-specific pleuritis in all specimens. The exact implication of the non-specific pleuritis in these cases remains unanswered and it should be elucidated further in the future. However, there is a strong question whether there is a specific entity of "non-specific (idiopathic) pleuritis" which is equivalent to the non-specific (idiopathic) inflammation of the pericardium[23]. Further studies will be required to give the final answer to this question.

It is quite interesting to note that there were 5 cases of pleurisy due to the paragonomiasis in the series of present study. The pathological finding of the biopsied specimens demonstrated the infiltration of signi-

ficant number of eosinophils and paragonimus Westermani antigen skin test was positive in all 5 patients. The pleural fluid if aspirated yields the predominant eosinophils in cell count and eosinophilia is found in peripheral blood. The method of treatment for the pleurisy due to the paragonomiasis is entirely different from the tuberculous pleuritis and early detection will save many hospital days and much morbidity. It is quite possible that some cases were classified among the non-specific pleuritis and specific attention is required in future for the detection of more cases of pleurisy due to paragonomiasis.

SUMMARY

1. The results of 245 pleural biopsies perfomed in 108 patients including 219 pleural needle biopsies and 26 pleural open biopsies were reported. The method of pleural biopsy seems to be superior to any other currently available diagnostic procedures for the etiological diagnosis of pleurisy.

2. When the pleural needle biopsy is compared with the pleural open biopsy, the former method has definite advantages over the open biopsy. The pleural needle biopsy is simple, repeatable and has almost no complication. The method of pleural needle biopsy is the initial method of choice as Donohoe correctly stated and should be employed in every cases of the pleurisy to confirm the etiological diagnosis. The open biopsy should be reserved only for those cases in whom the needle biopsy had not proved satisfactory.

3. Utilizing the method of needle biopsy, the pathological diagnosis was made in 86 per cent of our cases at the initial biopsy. By repeated needle biopsies, the results have improved to 91—92 per cent.

4. Most of the failures of the pleural needle biopsy were noted at the early stage of the study due to the unfamiliarity of the biopsy technique and later due to the incooperation of the patients.

5. The presence of the free pleural fluid serves as a convenient guide for the performance of the needle biopsy but successful needle biopsy was easily done without presence of pleural fluid when there is adequate pleural thickening.

6. 63—75 per cent of our diagnosed cases were proved to have granulomatous pleuritis, 13—31 per cent non-specific pleuritis and 5.4—5.8 per cent eosinophilic pleuritis due to paragonomiasis. The distribution of this pathological diagnosis seems to reflect quite well the actual picture of incidences of pleurisy of various different etiology in young adults in Korea.

7. The relationship of the success in obtaining adequate tissue by needle biopsy and interval between onset of symptom and biopsy was discussed. It was found that the interval has no significant effect on the production of adequate tissue by needle biopsy if the time elapsed is 4 weeks or more from the onset of symptom.

8. The significance of the pathological findings of granulomatous pleuritis at one biopsy and non-specific pleuritis at another biopsy in the same patient was discussed. It is concluded that the single finding of non-specific pleuritis at one needle biopsy cannot rule out the presence of granulomatous pleuritis and it is recommended that pleural biopsy be repeated whenever necessary.

9. The diagnostic significance of the chemical analysis of the pleural fluid was discussed in correlation with the results of the pleural needle biopsies. It is concluded that the number of examinations are not quite sufficient to draw any definite conclusion at the present stage of our study.

10. The finding of sanguinous pleural fluid in the patient of granulomatous pleuritis is quite high (72.7%) and it was found that the sanguinous pleural fluid was most frequently found in the patients with granulomatous pleuritis in non-cancerous age.

11. Two groups of pleurisy patients with or without parenchymal lung lesion on chest X-ray were discussed in correlation with the results of the needle biopsy. It was found that the incidence of the pathological evidence of granulomatous inflammation on the biopsy specimens in these two groups is almost the same regardless of the presence of the demonstrable parenchymal lung lesion.

12. Histopathological finding of granulomatous pleuritis was discussed in conjunction with the significance of two types of tubercles, the soft tubercles and hard tubercles. In all specimens diagnosed as granulomatous pleuritis granulomas were demonstrated ranging from large, conglomerate tubercles with central caseation or giant cells to small granulomas without central caseation or Langhans' giant cells.

13. Histopathological significance of the finding of non-specific pleuritis on the biopsy specimens was discussed and the existence of a specific entity of "non-specific pleuritis" which is equivalent to the non-specific inflammation of the pericardium.

14. Cases of pleurisy due to paragonomiasis were discussed and the need of specific attention for search of new cases was emphasized.

ACKNOWLEDGMENT

The author wishes to express his appreciation to ROK Army Surgeon General Brig. Gen. Hi-Sup Jueng for his support and encouragement, Prof. Shim-Suk Han, Seoul

Medical College, for his kindness of rendering the free use of the Vim-Silverman needle and his helpful suggestion and Prof. Ki-Yong Nam, Seoul Medical College, for his generous help. The author also gratefully acknowledges the generous assistance and help of Capt. Bin Hwang, Capt. Tae-Suk Chai, and the Clinical Laboratory Staff, Capital Army Hospital, Seoul, Korea.

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