Lung Cancer Cell Type as a Determinant of Bronchoscopy Yield*

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The accuracy of diagnosis of lung cancer obtained by fiberoptic bronchoscopy utilizing sputum cytology and bronchial biopsy depends on the size, location, and number of biopsy samples taken from the tumor. We have found that the accuracy of diagnosis also depends upon the histologic type of cancer. Fiberoptic bronchoscopy (brushing, washing, and biopsies) was performed and sputum cytology and bronchial tissue was obtained from 51 patients with histologically-proven lung cancer. The bronchial biopsy was more sensitive than the bronchial washing and brushing techniques in detecting primary bronchogenic and metastatic carcinoma. It was positive in ten of ten patients with small cell carcinoma, 12 out of 20 cases of squamous cell carcinoma, three of four cases of adenocarcinoma, and three of four patients with large cell cancer. The bronchial biopsy yield was influenced by the histologic cell type with the highest diagnostic yield being found with small cell carcinoma.

Fiberoptic bronchoscopy has substantially advanced the detection of malignant pulmonary lesions by improving visualization of peripheral bronchi.1,2 Bronchial biopsy, brushing, and washing are valuable procedures associated with the bronchoscopic evaluation of pulmonary carcinoma. As the incidence of lung cancer increases, and these diagnostic procedures are performed more often, it is vital to determine the diagnostic usefulness of each of these techniques. Review of the literature shows little uniformity as to what determinants affect the sensitivity of these three procedures in diagnosing pulmonary carcinoma.3,4 The purpose of this study was to determine if the sensitivity of the bronchial biopsy, brushing, and washing was affected by the histologic type of lung cancer.

Materials and Methods

This study was based on 54 bronchoscopies performed on 51 patients. The bronchoscopies were performed by the staff of the Pulmonary Division at Metropolitan Hospital, New York Medical College. The study encompasses the period from July 1978 to July 1981, and includes all patients undergoing bronchoscopy within this period who were histologically diagnosed as having lung cancer either by bronchial biopsy, sputum cytology, open thoracotomy, or post mortem examination. There were three patients who had two bronchoscopies performed because of the failure of the first procedure to provide a definitive diagnosis. Data were evaluated for statistical significance by means of the chi square test.

Bronchoscopy was performed under local anesthesia using a 2 percent lidocaine solution. A fiberoptic bronchoscope (Olympus BFB-3) was inserted transnasally, and the tracheobronchial tree was examined. Visualized lesions were brushed three times with a nylon brush (Olympus). The brush was withdrawn into a catheter before removing it through the aspiration channel. The brushing specimen was transferred onto two separate slides and preserved with Adams-Spraycyte fixative. Subsequently, they were treated, fixed, and stained using Papanicolaou's technique, (hematoxylin, OG-6, EA-65). Three to six bronchial biopsy specimens were obtained under bronchoscopic visualization. They were placed in formalin, dehydrated, embedded in paraffin, and stained with hematoxylin-eosin. The lesion was then washed with small amounts of sterile saline solution (3 ml), and the aspirated secretions were continuously collected in a Lumen trap. The bronchial washing was transferred to 95 percent alcohol and a cell block was prepared and examined pathologically.

Results

In a three-year period, 54 bronchoscopies were performed in 51 lung cancer patients. The age of the patients ranged from 22 to 84 years, with a mean age of 61.3. Thirty-six of the patients were men (70.5 percent) and 15 were women (29.4 percent). Forty-two patients had bronchogenic carcinoma (82.4 percent), and nine had metastatic pulmonary disease (17.6 percent). Analysis of the 51 cases of bronchogenic carcinoma showed 21 patients had squamous cell carcinoma (41.1 percent), ten had small cell carcinoma (19.6 percent), five had large cell carcinoma (9.8 percent), and four had adenocarcinoma (7.8 percent). In two cases with malignant cytologic findings, the histologic cell type of carcinoma was undetermined (3.9 percent). The following tabulation lists the primary origin of the nine cases of pulmonary metastasis:

- Carcinoma of the larynx
- Renal cell carcinoma
- Breast carcinoma
- Gastric carcinoma
- Cervical carcinoma
- Gastric carcinoma*
- Schminkes tumor*
- Renal cell carcinoma*
- Primary origin unknown*

*Primary carcinoma in which bronchoscopy failed to identify pulmonary metastasis.
The diagnosis of lung cancer was made by fiberoptic bronchoscopy and associated procedures in 37 of 51 patients. The remaining 14 patients were diagnosed as having pulmonary carcinoma either by sputum cytology, open lung biopsy, or at autopsy. Three patients had two separate bronchoscopic procedures, and each of these were negative.

Bronchoscopic procedures resulted in a diagnosis of lung cancer in 32 of the 42 cases of bronchogenic carcinoma (76.2 percent) and five out of nine cases of metastatic disease (55.5 percent). There were four metastatic lung neoplasms which were not detected bronchoscopically and their primary sites of origin are noted in the tabulation.

Utilizing all three diagnostic techniques, a histologic diagnosis was determined from bronchoscopy specimens in ten of ten patients with small cell carcinoma, 14 out of 21 patients with squamous cell carcinoma (66.6 percent), three of four with adenocarcinoma (75 percent), and three of five patients with large cell carcinoma (60 percent).

The sensitivity of the bronchial biopsy in detecting bronchogenic and metastatic pulmonary carcinoma was compared with the washing and brushing procedures. It is clear that the bronchial biopsy was the most sensitive method yielding a positive finding in 32 of 48 biopsies (66.6 percent). The washings were positive in 23 of 52 washings (44.2 percent), whereas the brushings were only positive in 18 of 51 procedures (35.3 percent).

The sensitivity of these diagnostic procedures varied with the cell type. The bronchial biopsy was positive in ten of ten patients with small cell carcinoma (100 percent), three of four cases of adenocarcinoma (75 percent), three of four instances of large cell carcinoma (75 percent), 12 of 20 cases of squamous cell carcinoma (60 percent), and four of ten procedures with metastatic lung carcinoma (40 percent). Biopsy was not performed in six procedures due to medical contraindications.

In contrast, bronchial washings were positive in five of nine procedures with small cell cancer (55.5 percent), nine of 22 washings of squamous cell carcinoma (40.9 percent), one of three instances of adenocarcinoma (33.3 percent), and in one of four cases of large cell carcinoma (25 percent). Five of 11 washings of patients with metastatic disease were positive for malignant cells (45.5 percent). In the two patients with undefined histologic cell type, the bronchial washings revealed malignant cells. Bronchial washings were not done in three procedures.

Brush cytology was positive in five of nine patients with small cell carcinoma (55.5 percent), one of three cases of adenocarcinoma (33.3 percent), seven of 22 instances of squamous cell carcinoma (31.8 percent), and in one of five brushings of patients with metastatic disease (30 percent). One of the two malignant cases with undefined cell type had a positive brush cytology. Brush cytology was not performed in three procedures.

The sensitivity of various combinations of the bronchial biopsy, washings, and brushings in detecting bronchogenic carcinoma and metastatic cancer was analyzed. The biopsy alone was positive in 13 instances (35.1 percent). The biopsy, washings, and brushings were all simultaneously positive in 15 instances (40.5 percent). Brushings and washings were both positive together in only three instances (8.1 percent). In two instances, the washings alone made the diagnosis of lung cancer. The combination of the biopsy and brushing were both simultaneously positive in only one instance (2.7 percent). The brushing technique alone was never positive.

**DISCUSSION**

Comparison of the relative sensitivity of bronchial biopsy, washings, and brushings with histologic cell type of lung cancer had not been emphasized. Previous studies have directly correlated the yield of these bronchoscopic procedures with the size and location of the tumor as well as special techniques used by the physician performing the bronchoscopy. Present chemotherapeutic, surgical, and radiologic management of cancer is largely dependent upon the identification of the cell type of the lung cancer as this study, therefore, compares the specific cell type of carcinoma with the various bronchoscopic procedures in an attempt to evaluate the sensitivities of these procedures with the histology of the lesion.

The lung cancer patient population studied consisted of 70.5 percent men and 29.4 percent women who closely corresponded to the 1981 National Cancer Institutes Surveillance Data. The incidence of occurrence of small cell carcinoma (19.6 percent) and squamous cell carcinoma (41.1 percent) was similar to that of other investigators. The occurrence of adenocarcinoma (7.5 percent) and large cell carcinoma (9.5 percent) was lower than that of others, but these groups had small numbers of patients. In our hands, fiberoptic bronchoscopy yielded a positive diagnosis of pulmonary carcinoma in 72.5 percent of patients proven to have lung cancer. This result was similar to some authors but somewhat lower than those of others. The latter's higher results might have been attributed to fluoroscopic guidance of the bronchoscope, the size and location of the tumors, as well as the inclusion of "suspicious" cytology as a classification of cancer.

The variation in bronchoscopic yield according to cell type is not fully explained. The bronchial biopsy yield was higher in detecting small cell carcinoma than squamous cell carcinoma (p<0.05) or large cell carcinoma (p<0.05). It was not significantly higher than...
adenocarcinoma (p<0.1). This is attributed to the intrinsic aggressiveness of small cell carcinoma with its greater surface area and micrometastases.

The study represents the complete and unselected experience of the pulmonary division at a metropolitan hospital, but because it is a retrospective series, certain bias may be present. Bronchial biopsy was not done in six patients because of medical contraindications perhaps favoring the diagnosis of small cell carcinoma. However, bronchial washings and brushings, which were completed in these six patients, were diagnostic in five or six instances, and in the remaining patient, a diagnosis of metastases from gastrointestinal carcinoma was made by open lung biopsy, thus minimizing sample error. Were the number of biopsy samples (three to six) optimal? Three to six bronchial biopsy specimens which were satisfactory to the bronchoscopist were obtained under bronchoscopic visualization to provide adequate material for histologic examination. The number of samples seems to be optimal when compared to the literature. Since each patient's tumor was sampled in a similar manner, our technique probably did not induce significant bias.

The lower yield of adenocarcinoma may have occurred because this tumor is more likely to be peripherally located. While it is recognized that peripheral tumors not visible with the fiberoptic bronchoscope are more difficult to diagnose than those that are visible, the failure in diagnosing peripheral adenocarcinoma was minimized because 80 percent of our patients had proximal visualized lesions. Of the remaining peripheral lesions, only one patient had adenocarcinoma which was diagnosed by biopsy. The accuracy in making a tissue diagnosis of bronchogenic carcinoma was optimized in those patients who had lesions beyond the visible range of the bronchoscope by using fluoroscopic guidance with image intensification.

An analysis of the yield from bronchial washings and brushings revealed variability in the sensitivities of these procedures when correlated with the histologic cell type. Yields were higher when the patients had small cell carcinoma; however, this was not statistically significant.

We found the biopsy procedure consistently more sensitive than either the brushing or washing procedure in patients with bronchogenic carcinoma. However, bronchial washings gave a slightly higher yield in patients with metastatic disease. In addition, two instances of bronchogenic carcinoma were diagnosed on the basis of the washing aspirate alone. Thus, despite the low yield of bronchial washings, the technique is still useful. In conclusion, this review suggests that bronchial biopsy yield was directly influenced by histologic cell type of the lesion. The highest yield was in patients with small cell carcinoma of the lung, and this was probably due to the aggressive nature of the lesion.

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