Open Lung Biopsy; A Strong Stand*

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The purpose of this study was to ascertain if the results of open lung biopsy could be appreciably improved by extending the procedure to include hilar lymph nodes. Triple biopsy (pleura, lung and hilar lymph nodes) was performed on 89 patients with diffuse pulmonary disease and/or hilar adenopathy and persistent pleural effusion. The result was a definitive diagnosis in 62 and an additional 22 in whom nonspecific pleuritis was the only finding. Of particular interest was the finding of 25 patients with proved tuberculosis which had escaped definitive diagnoses by all techniques other than biopsy. A series of 24 open lung biopsies (pleura and lung only) were reported by this institution in 1963 with only three cases of proved tuberculosis.

Open lung biopsy for diffuse pulmonary disease has been accepted as a safe and essential diagnostic procedure in recent years, since the first large series reported by Klassen et al1 in 1949. This approach was developed to fill a void incurred by the inability of the many indirect and more conservative procedures to establish satisfactorily the diagnosis in such lesions. Open lung biopsy, though initially utilized infrequently, more recently has been considered earlier in the diagnostic work-up, to obviate the protracted period of hospitalization associated with the myriad diagnostic procedures currently in vogue.

At this facility, a pulmonary disease center for the Navy, we have long advocated a somewhat more aggressive approach to open biopsy,2–3 preferring to enter the chest through a lateral incision and carry out a limited exploration of the lung and hilum. In this manner, we have been able to select areas of greater disease involvement for biopsy. In the past three years, in an attempt to standardize the procedure, we have come to the concept of the triple biopsy, in which each patient has the benefit of a biopsy of the parietal pleura, a portion or portions of lung, and one or more hilar nodes. We have not had cause to regret this approach. From January, 1964 through June, 1968, 89 open biopsies for diffuse pulmonary disease have been performed, and presented herein is the technique of triple biopsy and a resume of the results in this series.

**Technique**

Under general endotracheal anesthesia, the patient is positioned in the lateral decubitus position as for a standard posterolateral thoracotomy. The side selected for biopsy is determined by historic and radiologic evidence of disease or greater involvement, so as to anticipate the best yield. The incision is made 4 cm below the tip of the scapula, 6–8 inches in length, with the major portion of the incision anterior to the fold of the latissimus dorsi. The muscles are divided with the electrocautery and entry into the thorax made through the fifth, sixth, or seventh intercostal space, whichever one lies comfortably within the incision. A 2 x 4 cm strip of parietal pleural is excised for a specimen during entry, when the pleura is well exposed. With the ribs spread, a hand can be inserted into the thoracic cavity for a limited exploration. Focal areas of pathology can be gently brought into view and a wedge of lung taken over Buie clamps, oversewing the defect with a double row of 3-0 swedge chromic suture, to obtain airtight closure. Very little of the lung is out of reach of this incision for biopsy purposes. Hilar nodes anterior and posterior to the lung root are accessible, and a suitable specimen is obtained by incising the overlying pleura and shelling out the node by blunt and sharp dissection, taking

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Table 1—Triple Biopsies, 89 Patients
(Microscopic Diagnosis)

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number</th>
<th>Percent</th>
</tr>
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<tbody>
<tr>
<td>Non-caseating granuloma (sarcoid)</td>
<td>17</td>
<td>19</td>
</tr>
<tr>
<td>Tuberculosis</td>
<td>25</td>
<td>28</td>
</tr>
<tr>
<td>Caseating granuloma</td>
<td>14*</td>
<td></td>
</tr>
<tr>
<td>Non-caseating granuloma</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Tuberculosis pleuritis</td>
<td>7</td>
<td></td>
</tr>
<tr>
<td>Fungi</td>
<td>4</td>
<td>4</td>
</tr>
<tr>
<td>Histoplasmosis</td>
<td>2*</td>
<td></td>
</tr>
<tr>
<td>Cryptococcosis</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Neoplasms</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Primary</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Metastatic</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Lymphogenous</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pleuritis, nonspecific</td>
<td>22</td>
<td>24</td>
</tr>
<tr>
<td>Granulomatous inflammation, nonspecific</td>
<td>6</td>
<td>7</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>9</td>
<td>10</td>
</tr>
<tr>
<td>Diffuse interstitial fibrosis (Hamman-Rich)</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pulmonary fibrosis, nonspecific</td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>Chronic interstitial pneumonitis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Pulmonary arteriosclerosis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Emphysema</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

*One case had both etiologic agents

care to stay right on the nodal surface. Small bleeders are readily controlled with sponge pressure and it has rarely been necessary to electrocautery or ligate persistent bleeders. Two large Koroseal tubes are placed to the apex and costophrenic sulcus for expansion and drainage, and the wound is closed in a standard fashion. Each of the three tissue specimens (pleura, lung, and node) is divided in half; one half to go for routine microscopic examination and one half to be divided in three parts for culture for bacteria, fungus, and tuberculosis.

EXPERIENCE

Table 1 shows our results in 89 open triple biopsies, as reported on microscopic diagnosis. The relatively large percentage of tuberculosis is attributable to the fact that the Naval Hospital, St. Albans, is the East Coast treatment center for tuberculosis in the Navy. The diagnosis of tuberculosis was established by visualizing the bacillus on special stains (Ziehl-Neelsen and auramine-O) and/or growing out the organism on culture. In like manner, the diagnoses of the four cases of fungal disease were established by identifying the organism on the microscopic examination and/or culturing out the organism on the appropriate culture medium. Seven of the tuberculosis group had had a prior tissue diagnosis of sarcoidosis, ie non-caseating granuloma, on cervical node biopsy. Similarly, one of the cryptococcosis cases had had a cervical node diagnosis of sarcoid prior to open biopsy.

The complications consisted of rare instances of atelectasis requiring transtracheal suction and other local measures, and collection of pleural fluid or air, requiring thoracentesis or re-insertion of a chest tube. These problems virtually always occurred with the use of only one chest tube early in the series and were not seen with the routine use of two chest tubes.

Two deaths occurred within 30 days of surgery in this series (2.2 percent), and neither was related directly to the thoracotomy. One was a 45-year-old man operated upon for right pleural effusion, who was found to have anaplastic bronchogenic carcinoma with pleural metastasis. There was an history of deep thrombophlebitis prior to surgery, and on the 12th postoperative day, the patient died of a pulmonary embolus. The other was a 77-year-old man, the oldest patient in the series, who was operated on for left pleural effusion, found to have bronchogenic carcinoma with pleural metastasis, and died of carcinomatosis on the medical service on the 25th postoperative day.

Three case reports are presented to illustrate the value of direct, open biopsy.

CASE REPORTS

CASE 1 (Figures 1 and 2)

A 34-year-old Negro woman was admitted to the medical service on August 4, 1967 for evaluation of chest pain and fever. Sixteen months earlier, she had been admitted with a six-month history of progressive generalized lymphadenopathy. The Kveim test was positive, and a cervical node biopsy returned non-caseating granuloma, consistent with Boeck's...
AARON ET AL

FIGURE 2. Lateral radiographic examination of the chest shows generalized interstitial infiltrate with elevation of the left hemi-diaphragm.

Sarcoïd. Eleven months later, she developed intermittent fever with chest pain and progressive pulmonary parenchymal interstitial infiltrates in the right middle lobe, right lower lobe, and left lower lobe. In July, 1967, because of increasing fatigueability and exertional dyspnea, she was started on prednisolone, 40 mg daily, with some improvement. Ten days prior to this admission, she developed bilateral pleuritic chest pain associated with a nonproductive cough, chills, and fever.

Physical examination on admission revealed a temperature of 103.6°F, splinting respirations, splenomegaly, and generalized lymphadenopathy. Pertinent laboratory data showed 17,500 white blood cells with a shift to the right and a sedimentation rate of 36 mm/hr; normal serum calcium; phosphorus; total serum proteins were 9.3 gm percent albumen; protein electrophoresis revealed marked hypergamma-globulinemia. Radiographic examination of the chest revealed generalized interstitial infiltrate with obliteration of the left costophrenic sulcus.

On bed rest and penicillin therapy, plus prednisolone 40 mg daily, she rapidly became afebrile with improvement in the pleuritic pain. Because of the strong suspicion of tuberculosis, open biopsy was elected, and performed on the left lung on August 30, 1967. The lung and pleura grossly showed diffuse nodularity; histologic examination revealed non-caseating granuloma which on special stains demonstrated multiple budding organisms; subsequent cultures identified Cryptococcus neoformans. Development of cryptococcal meningitis necessitated a course of amphotericin-B, and though her convalescence was prolonged, she was eventually discharged six months postoperatively in satisfactory condition.

CASE 2 (Figures 3 and 4)
A 27-year-old Caucasian woman was admitted on May 30, 1966 with a complaint of retrosternal pleuritic chest pain of two weeks' duration. She had had similar pains periodically for two years, but they were worse recently and were

FIGURE 3. Posterior-anterior chest x-ray film shows huge hilar and bronchopulmonary nodes.

FIGURE 4. Lateral chest x-ray film shows huge hilar and bronchopulmonary nodes.

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associated with weakness, malaise, shortness of breath, weight loss and migratory arthralgia. Examination was within normal limits except for minimal hepatomegaly. Laboratory examination, including complete blood count, serum protein, albumin, calcium, and phosphorus were within normal limits. Skin tests with PPD-S, PPD-B, blastomycin, coccidioidin, and histoplasmin were negative. X-ray examination of the chest showed huge hilar and bronchopulmonary nodes.

She subsequently developed arthritis in the wrist and erythema nodosum over both pretibial areas, and splenomegaly became evident. On June 7, 1986, through a right thoracotomy, triple biopsy was done with the following results. The node and lung showed caseating granuloma with acid-fast bacilli seen on Ziehl-Neelsen and auramine-O fluorescent stains. She was deemed to have primary tuberculosis with lymphogenous spread and was started on isoniazid and paraaminosalicylic acid with gradual improvement.

CASE 3 (Figure 5)

A 47-year-old Caucasian man noted onset of left lateral pleuritic chest pain, nonproductive cough, and low grade fever, associated with left pleural effusion in August, 1966. Work-up included sputum studies which were negative for tuberculosis and malignant cells, negative bronchoscopy, needle pleural biopsy which showed nonspecific chronic inflammation and pleural fluid with lymphocytosis and negative smear for acid-fast bacilli, and negative skin tests for tuberculosis, histoplasmosis, and coccidioidomycosis. On October 20, 1966 he underwent left thoracotomy for triple biopsy, revealing a markedly thickened pleura and edematous adjacent lung. Biopsy of the pleura and lung showed no granulomata, no acid-fast bacilli on Ziehl-Neelsen, but did show fluorescent staining bacilli resembling mycobacteria, on auramine-O examination.

He was placed on INH and PAS therapy, on which regimen the effusion and painsubsided. In March 1967, he developed a left-sided effusion. Examination of this fluid and a needle pleural biopsy revealed acid-fast bacilli morphologically resembling Mycobacterium tuberculosis on Ziehl-Neelsen smear and Auramine-O. He was continued on antituberculosis treatment with eventual resolution of the effusion on the left as well.

DISCUSSION

Upon reviewing the various series concerning this subject, one is impressed that "diffuse pulmonary disease" is a phrase intended to cover all forms of pulmonary parenchymal pathology except for the coin lesion and the expanding hilar mass, though a definition is never rendered. Open lung biopsy, as originally espoused, emphasized the bilateral nature of the disease, and some workers still limit the use of open biopsy to this smaller group of lesions. The trend in recent years, however, has been to utilize open biopsy for all manner of diffuse lung lesions which defy diagnosis by more conservative means.

We have expanded this to include those patients who may have pleural effusion or significant hilar adenopathy, considering that involvement of these areas is almost invariably linked to some form of underlying pulmonary disease. Our criteria for triple biopsy, therefore, are: 1) an undiagnosed pulmonary infiltrate, of any nature, unilateral or bilateral, 2) persistent pleural effusion, unilateral or bilateral, the nature of which was not revealed by study of aspirated pleural fluid, 3) hilar adenopathy, when associated with pulmonary parenchymal disease.

Obviously, the incision we use is more extensive than the more conventional incision, and actually is somewhat larger than advocated by our predecessors at this institution. We accomplish more through our incision. It must be large enough to slip a hand through comfortably to explore and to control hemorrhage if necessary. We believe this has not added to our morbidity and this is supported by Gaensler et al who determined that morbidity was not related to the size of the wound. We are convinced, as are other observers, that the problems which arise attendant to this procedure are incurred through inadequate drainage of the pleural space, and so two large caliber pleural drainage tubes are utilized as with all other types of pulmonary resection.

The results of our series are comparable to others reviewed, but vary in certain aspects, as follows. The high percentage of tuberculosis lesions (28 percent) has been noted earlier. The inclusion of pleural effusion as an indication for triple biopsy has resulted in the category of "nonspecific pleuritis" which comprises 24 percent of our series; this category does not appear in the other series re-
viewed. The absence of the various entities of pneumoconiosis must be due to the military population with which we deal, both active duty and retired, few of whom have been exposed during their working lives to the industrial atmospheres containing asbestos, beryllium, silicone dust, or the like. A particularly interesting by-product of our aggressive approach has been the discovery of a number of cases of active tuberculosis masquerading as sarcoidosis, thus providing early treatment and control. Our yield of positive diagnoses (65 percent) is lower over-all, than that reported by others, which ranged from 95 percent1 to 71 percent3, but if one excludes the group of nonspecific pleuritis, as the other studies have, our yield for the remainder of the cases in our series is 84 percent positive diagnosis.

The complication rate in our series has been negligible, for the above cited reason, ie adequate tube drainage. Reoperation for hemorrhage, or air leak, or occurrence of empyema has not been required, we believe for the same reason, that of rapid obliteration of the pleural space and continued effective drainage. The two deaths which occurred within 30 days of the thoracotomy were perhaps contributed to by the operation, but were directly related to the underlying disease process. Our mortality figures of 2.2 percent correlate well with the 2.6 percent of Klassen and Andrews,7 the 1.4 percent of the Rubin’s collected series of 494 cases.8 The two deaths involved extensive neoplastic disease, as have the vast majority of the deaths cited in the literature.

REFERENCES

Population Explosion

There is an apparent mathematical relationship between the different kinds of multiple births. Twins occur in one out of approximately 87 births. Triplets occur in one out of approximately 7,569 births. Quadruplets occur in one out of approximately 658,507 births. Quintuplets occur in one out of approximately 57,289,761 births. There are two kinds of twins: identical (monozygotic, one-egg) and fraternal (dizygotic, two-egg) twins. Identical twins are always of the same sex and contain the same set of genes, and so closely resemble each other that they are hardly distinguishable. Fraternal twins may be of the same or the opposite sex, and resemble each other no more closely than do brothers and sisters born at different times. A little more than one-fourth of all sets of twins are born identical; the other three-fourths are fraternal. The frequency of monozygotic twins is fairly constant for all the populations of the world, namely, three to four per 1,000. There are, however, marked differences in dizygotic rates for Negroes and whites. The average dizygotic rate for white is about seven per 1,000, whereas a rate of 20 per 1,000 is common throughout Negro Africa, reaching 40 per 1,000 at Ibadan, Nigeria. The dizygotic rate among Negroes outside Africa is 12–13 per 1,000—a difference that may be due to admixture with whites.