EXPERIMENTAL STUDIES AND CLINICAL APPLCATION OF INTRATHORACAL BIOPSY USING THORACOSCOPE AND TISSUE ADHESIVE

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1. Fundamental experiment

MATERIALS AND METHODS

Eighteen adult rabbits were anesthetized with pentobarbital 30 mg/kg and intratracheal intubation was done. A left thoracotomy was performed. About 0.5 cm^2 segment of lower lobe of the lung was excised by biopsy forceps. Bleeding from the excised lesion was galvanically cauterized. Air leakage from the same site was covered by the tissue adhesive (alpha-cyanoacrylate monomar) or and thin fibrin film. Eighteen rabbits were divided into

Fig. 1 On 7 th day, arrow showing the site of biopsy.

Fig. 2 On 14 th day, arrow showing the site of biopsy.

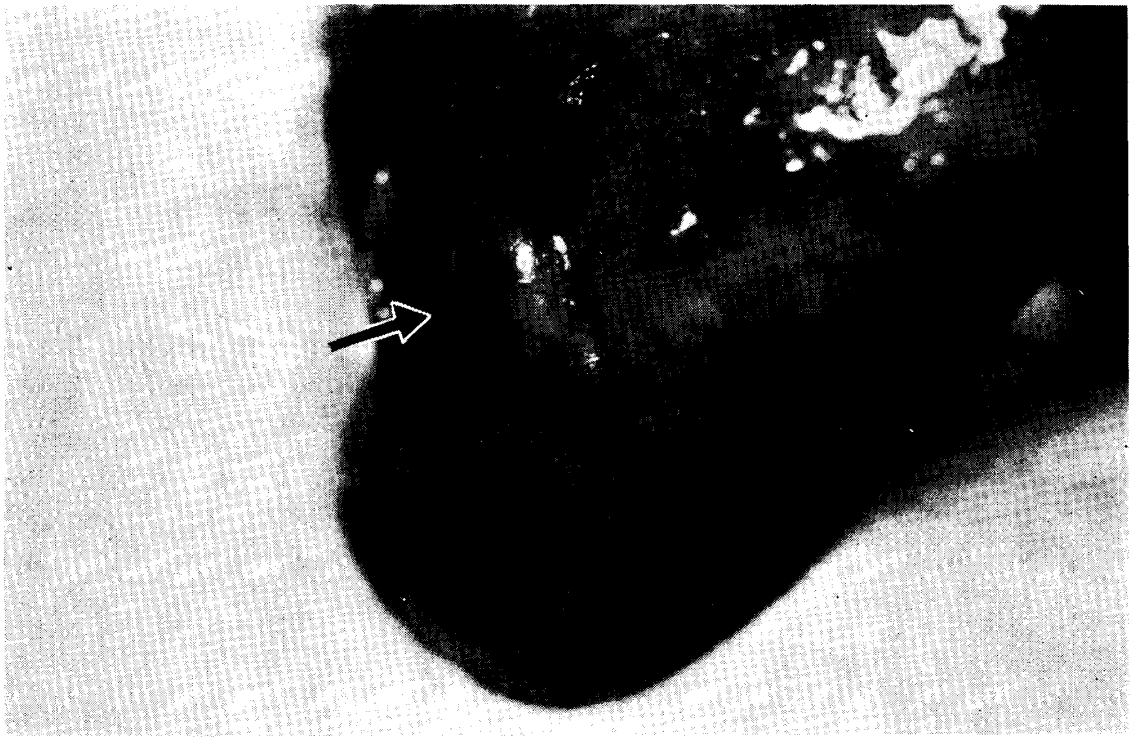


Fig. 3 On 28 th day, arrow showing the site of biopsy.

two groups, A and B. Of A-group, only tissue adhesive 0.1 ml was applied on the biopsied regions. Of B-group, thin fibrin film with thickness of 0.15 mm was placed on the defect of the lung and fixed with tissue adhesive after biopsy. After these procedures, the lung was re-inflated by increasing the intratracheal pressure. Postoperatively, cephalosporin 100 mg/kg was injected in all rabbits intramuscularly.

RESULTS

Each three rabbits in both A and B group were sacrificed on 7th, 14th and 28th postoperative day, respectively, to be examined histologically. Neither postoperative death nor postoperative complications such as bleeding, pneumothorax, pleural effusion and infection were not observed at all. No adhesion between the site of biopsy and parietal pleura occurred.

Macroscopic differences between A and B group were not observed. On 7th day, biopsied region was covered with yellowish white and thin membrane and surrounded by mild redness and swelling (Fig. 1). On 14th day, it was covered with thicker and greyish white membrane

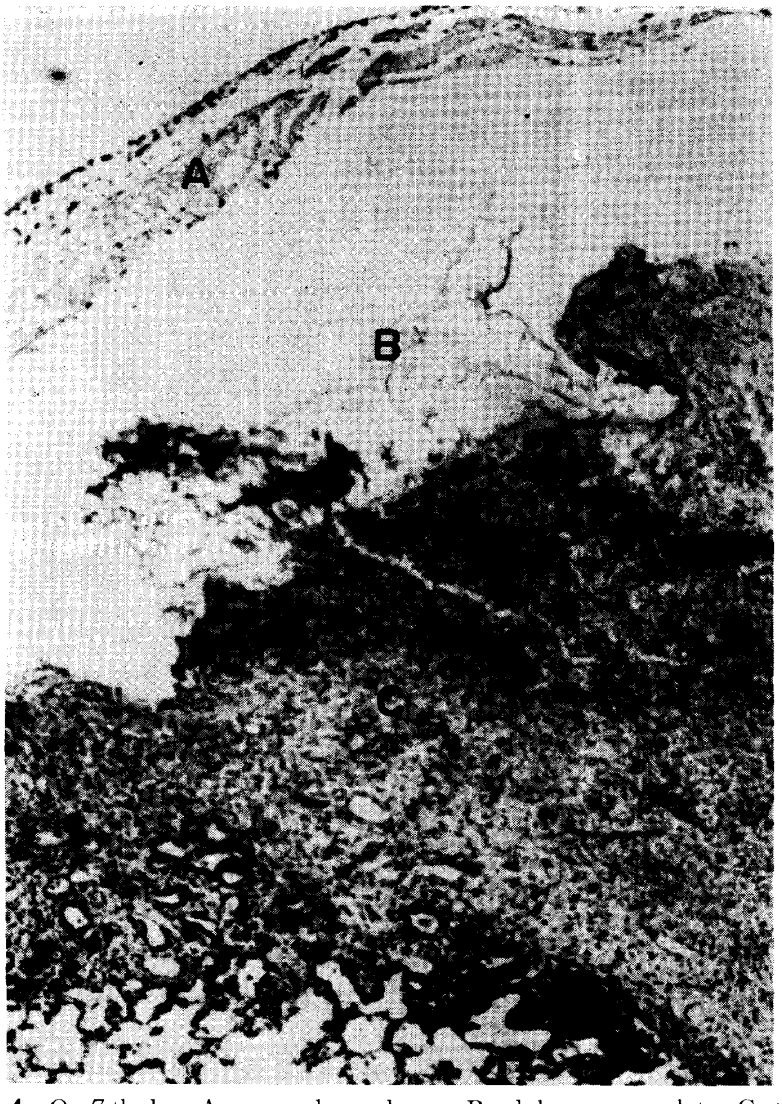


Fig. 4 On 7 th day, A: covered membrane, B: alphacyanoacrylate, C: tissue of the lung (H. E. ×40)

(Fig. 2). On 28th day, tissue adhesive and fibrin film adhered to the biopsied parts without desquamation. The surface of the tissue adhesive or fibrin film, was covered by thick and smooth membrane and its border to normal lung was not distinct (Fig. 3). Specimen which contained tissue adhesive, fibrin film and lung was stained by H.E. and elastica-Domagk. Microscopic examination was done in each group.

A-group: On 7th day, fibrin and fibroblasts were seen on the surface of cyanoacrylate. Coagulation necrosis was seen at the cauterized lesion which was surrounded by the infiltration of eosinophilic leukocytes, lymphocytes, fibroblasts and foreign body giant cells. Regeneration of vessels and alveoli were also recognized. The walls of neighbouring alveoli were observed to be thickened with occaisional desquamative changes (Fig. 4). On 14th day, the coagulation necrosis was replaced partially by granulation containing lymphocytes, eosinophilic leukocytes and foreigh body giant cells (Fig. 5). On 28th day, tissue was surrounded by edematous granulation. In the adjoining lung tissue, alveolar wall was thicken and cystic degeneration was seen. Foreign body giant cells, eosinophilic leukocytes and lymphocytes were not observed

Fig. 5 On 14 th day, A: covered membrane. B: alphacyanoacrylate, C: tissue of the lung (H. E. ×40)

Fig. 6 On 28 th day, A: covered membrane, B: alphacyanoacrylate, C: tissue of the lung (H. E. ×40)

on this stage (Fig. 6). In conclusion, tissue adhesive was surrounded by granulation without desquamation and the damage of neighbouring lung tissue was minimum.

B-group: On each stage, local reaction was similar as well as A-group. Fibrin film was observed on 7th day and 14th day. On 28th day, however, it disappeared and was replaced by granulation.

These experimental results suggested that the possibility of severe postoperative complications such as bleeding, pneumothorax and infection would hardly be occurred. Fibrin film was proved safely and simply to cover the defect after biopsy of relatively large amount of the lung tissue.

2. Clinical application

Since the lung biopsy under the view of thoracoscopy might obviate serious postoperative complications as was evidenced by the fundamental experiment described above, it would be

expected to enhance its diagnostic value in order to differentiate bilateral disseminated lung disease, pleural lesions, mediastinal lesions and solitary lesions of subpleural location.

METHODS

Apparatus for this method was shown in Fig. 7. After confirming the free pleural space by the artificial pneumothorax apparatus, patient was put under general anesthesia by intratracheal intubation. Two trocars were then inserted via two skin incision, the one for the guidance of thoracoscope and the other for forceps or probe. Under the view of thoracoscope, lesions were palpated with the probe and photographed, if necessary, according to the conventional procedure. If pleural fluid was present, specimen was collected for the cytological and bacteriological examination and it was removed finally. Then, forceps for biopsy was inserted into the thoracic cavity through trocar, obtaining several layer specimen of the lung enough for tissue examination as well as parietal pleura and mediastinum, if necessary. Specimen was biopsied from more than two sites. Rigid thoracoscope is thought to be suitable for biopsy, whereas flexible one is more suitable for the observation of the overall thoracic cavity.

Bleeding from the tissue defect due to biopsy necessarily occurred, more or less, in all cases, so that the galvanic was applied keeping blood suction through a metalic suction tube at the same time (Fig. 8).

Air leakage was negligible when biopsy was done in case of lung cancer, consolidation and pleural callosity. On the contrary, in case of small lesion such as diffuse bilateral pulmonary disease or pulmonary emphysema, an air leakage after biopsy was frequently observed. Tissue adhesive (alpha-cyanoacrylate) was applied at the site of air leakage. It was applied via a slender polyethylen tube. If biopsied specimen was relatively larger, a piece of thin fibrin

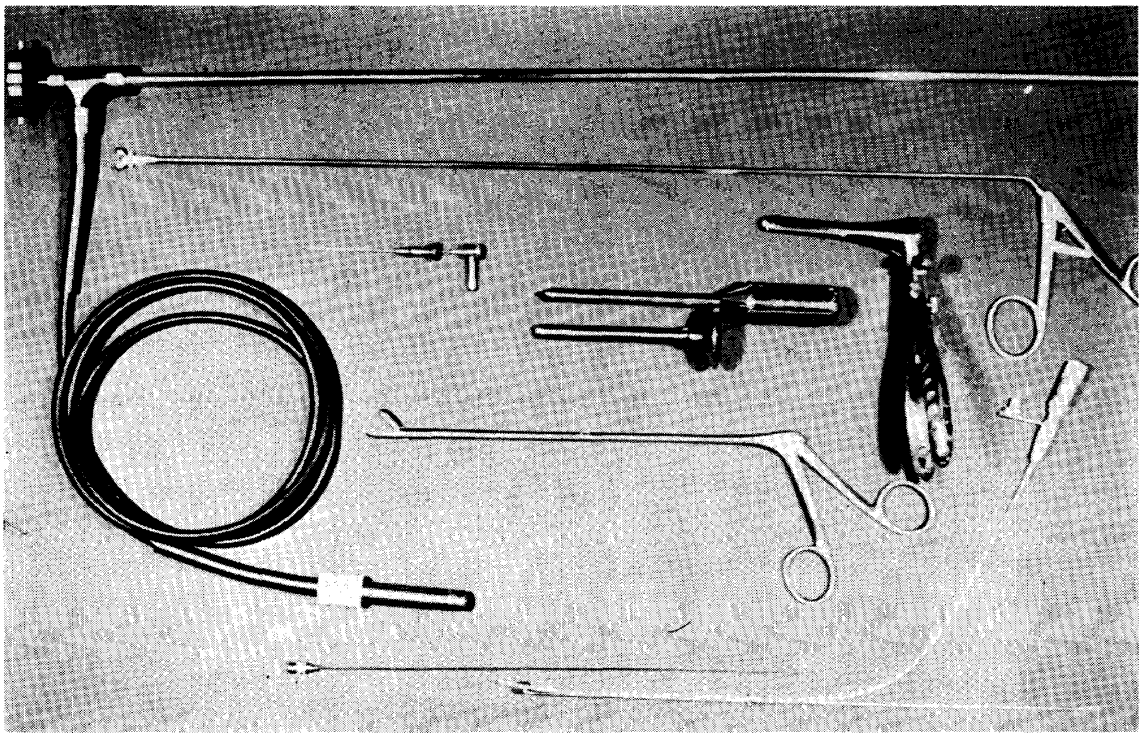


Fig. 7 Apparatus for thoracoscopic lung biopsy

Fig. 8 The defect after thoracoscopic lung biopsy has been galvanically cauterized

Fig. 9 Fibrin membrane is placed on the defect of the lung with biopsy forceps

film (0.15 mm in thickness) was applied on the defect with the additional application of the tissue adhesive, otherwise a large amount of tissue adhesive was liable to be detached due to its delay of fixation on the defect (Fig. 9). After those procedures, abscence of bleeding and air leakage was confirmed by increasing intratracheal pressure. Antibiotics was put into thoracic cavity. Then the trocars were drawn out and single skin suture was done under increased intratracheal pressure. None of the intercostal drainage was necessary.

RESULTS

The thoracoscopic examination was undergone in 133 cases (Table 1). The thoracoscopic observation without biopsy was applied in 55 cases. In the remaining 78 cases, the thoracoscopic biopsy was performed. The biopsy was taken from the localized lesions and its neighbouring region in various cases, comprising the lung cancer, pulmonary tuberculosis, sarcoidosis, benign tumor, chronic pneumonitis, diffuse pulmonary fibrosis, alveolar proteinosis and alveolar microlithiasis. Final diagnosis was established by the present procedure in 98 per cent of all cases.

In the case of tuberculous or fibrinofibrinous pleural effusion and mesothelioma, every cases could be established its final diagnosis. In the mediastinal tumor, the biopsy was not attempted because of its rigidity as was observed by the thoracoscopy. In the case of spontaneous pneumothorax, a presence of bullae, blebs or pin holes was confirmed without biopsying the tissue sample. The plausible complications following the thoracoscopic lung biopsy was

Table. 1

	round, coin and massive lesion	nodular and reticular lesion	infiltrative shadow	pneumo-thorax	pleural effusion	total
cancer of the lung	27	9	8	2	5	51
mediastinal tumor	24					24
spontaneous pneumothorax				15		15
tuberculous & fibrino-fibrous pleurisy					9	9
pulmonary tuberculosis	1	6	2			9
pulmonary sarcoidosis		6				6
pulmonary fibrosis		6				6
benign tumor of the lung	5					5
chronic pneumonitis		2	2			4
pulmonary alveolar proteinosis		1				1
pulmonary alveolar microlithiasis		1				1
pleural mesothelioma					1	1
bronchogenic cyst				1		1
total	57	31	12	18	15	133

postoperative hemorrhage and pneumothorax. Since the definite application of the galvanic cauterization to the hemorrhage could be done under the view of the thoracoscope, neither postoperative bleeding nor hemothorax was recognized; whereas the application of the tissue adhesive for the air leakage could be beneficial without any of such complication of air leakage except for one case. This case with the air leakage was experienced in our initial series, whom the desquamation of the tissue adhesive followed by pneumothorax was observed. In considering this failure, the additional fibrin film was decided to apply as a support of tissue adhesive in a case of massive biopsy and any of pneumothorax has not been experienced since then. In addition of these complications, any of the air embolism and empyema did not occur.

DISCUSSION

Conventional methods of lung biopsy are consisted of the percutaneous needle biopsy[19–27], the transbronchial biopsy[28–30], open lung biopsy[31–36] and thoracoscopic biopsy. Since the initial attempt of the lung puncture have been reported by Leyden in 1882, various methods of needle biopsy such as suction excision biopsy, needle aspiraton biopsy. Cutting needle biopsy, trephine lung biopsy and transbronchial lung biopsy were reported. Although needle lung biopsy is considered to be a simple method only necessitating local anesthesia, accurate biopsy of lesions may be difficult without viewing the lesions only providing with cytological examination. Moreover, bleeding and air leakage is difficult to stop for the

same reason.

On the contrary, the open lung biopsy initially reported by Klassen, has established the most reiable diagnostic value. Nevertheless, the minor thoracotomy for biopsy necessitate operative as well as postoperative trouble to the patient such as continuous drainage, which might be inconvinient in order to repeat the biopsy for follow-up studies.

Thoracoscopic biopsy requires only a small incision without serious discomfort to the patient, and the biopsy under inspection facilitates to establish the accurate tissue diagnosis owing to its definite localization of pleural and pulmonary lesions. Postoperative air leakage and hemorrhage, however, has been accused of its serious sequelae, which is proposed to overcome by the continuous drainage by Heine. According to our method, these complications have been overcome by the galvanic cauterization for bleeding and the tissue adhesive with the fibrin film for air leakage. Necessity for the postoperative continuous intrathoracal drainage has been able to be eliminated. This operative abbreviation was appeared to be favorable to the patient without any remarkable pain or troubles such as postoperative hemorrhage, pneumothorax, pleural effusion and empyema. Furthermore, minimum traumatic procedures might safely be applicable even to the patient with pulmonary insufficiency or large quantity of expectoration. For the same reason, this method is considered to be repeatable not only for the purpose of differential diagnosis but also for the establishment of the therapeutic guide. On the contrary, the open lung biopsy may be indicated for the case with the extensive pleural adhesion and the case whose massive lung tissue necessitates. Use of the flexible fiberoptic thoracoscope[8,37], instead of the rigid one, facilitates to observe every corners of the chest cavity, but is less convenient for the biopsy to be located than that of the rigid one.

The merits of the present method will described in each disease as follows;

a. Diffuse bilateral pulmonary disease; tissue examination is obtained under this new method of thoracoscopic biopsy which is superior to the needle biopsy only providing with the cytological examination (Fig. 10). In the case of deep parenchymal lung lesion such as bronchtis obliterans, open lung biopsy is excellent than the thoracoscopic biopsy.

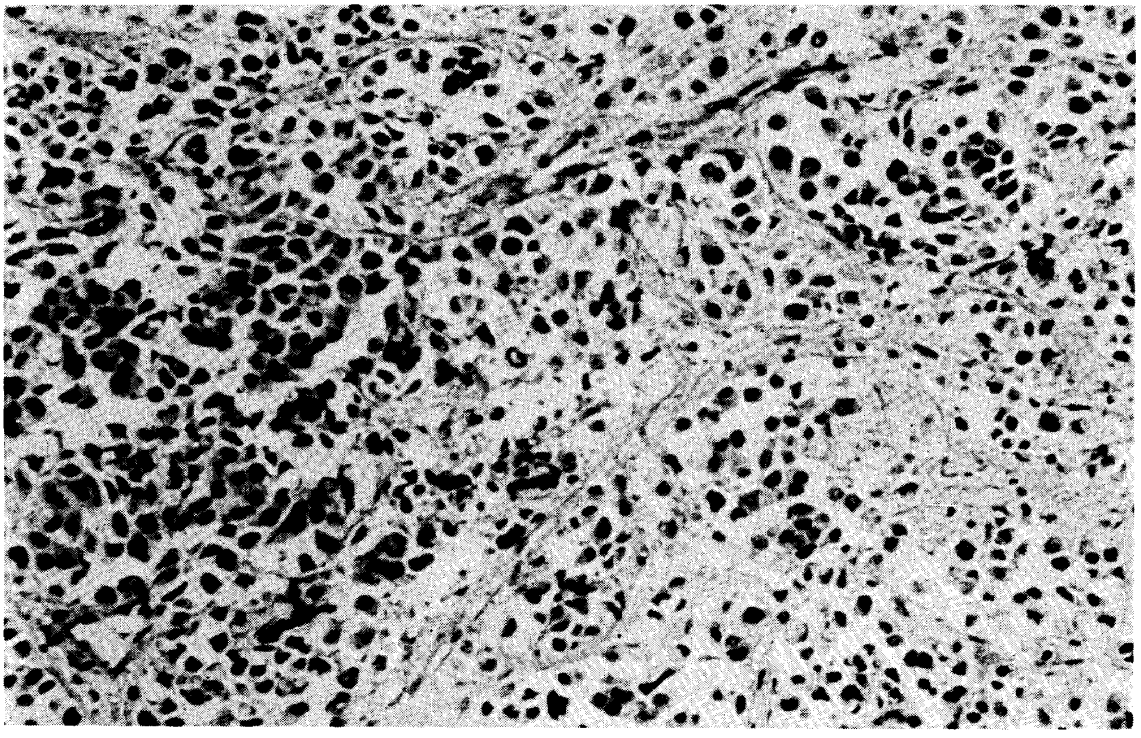
b. Cancer of the lung; Following states can be observed that invasion to the chest wall, dissemination into the thoracic cavity (Fig. 11) and hilar metastasis especially at the posterior and lower part of hilum where the mediastinoscopy is difficult to examine, so that the resectability and tissue diagnosis of cancer can be decided. Subpleural small cancer and lesion with the pleural invasion are better indication for the thoracoscopic examination than the needle biopsy.

c. Spontaneous pneumothorax; Presence of the bullae (Fig. 12), blebs or pin hole without any radiological evidences is confirmed by the thoracoscopic inspection in order to establish the indication for the operation. A case with spontaneous pneumothorax who is in cancer age without any abnormal shadow and cystic lesions on chest roentogenogram should be examined under thoracoscope. For example, two cases with spontaneous pneumothorax in the age of 69 and 71 were diagnosed as a small primary cancer of the lung and a pleural mesothelioma by thoracoscopic biopsy.

d. Pleural effusion; Under the thoracoscopic inspection, accurate biopsy of pleural lesion can attained in comparison with the cytological examination by puncture and needle biopsy.

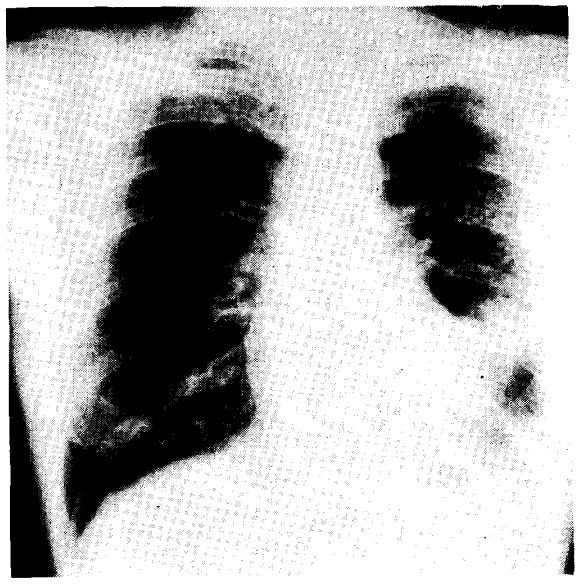
(a)

(b)



(c)

Fig. 10 (a). 71 yr. man, anteroposterior roentogenogram showing bilateral homogeneous and reticulonodular shadows (b). many nodules shown under the thoracoscopic inspection (c). invasion of squamous cell carcinoma (H. E. ×100)



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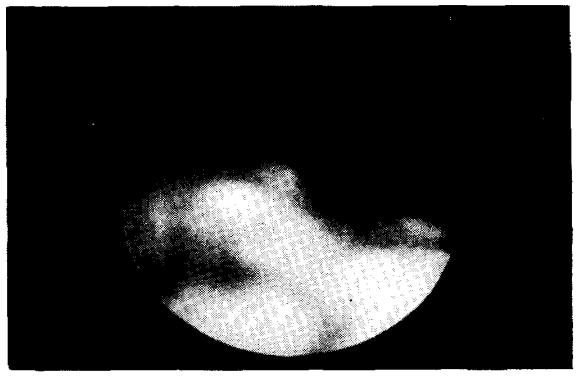

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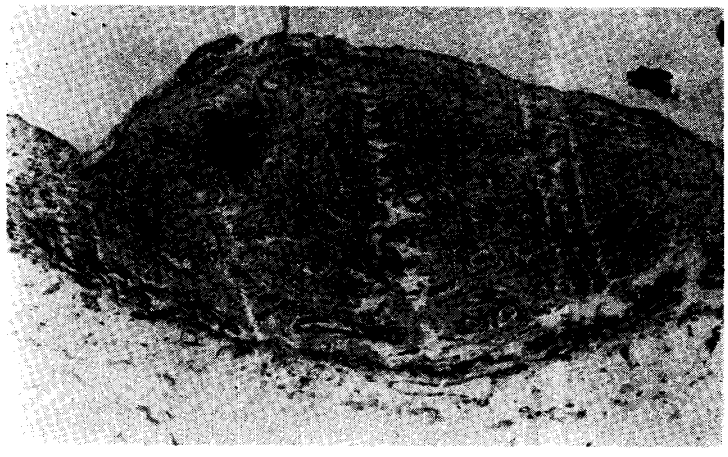

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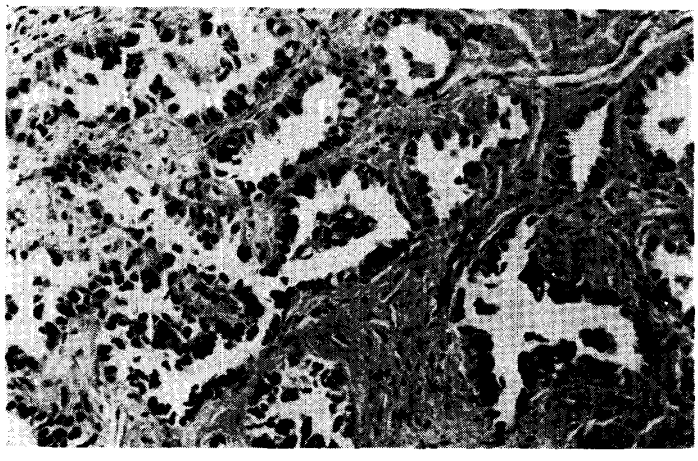

(d)

Fig. 11 57 yr. woman. (a). anteroposterior roentogenogram showing the pleural effusion and massive homogeneous shadow of left lower field (b). many nodules disseminated in the thoracic cavity are observed by thoracoscopy (c). biopsied specimen from pleural nodules (H. E. ×40) (d). its diagnosis was adenocarcinoma (H. E. × 100)

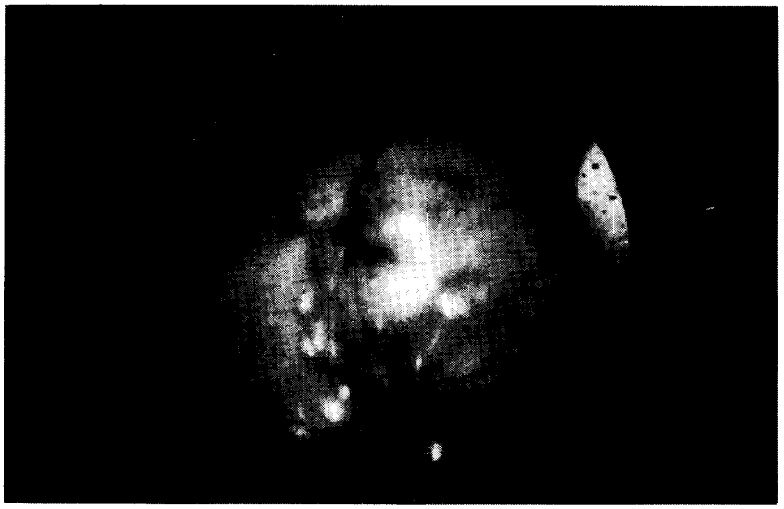

Fig. 12 Thoracoscopic photograph shows bullae, a case of spontaneous pneumothorax of 21 yr. man

In conclusion, the merits of our method are summarized as follows;

1. Various pleural lesion, diffuse pulmonary disease and subpleural solitary lesions are thought to be the indication for this method.
2. Any of remarkable trouble and postoperative complictaions such as hemorrhage, pneumothorax, pleural effusion and empyema are not observed.
3. Even in the case with pulmonary insufficiency, this method can be safely applied.
4. Accurate diagnosis of the lesions in the most part of the thoracic cavity is possible under thoracoscopic inspection.
5. Tissue diagnosis with enough sample can be made.
6. Repetitive follow-up studies can be made.

The weak points of this method are summarized as follows;

1. Parenchymal lesion in a deeper location such as bronchiolitis obliterans is difficult to be biopsied.
2. The case with pleural adhesion is difficult to be observed and biopsied.

SUMMARY

In order to facilitate the preventive measures against postoperative complications such as hemorrhage and air leakage after thoracoscopic lung biopsy, combined application of the galvanic cauterization for hemorrhage and the tissue adhesive for air leakage was attempted. On the basis of experimental substantiation of this method, clinical application was done successfully in 133 patients with diffuse pulmonary disease and pleural or subpleural lesions.

No complications such as bleeding, pleural effusion and empyema has not been experienced except for one case of postoperative pneumothorax.

The method was proved to be excellent in that the relatively large size of biopsy specimen could be obtained to make diagnosis without any serious complication on the basis of cytological as well as histological study.

Since the introduction of the thoracoscopy by Jacobaeus in 1910[1], it had been of limited

usage for the purpose of cauterizing dissection of pleural adhesion combined with therapautic pneumothorax for the treatment of pulmonary tuberculosis. Now that therapeutic value of artificial pneumothorax has been lost completely, thoracoscopy itself is being widely accepted as one of diagnostic measures in chest clinic not only by visualizing the intrathoracic lesions with the least traumatic procedure, but also by facillitating an authentic biopsy of pleural or subpleural parenchymatous lesions of lung[2-9]. The procedure because of the small incision might, in turn, make difficult to confirm a presence of postoperative complication such as hemorrhage or air leakage. For this reason, supplemental procedures comprising galvanic cauterization for hemorrhage and tissue adhesive (alpha-cyanoacrylate) for air leakage has been recommended[10-18].

Since 1968, we have attempted thoracoscopic biopsy with this supplemental procedures in 133 consecutive cases without any postoperative complications except for one case with postoperative pneumothorax. In this connection, additional application of thin fibrin film to the point of air leakage with tissue adhesive has been attempted.

This paper will be concerned with the experimental study and clinical application of the additional improvement of repairment technique against tissue caused by biopy using adhesive under the thoracoscopic examination.

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