Comparative study of bronchoalveolar lavage, bronchial brushing, and FNAC in diagnosing malignant neoplasms of lungs

ABSTRACT
Background: Lung cancer is the leading cause of death in developed countries and is increasing at alarming rates in developing countries. Cytological techniques such as bronchoalveolar lavage (BAL), bronchial brushing (BB), and fine needle aspiration cytology (FNAC) can aid in the early diagnosis of lung malignancies.

Materials and Methods: A total of 67 cases, suspected of lung cancer between January 2010 and December 2012, were selected where samples of BAL, BB, FNAC, as well as biopsy were obtained and processed according to the standard procedures of cytology and histology. The aim of this study was to compare the diagnostic efficacy of the three modalities, i.e., BAL, BB, and FNAC in diagnosing malignant neoplasms of the lung. Biopsy was considered to be the gold standard diagnostic test.

Results: Sensitivity of BAL, BB, and FNAC was found to be 47.61, 65.07, and 88.88%, respectively, whereas specificity of BAL, BB, and FNAC was 75, 75, and 100%, respectively.

Conclusions: FNAC is the best technique among the three for the diagnosis of lung cancers.

Key words: Bronchial brushing; bronchoalveolar lavage; diagnostic efficacy; FNAC

Introduction
Lung cancer is the leading cause of death in developed countries and is increasing at alarming rates in developing countries. Although lung carcinoma remains more common in males than females, the difference is decreasing. Cytological methods in the diagnosis of malignant lesions of the lungs has been generally considered to be one of its most successful applications. Flexible fiberoptic bronchoscope revolutionized respiratory cytology as techniques such as bronchial brushing (BB), bronchoalveolar lavage (BAL), and bronchial biopsy became more easy, accessible, and popular.

Fine needle aspiration cytology (FNAC) has proved to be the most helpful method for the diagnosis of lung tumors. Our aim was to compare the efficacy of these three cytological techniques in lung malignancies by correlating them with histopathological diagnosis by bronchial biopsy.

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Materials and Methods

In our study, out of all the suspected cases of lung carcinoma from January 2010 to December 2012, 67 cases were selected where BAL, BB, and FNAC samples, as well as bronchial biopsy were available. If any of the three samples was inadequate or not received, the case was not included. Bronchial biopsy was considered as the gold standard method. The samples were obtained by the pulmonologist with the help of flexible fiberoptic bronchoscopy. The samples were received as follows: (1) BAL samples were received as 20 ml aliquots of normal saline in sterile vials. Samples were centrifuged in cytospin and prepared into air-dried and wet-fixed smears. (2) BB samples were received as air-dried and wet-fixed slides. (3) FNAC samples were received as air-dried and wet-fixed smears obtained by ultrasonography (USG) or computed tomography (CT)-guided transthoracic or transbronchial approach. The air-dried smears were stained with May Grunwald Geimsa and the wet-fixed slides with Papanicolaou and Hematoxylin and Eosin stains. (4) Bronchial biopsies were received in 10% formalin, processed and stained with Hematoxylin and Eosin stain, special stains, and immunohistochemistry wherever required.

Results

In our study of 67 cases suspected of lung cancer, 45 were males whereas 22 were females. Four cases were negative for malignancy on biopsy, 63 cases were found to be positive, thereby giving a male: female ratio of 2.15. Their age ranged between 35 and 85 years. Maximum cases were seen between the fifth and seventh decade. Majority of the cases were found to be associated with smoking in early age group.

In our study, BAL showed 30 true positive cases and 3 true negative cases, which was confirmed by biopsy. However, 1 case was diagnosed as false positive and 33 cases as false negative by BAL. BB showed 41 true positive cases and 3 true negative cases with only 1 case as false positive and 22 cases as false negative. FNAC gave the best result with 56 true positive cases and 4 true negative cases. Moreover, 7 cases were false negative and no false positive case [Table 1].

Sensitivity of BAL was 47.61% and of BB was 65.07%; it was highest for FNAC at 88.88%. Specificity of BAL was 75%, BB was 75%, and that of FNAC was 100%. Similarly, positive predictive value and negative predictive value of FNAC were far better than that of BAL and BB. Accuracy of BAL was 44.77%, BB was 65.67%, and that of FNAC was 89.55% [Table 2].

Of the 30 cases diagnosed by BAL as lung cancer, 11 were squamous cell carcinoma, 14 adenocarcinoma, 3 small cell carcinoma, and 2 cases were undifferentiated large cell carcinoma. In 41 cases diagnosed by BB as lung cancer, 18 were squamous cell carcinoma, 18 adenocarcinoma, 3 small cell carcinoma, and 2 of undifferentiated large cell carcinoma. Out of the 56 cases diagnosed by FNAC as lung cancer, 22 were squamous cell carcinoma, 26 adenocarcinoma, 4 cases small cell carcinoma, 2 undifferentiated large cell carcinoma, and 1 each adenosquamous carcinoma and metastatic ductal carcinoma [Table 3].

Figure 1 (a) Fine needle aspiration cytology (FNAC) of adenocarcinoma showed pleomorphic cells with abundant cytoplasm and prominent nucleoli (Hematoxylin and Eosin, 400×), (b) Bronchial brush smear of squamous cell carcinoma showed pleomorphic and hyperchromatic cells in sheets (Hematoxylin and Eosin, 200×). (c) FNAC smear of Small cell anaplastic carcinoma showed loose clusters, round cells with scant cytoplasm, nuclear moulding, and streak of nuclear trail (Giemsa, 200×). (d) Bronchial brush smear of Large cell undifferentiated carcinoma consisted of large pleomorphic cells, hyperchromatic pleomorphic nuclei, multinucleated cells, and atypical mitotic figures (Hematoxylin and Eosin, 200×).

| Test result | FNAC | BB | BAL |
|-------------|------|----|-----|
| TP*         | 56   | 41 | 30  |
| TN‡         | 1    | 1  | 1   |
| FP‡         | 0    | 22 | 33  |
| FN‡‡        | 7    | 1  | 1   |

Statistics

Sensitivity (TP*/TP + FN‡‡) 88.88
Specificity (TN‡/TN + FP) 70.75
Positive predictive value (TP/TP + FP) 97.61
Negative predictive value (TN‡/TN + FN) 83.38
Accuracy (TP + TN‡/TP + TN‡ + FP + FN) 89.55

| Test result | FNAC | BB | BAL |
|-------------|------|----|-----|
| Squamous cell carcinoma | 22 | 18 | 11 |
| Adenocarcinoma | 26 | 18 | 14 |
| Small cell carcinoma | 4 | 3 | 3 |
| Undifferentiated large cell carcinoma | 2 | 1 | 2 |
| Adenosquamous carcinoma | 1 | 1 | 0 |
| Metastasis | 1 | 0 | 1 |
The sensitivity of BAL for diagnosing lung cancers [Table 1]. In our study, the values of sensitivity, specificity, and overall accuracy of BB were 65.07, 75.0, and 65.67%, respectively.

The sensitivity of FNAC involves sampling the lesion with the help of a fine needle usually 25–26 gauze. The success of FNAC depends on four requirements: (1) samples must be representative of the lesion investigated; (2) Samples must be adequate in terms of cells and other tissue components; (3) Samples must be correctly smeared and processed; and (4) the biopsy must be accompanied by relevant and correct clinical/radiological information. Definitive diagnosis cannot possibly be made if these requirements are not fulfilled. Its accuracy in many situations can approach that of histopathology in providing an unequivocal diagnosis. However, it is not a substitute for conventional histopathology.

FNAC showed sensitivity, specificity, and accuracy as 88.88, 75.0, and 89.55%, which were much superior to those of BAL. In our study, the sensitivity, specificity, and accuracy of BAL were 47.61, 75, and 44.77%, respectively, when a single sample of BAL was collected.

In our study, the sensitivity, specificity, and accuracy of BB were 65.07, 75.0, and 65.67%, respectively.

Complications of bronchoscopy are rare (0.5 and 0.8% for major and minor complications, respectively), and include laryngospasm, bronchospasm, disturbances of cardiac conduction, seizures, hypoxia, and sepsis. The incidence of major complications is higher for transbronchial biopsy (6.8%). Cytological sampling by BAL relies mainly on cells “exfoliated” from the malignant lesion. Exfoliated cells that are lying in the bronchus start developing degenerative changes, thus progressively losing their morphological details, which are important in differentiating them from nonmalignant cells that are shed off by the normal bronchial epithelial lining. With BAL, the bronchoscope is wedged into position as far as it goes, and the distal airways are flushed with several aliquots of sterile saline, usually approximately 20 mL. The first aliquot is more representative of the cellular material from larger airways, whereas subsequent aliquots reflect the alveolar compartment. BAL is also used for the diagnosis of malignancy, with sensitivity ranging from 35 to 70%.[9,10] The sensitivity of BAL for detecting malignancy is higher for multifocal or diffuse tumors such as bronchioloalveolar carcinoma.[11] False positive results are occasionally encountered as a result of atypical type II pneumocytes in the setting of pneumonia, diffuse alveolar damage, bone marrow transplantation, and chemotherapy.[12,13]

In BB, fiberoptic bronchoscopy allows direct visualization and sampling of the tracheobronchial tree. A brush is applied to the surface of an endobronchial lesion, and the entrapped cells are either smeared onto a glass slide or rinsed in a collection medium for thin layer or cell block preparation. If smears are made, immediate fixation (by immersion into 95% ethanol or spray fixation) of the smears is essential to preserve morphologic detail.[14]

Discussion

A pivotal improvement in sampling cells from the lower respiratory tract occurred with the development of the flexible bronchoscope in the late 1960s. Today, any part of the respiratory tract can be sampled with this device. With this, the emphasis shifted from the diagnosis of malignancy in operable patients and confirmation of metastases to the use of cytology as a first line diagnostic procedure on which crucial management decisions could be based.[11,12] In our study, in comparison to BAL, BB gave higher number of true positive and true negative cases, and much lesser number of false positive and false negative cases, showing its superiority over BAL in diagnosing lung cancers [Table 1].

Figure 1: (a) Fine needle aspiration cytology (FNAC) of adenocarcinoma showed pleomorphic cells with abundant cytoplasm and prominent nuclei (H&E stain, x400). (b) Bronchial brush smear of squamous cell carcinoma showed pleomorphic and hyperchromatic cells in sheets (H&E stain, x200). (c) FNAC smear of Small cell anaplastic carcinoma showed loose clusters, round cells with scant cytoplasm, nuclear moulding, and streak of nuclear trail (Giemsa stain, x200). (d) Bronchial brush smear of Large cell undifferentiated carcinoma consisted of large pleomorphic cells, hyperchromatic pleomorphic nuclei, multinucleated cells, and atypical mitotic figures (H&E stain, x200)

Complications of bronchoscopy are rare (0.5 and 0.8% for major and minor complications, respectively), and include laryngospasm, bronchospasm, disturbances of cardiac conduction, seizures, hypoxia, and sepsis. The incidence of major complications is higher for transbronchial biopsy (6.8%). Cytological sampling by BAL relies mainly on cells “exfoliated” from the malignant lesion. Exfoliated cells that are lying in the bronchus start developing degenerative changes, thus progressively losing their morphological details, which are important in differentiating them from nonmalignant cells that are shed off by the normal bronchial epithelial lining. With BAL, the bronchoscope is wedged into position as far as it goes, and the distal airways are flushed with several aliquots of sterile saline, usually approximately 20 mL. The first aliquot is more representative of the cellular material from larger airways, whereas subsequent aliquots reflect the alveolar compartment.[7,8] BAL is also used for the diagnosis of malignancy, with sensitivity ranging from 35 to 70%.[9,10] The sensitivity of BAL for detecting malignancy is higher for multifocal or diffuse tumors such as bronchioloalveolar carcinoma.[11] False positive results are occasionally encountered as a result of atypical type II pneumocytes in the setting of pneumonia, diffuse alveolar damage, bone marrow transplantation, and chemotherapy.[12,13]

FNAC showed sensitivity, specificity, and accuracy as 88.88, 100, and 89.55%, which were much superior to those of BAL and BB [Table 3]. The sensitivity of 88.88% for FNAC was in agreement with other researchers such as Rivera and Mehta et al. (90.0%) and Tuladhar and Panth (84.0%).[17,19]
In the present study, bronchial biopsy classified 39.68% cases (25/63) as squamous cell carcinoma whereas FNAC diagnosed 39.28% cases (22/56) as squamous cell carcinoma. On the other hand, BB could diagnose 43.90% of the cases (18/41) as squamous cell carcinoma, BAL was able to diagnose only 36.66% cases (11/30) as squamous cell type. Similarly, 46.03% cases (29/63) were diagnosed as adenocarcinoma by biopsy. FNAC showed 46.42% cases (26/56) of all the cases to be of adenocarcinoma, whereas BB samples classified 43.90% cases (18/41) as adenocarcinoma. While in BAL samples, 46.66% cases (14/30) were morphologically diagnosed as adenocarcinoma, 7.93% cases (5/63) were diagnosed as small cell carcinoma by biopsy. FNAC classified 7.14% (4/56) as small cell carcinoma. BB samples showed 7.31% cases (3/41) as small cell carcinoma, whereas in BAL samples, 10% cases (3/30) were of small cell type.

Thus, FNAC promises to be a very convenient, efficient, time saving diagnostic technique, which can be performed for screening of suspicious cases and early diagnosis of malignancies in the lung. However, FNAC has its limitations because it gives more false negative results than biopsy. Therefore, cases that are highly suspicious for malignancy on radiology and clinical examination, which were negative on FNAC, may later be biopsied to confirm the morphological typing of the malignant lesion.

Conclusion

To conclude, FNAC is a significantly superior cytological technique in the diagnosis of malignancies in the lung because it demonstrates far better specificity, sensitivity, and accuracy in comparison to BAL and BB.

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Conflicts of interest

There are no conflicts of interest.

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