Cytologic Diagnosis of Lung Lesions
by Bronchial Brushing

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ABSTRACT

Material obtained by the bronchial brushing technique from 205 patients with radiographically demonstrable lung lesions was evaluated. The bronchial smears showed well-preserved cellular elements which provided for evaluation of the type of cancer, as well as differentiation of cancer cases from inflammatory lesions. Lung carcinoma was diagnosed by bronchial brushing in 66 percent, by sputum cytology in 40 percent and by bronchoscopic aspirate in 19 percent. These gave an over-all positive cytologic diagnosis of 77 percent. Pitfalls in the cytologic interpretation were pointed out. The bronchial brushing technique is an important tool in the diagnosis of pulmonary lesions which are not accessible by bronchoscopy, and in which sputum failed to show tumor cells. The procedure is simple, is performed under local anesthesia with fluoroscopic control and is free of significant complications.

Introduction

The value of cytology as an aid in the diagnosis of lung lesions, especially in the early detection of pulmonary cancer, has been well recognized. Different methods are available for obtaining specimens used for cytologic interpretation of lung lesions.

Preoperative sputum and bronchial aspirates or washings have long been utilized for cytologic diagnosis of exfoliated cells.9 It has been recognized that a series of good sputum specimens from a deep cough give a better yield of malignant cells than bronchial aspirates. The proportion of cytologically proved cases varies directly with the number of sputum examinations, the attention to detail in the collection and preparation of the specimens and the experience of the examiner.10 The greater the size of the tumor and the more the tumor is centrally located, the more likely are malignant cells to be discovered in the sputum.

Bronchoscopic biopsy usually provides a diagnosis if the lesion is visualized and within reach of the bronchoscope. Blind bronchial biopsies usually yield unsatisfactory results.
These above diagnostic methods provide diagnosis mainly in centrally located lesions. Cancer cells from peripheral lesions do not exfoliate readily and they are not accessible by bronchoscopy. Needle biopsies of lung lesions have been attempted with the use of transthoracic needle aspiration. In 1959, Tsuboi et al and in 1964, Hattori and co-workers developed the bronchial brushing technique with fluoroscopic visualization for obtaining specimens for cytologic evaluation of lung cancer. The technique was modified by Fennessy in 1965. This method made possible a direct approach to the lesion and provided concentrated material for examination.

The purpose of this paper is to evaluate the adequacy of material obtained by the bronchial brushing technique, its diagnostic accuracy in peripheral lung lesions, pitfalls in cytologic interpretation and its role not only in lung cancer diagnosis but also in non-neoplastic lesions.

Materials and Methods

Two hundred-five patients have been examined in our institution by the bronchial brushing technique. A majority of these patients presented peripheral lung lesions, and the usual sputum studies were not diagnostic. In our studies, peripheral lung lesion is classified as one which is not visualized by the standard rigid bronchoscope and right angle lens. In most of these cases, bronchial brushing was performed as an out-patient procedure. Topical anesthesia was used exclusively. A premoulded selective bronchial catheter of polyethylene was maneuvered with a Seldinger guide wire into the diseased bronchial segment under image intensification fluoroscopic control. Disposable Fennessy bronchial brushes were then passed through the catheter to obtain direct samples. Biplane spot films were obtained for a permanent record of the position of the brush. More recently, one wire brushing sample was also obtained from each patient. The specimens were smeared on glass slides. Those for cytologic examination were fixed immediately in ether-alcohol. Those for microbiologic smears were stained by Gram, Giemsa and Ziehl-Neelsen methods for a search of acid-fast and fungal organisms.
Usually, two satisfactory glass smears could be made from a single nylon brush. After the smears were made, the disposable nylon brushes were cultured for acid-fast and fungal organisms. The wire brushes were fixed in 10 percent formalin and then, by using a fine hypodermic needle, bits of tissue were removed from the bristles and made into permanent paraffin block sections which were stained with hematoxylin and eosin.

**Results**

Of the 205 cases that were studied, 91 (45 percent) proved to be carcinoma, 72 (35 percent) proved to be inflammatory lesions, 8 (3.9 percent) were miscellaneous benign conditions and 34 (17 percent) were held for the results of culture of microorganisms or follow-ups. In table I are shown the comparative results obtained from the different procedures instituted in this series of cancer cases.

Cytologic interpretation of the neoplastic group was not a problem as long as the bronchial brush was properly positioned. The type of tumor could be discerned, based on specific cellular characteristics. The keratinizing type of epidermoid carcinomas showed a striking orangeophilic-staining keratin in the cytoplasm, in addition to the more characteristic neoplastic changes of hyperchromasia an increase in nuclear cytoplasmic ratio and pleomorphism (figure 1).

The undifferentiated small cell carcinoma showed a characteristic finding of small, dark-staining, pleomorphic nuclei appearing in small loose clusters. Nuclear chromatin was hard to delineate owing to hyperchromasia of the nuclei. Cells were often devoid of cytoplasm or a faint basophilic rim could be seen (figure 2). These cells are to be differentiated from groups of basal (reserve) cells; the latter usually occur in tight clusters. Their nuclei are homogeneous and regular. It may be noted that the cells on the periphery of the clusters of reserve cells present a more abundant cytoplasm and the centrally located cells are devoid of cytoplasm. These peripheral cells represent the differentiation towards the superficial columnar cells (figure 3).

The cases interpreted cytologically as adenocarcinoma in our series include both adenocarcinoma originating from the parabronchial glands (figure 4) and alveolar cell carcinoma (figure 5). Similar cellular characteristics are found in both types when using the bronchial brushing technique. The adenocarcinoma cells were large with moderate pleomorphism. Their nuclei showed indentation and/or lobulation. The

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**TABLE I**

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<th>Cytologic Diagnosis in Cancer Patients*</th>
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<tr>
<td>Bronchial brushing</td>
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<td>Sputum cytology</td>
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<tr>
<td>Bronchoscopic aspirate</td>
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<td>Over-all positive cytologic diagnosis</td>
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* Majority of cancer patients had peripheral lung lesions and nonproductive sputum.
Figure 4. Malignant cells with markedly enlarged nuclei, prominent nucleoli and fair amount of cytoplasm characteristic of adenocarcinoma.

Figure 5. Malignant cells from alveolar cell carcinoma, on the right, in contrast to a small group of well-preserved ciliated columnar cells on the left. (500X)
The cellular alterations in inflammatory conditions are so accentuated in preparations obtained from the bronchial brushing samples that the inexperienced person may interpret such altered cells as cancer cells of the well-differentiated adenocarcinoma type. Such cellular changes are not commonly found in sputum samples. It should be kept in mind that terminal bronchioles and alveoli may have very active cuboidal lining cells in chronic pneumonitis and that this type of cell may easily be picked up by the bronchial brush during the procedure. These reactive cells present themselves as cuboidal cells with active nuclei and prominent nucleoli; they have, however, been observed to form small clumps with regular cellular borders (figure 8). In severe cases, they may be hard to differentiate from a well-differentiated adenocarcinoma. Viral infections also present bizarre cellular changes in exfoliated material. Large atypical metaplastic squamous cells and multinucleated cells are seen in sputum smears. Squamous metaplasia is another pitfall in the cytologic diagnosis of cancer. This may be confused with a well-differentiated epidermoid carcinoma. Metaplastic cells usually occur in clusters, have uniform nuclei and are closely adherent to one another.

In this series, three false-positive cases have been examined. Each one is an example of the pitfalls in the cytologic diagnosis of the bronchial brushing specimen named in the above discussion.

Comments

The specimen obtained by the bronchial brushing technique enables the examiner to
These cytologic findings open surgical procedures can be deferred, on occasion, to await culture results. In some circumstances, it is necessary to ascertain that the material is obtained directly from the involved area and that the position is confirmed by biplane radiologic techniques.

The bronchial brushing technique is very helpful in obtaining a definitive cancer diagnosis in inoperable cases, prior to radiation or chemotherapy. By obtaining a positive cancer diagnosis by bronchial brushing technique, not only are mistakes in diagnosis avoided but also the inoperable patient need not undergo a diagnostic thoracotomy. A definite cytologic diagnosis by this technique appears to be reliable.

The confirmation of the diagnosis of inflammatory conditions of the lung in our series was based upon the following criteria: (1) surgical specimens, (2) positive culture with a compatible clinical course (3) complete clearing of lesion with a minimum of six months' follow-up (4) stable or smaller lesions with a minimum follow-up of two years.

References


“Life affords no higher pleasure than that of surmounting difficulties, passing from one step of success to another, forming new wishes and seeing them gratified. He that labors in any great or laudable undertaking has his fatigues first supported by hope and afterwards rewarded by joy.”

Samuel Johnson