Efficacy of Pleural Needle Biopsy and Pleural Fluid Cytopathology in the Diagnosis of Malignant Neoplasm Involving the Pleura*

W. R. Salyer, M.D.,** J. C. Eggleston, M.D.,† and Y. S. Erozan, M.D.‡

A comparison was made of the efficacy of pleural needle biopsy and pleural-fluid cytopathology in the diagnosis of pleural tumor in a group of 271 patients. A malignant tumor involving the pleura was present in 95 cases. Needle biopsy alone provided a diagnosis of tumor in 53 instances, and cytopathologic preparations were diagnostic in 69 patients. A diagnosis was established on either the biopsy or cytopathology, or both, in 86 cases (90 percent). These results indicate the value of using both biopsy and fluid cytology in the evaluation of pleural effusion, which often is due to involvement of the pleura by malignant neoplasm.

Pleural effusions of unknown etiology are frequent and often difficult clinical problems. A variety of diseases may be associated with pleural effusions, and several techniques are employed to determine a diagnosis.

A common cause of effusion in the adult population is malignant tumor involving the pleura. The following study compares the efficacy of closed needle biopsy and of cytology of pleural fluid in establishing a diagnosis of pleural neoplasm.

METHODS

Three hundred and forty-eight consecutive patients who underwent needle biopsy of the pleura between 1966 and 1972 were identified in the surgical pathology files of The Johns Hopkins Hospital. The biopsies were performed with the Abrams pleural punch biopsy needle. Of these, cytopathologic examination of pleural fluid had also been performed, and follow-up information was available on 271 patients. This group forms the basis of the study.

The clinical records of these 271 patients were reviewed to determine the final diagnosis regarding the etiology of the effusion. A diagnosis of malignant tumor involving the pleura was accepted for patients who had persistent effusions unresponsive to therapy for infections and congestive heart failure and who died of tumor or had widespread metastases within two years.

Diagnoses of tuberculosis, congestive heart failure, bacterial pneumonia, pulmonary emboli, viral pleuritis, collagen vascular disease, and nephrotic syndrome were accepted with an appropriate clinical setting, additional bacteriologic data, response to therapy, and consistent clinical course. None of the patients regarded as having an effusion due to a non-neoplastic disease had evidence of tumor two years after the pleural biopsy.

Histologic and cytologic material from the 271 patients was reviewed. Routinely prepared tissue sections were stained with hematoxylin and eosin. Each biopsy was subserially sectioned, and three slides per biopsy were stained.

Cell spreads, millipore filters, and cell blocks were prepared for cytologic study from heparinized, fresh pleural fluid. These were then fixed in 95 percent ethyl alcohol except for one air-dried cell spread which was stained with the Giemsa stain. The other cell spreads and the millipore filters were stained with a modified Papanicolaou stain. Two sections of the cell blocks were stained either with hematoxylin and eosin or with the Papanicolaou stain, and two with PAS and alcian blue. The cytologic preparations were reported as one of the following: diagnostic of cancer; strong possibility of cancer; cellular abnormalities present, probably not representing cancer; or no evidence of cancer.

RESULTS

The causes of the pleural effusions of the 271 patients are shown in Table 1. A malignant tumor involving the pleura was present in 95 cases. The effusions were due to various non-neoplastic diseases in 176 instances. The most common of these was tuberculosis (56 cases), followed closely by congestive heart failure (46) and bacterial pneumonia (45).

The types of neoplasms involving the pleura in the 95 patients are listed in Table 2. The lung and breast were the most common primary sites. In 17 patients, the primary site was not determined.
Neoplastic disease of the pleura was evident in the pleural biopsy in 53 of the 95 cases (56 percent). These data are presented in Table 3. The first biopsy was diagnostic in 47 instances and the second biopsy in six.

Sixty-nine of the 95 patients (72 percent) had diagnostic pleural-fluid cytology (Table 4). The diagnosis was established on the first specimen in 50 cases, on the second in 11, on the third in 5, and on a specimen after the third in three. An additional 14 cases (15 percent) were diagnosed as strongly suggestive of cancer on one or more specimens.

A comparison of the results of biopsy and cytology in the diagnosis of pleural tumor is presented in Table 5. It is apparent that cytologic study provided a considerably higher rate of tumor diagnosis. However, it should be noted that in 17 cases, the biopsy provided the diagnosis when the cytology was less than diagnostic, making the result of both biopsy and cytology examinations much more profitable than either of the two alone.

Among the 176 patients with benign diseases of the pleura, there were no "false-positive" diagnoses on either the biopsies or the cytologic specimens. Cancer was suspected on the pleural fluids of these patients in eight instances (4 percent).

**Discussion**

The findings of this study confirm the usefulness of closed needle biopsy of the pleura and of cytologic study of pleural fluid in the diagnosis of malignant tumor involving the pleura. Although biopsy or cytology alone yielded definite diagnoses in a relatively high percentage of cases, the two used together provided a diagnosis in 90 percent of the patients.

Considering the focal nature of pleural involve-
ment by metastatic tumor, it is not surprising that the success in diagnosis for biopsy would be less than that of cytology. The use of the fiberoptic bronchoscope for pleuroscopy and pleural biopsy, allowing direct visualization of focal pleural lesions, should improve the results of biopsy alone. Although some authors have reported a greater yield by biopsy than with cytology, the experience in other series is similar to ours in this regard.

The success in diagnosis of tumor by biopsy alone in this series is similar to the experience of others. Several authors have reported a higher percentage of "positive" diagnoses, and others have recorded a lower yield (Table 6).

The results of cytopathologic examinations in this series also compares favorably with previous reports. As previously noted, possible reasons for the high yield obtained by cytopathologic examination including the use of multiple techniques—cell spreads, membrane filters, and cell blocks, and the submission of the specimens, fresh and heparinized. The value of examining multiple specimens is again emphasized by the results of this study. A definitive cancer diagnosis was established in repeat specimens in 19 cases. Not only do multiple specimens allow examination of more material, but pleural fluid which has recently accumulated following a thoracentesis is likely to contain freshly shed and better preserved cells.

The difficulties in distinguishing malignant tumor from reactive mesothelial proliferation in both needle biopsies and cytologic preparations are well recognized. One observation, however, deserves comment. Several authors have stated that the presence of cells ramifying among adjacent intercostal muscle fibers is a useful diagnostic feature of pleural tumor. While we agree that the presence of obvious invasion of skeletal muscle or lung is extremely helpful, we occasionally have observed cells apparently "invading" attached muscle in biopsies with no other features of malignant tumor. It is probable that the cells are forced into this position mechanically during the needle biopsy procedure. The finding of individual cells and groups of cells within muscle thus should not be used as an absolute indication of tumor.

**CONCLUSION**

This report has compared the efficacy of pleural needle biopsy and pleural fluid cytopathology in the diagnosis of pleural neoplasm. Cytologic studies alone yielded a higher percentage of cancer diagnoses than did the biopsies alone. A diagnosis was established in 90 percent of the patients with pleural tumor when both studies were performed. These findings indicate the value of utilizing these techniques concomitantly in the evaluation of patients with pleural effusion, which in the adult is often due to involvement of the pleura by malignant tumor.

**REFERENCES**

Thoracic Outlet Compression Syndrome

There are a great many instances in medical nosology which attest to inaccurate assumptions prior to the identification of the essence of a clinical entity. The item given in the title is an example in this regard. This term was introduced by Rob, C G et al (Br M J 2:709, 1958). Related conditions were labeled as one of the following syndromes: cervical rib, first thoracic rib, costodorsal outlet, costo-clavicular, scalenus anterior, pectoralis minor, Paget-Schroetter’s, Wright’s. Thoracic outlet compression syndrome is likely to be encountered in younger and middle-aged persons, with substantially higher incidence in females than in males. The basic event in its pathogenesis is, according to well documented findings, compression of the brachial plexus and/or subclavian artery and subclavian vein. The compression results from scissors-like approximation of the clavicle superiorly and the first rib below it. Adkins, P C (in Blades, B (ed): Surgical Diseases of the Chest, St. Louis, Mosby, C V, 1966) expressed the view that various musculoskeletal factors might cause the same clinical manifestations. These factors include bony anomalies, observed in about 30 percent of instances, such as cervical rib which may be attached to the first rib, bifid first rib, fusion of first and second ribs, attachment of the first rib to the second rib anteriorly instead of the sternum, deformity of the clavicle. Cervical ribs occur in 1 percent of the population, 80 percent of them being bilateral. Sixty percent of unilateral cervical ribs are on the left side. Only 10 percent of cervical ribs cause bilateral. Cervical rib syndrome was reported first by Wilshire, W H (Lancet 2:633, 1860). Other possible etiologic factors are trauma, particularly whiplash injury to the neck, fracture of the clavicle, occasionally, babbiness of the suspensory muscles resulting in sagging shoulder, tumors of the first rib, superior sulcus tumor, enlarged cervical lymph nodes. The syndrome may be associated with pregnancy. One of its symptoms is diffuse pain usually of gradual onset in the arm, hand, shoulder. Pain is likely to be more pronounced in the recumbent position and when the arm is elevated above the shoulder. Occasionally, pain appears suddenly; it may be severe and it may radiate to the anterior chest wall, to the neck or to the parascapular area. Urschel, H C Jr et al (Ann Thorac Surg 16:239, 1973) reported 44 patients in whom thoracic outlet compression syndrome masqueraded as coronary artery disease (pseudoangiitis). Other symptoms are weakness, easy fatigability of the arm, tingling, numbness, coldness, claminess of the hand. Physical examination may reveal ischemia, superficial vein distention of hand, arm, shoulder and neck, cyanosis and edema of arms, diminution or absence of radial pulse, trophic changes, Raynaud’s phenomenon. According to Nelson, R N et al (Ann Thorac Surg 8:437, 1969) Adson’s test (disappearance of radial pulse on hyperabduction of the arm and rotation of the neck with the head toward the abducted arm) is unreliable. In addition to pertinent x-rays, diagnostic workup may require subclavian arteriography, phlebography, sphygmomanometry, cervical myelography, mercury strain gauge plethysmography, and ulnar nerve conduction velocity determination. Normal conduction velocity, 72 m/second, is reduced in thoracic outlet compression syndrome. A great array of clinical entities may present some of the symptoms and signs of this condition. They include pathologic changes in the spine, spinal cord, lung, mediastinum; also, inflammatory and degenerative musculoskeletal and vascular alterations in one of the upper extremities, trauma, metal intoxication, diabetes mellitus, hypovitaminosis and others. Mild manifestations can be managed successfully by conservative measures, such as physical therapy and muscle relaxants. On the basis of their extensive experience, Urschel, H C Jr et al (cited above) state that if ulnar nerve conduction velocity is less than 55 m/second initially, surgical excision of the first rib by transaxillary approach is usually a successful treatment.

Andrew L. Banyai, M.D.