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DIAGNOSTIC UTILITY OF BRONCHOSCOPY IN BRONCHOSCOPICALLY NON-VISIBLE (PERIBRONCHIAL) TUMORS INCLUDING TBNA: STUDY OF 150 CASES IN TERTIARY CARE SETTING IN INDIA

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ABSTRACT

Background: Lung cancer is the leading cause of cancer deaths around the world. Globally, lung cancer is the largest contributor to new cancer diagnosis and to death from cancer. Various conventional diagnostic techniques (CDTs) such as endobronchial forcep biopsy (FB), bronchial washing (BW) and bronchial brushing (BB), and transbronchial needle aspiration cytology (TBNA) are employed during fiber-optic bronchoscopy. **Methods:** Prospective, two tertiary care center study conducted between November 2012 and February 2014 at Bronchoscopy unit of MIMSR Medical College Latur, & Venkatesh chest hospital Latur India, to find the role of TBNA in bronchoscopically nonvisible (peribronchial) lesions (PBL) in confirming the diagnosis of lung cancer and to find additive yield over other techniques such as BB, BW and FB, and included 150 patients on the basis of clinical and radiological features of malignancy. In Peribronchial lesions during bronchoscopy documented findings are narrowing of airway due to extrinsic compression by tumour or Lymphadenopathy, or predominant feature of 'bulge' seen in the lumen. TBNA, FB, BB and BW were performed in all the cases during FOB. Histopathological and cytological examinations of specimens were performed at Pathology department. The statistical analysis was done using chi square test. **Results**: Total 150 patients, on the basis of clinical and radiological signs of malignancy, between age group 21-87 years with mean age 59.16 years. Males were 81.33% of total, of which 79% were smoker with 57.87% cases were having >40 pack years smoking history. Commoner symptoms were cough (92.33%), Shortness of breath (66.33%) & chest pain (61.33%), while commoner radiological presenting features were hilar mass (51%), parahilar opacity (21%), collapse segmental/lobar (18%). In PBL, diagnostic yield of TBNA, FB & CDTs were 68.66% & 27.33% & 41.33% respectively. Additional CDTs like BB cytology and BW has additive yield to FB from 27.33% to 41.33% in PBL (P<0.00001). Sensitivity of TBNA in PBL is 96.19% while that of CDTs is 59 (P<0.00001). IHC on TBNA specimens had increased histological type confirmation. **Conclusion:** Transbronchial needle aspiration is a beneficial, safe and minimally invasive bronchoscopic technique with insignificant side effect in the diagnosis bronchogenic carcinoma. TBNA in peribronchial lesions is most sensitive modality over conventional techniques and considered as 'gold standard' in these lesions. TBNA will definitely decrease need for repeat bronchoscopy.

KEYWORDS: TBNA, Bronchoscopy, peribronchial lesions (PBL), Lung cancer.

INTRODUCTION

Lung Cancer is the leading cause of cancer deaths around the world. Globally, Lung cancer is the largest contributor to new cancer diagnosis (1,350,000 new cases and 12.4% of total new cancer cases) and to death from cancer (1,180,000 deaths and 17.6% of total cancer deaths).[1] The World Health Organization (WHO) estimates that Lung cancer deaths worldwide will continue to rise, largely as a result of an increase in global tobacco use, especially in Asia. Tobacco use is the principal risk factor for Lung cancer, and large proportions of all pulmonary carcinomas are attributable to effects of cigarette smoking.[2]

In 1968, Machita and Olympus both introduced commercially available fiberoptic bronchoscopes. Since its introduction; fiberoptic bronchoscope has become an increasingly important diagnostic and therapeutic tool in respiratory diseases including lung cancer.[3] First time, TBNA done through rigid scope by Schieppati, thereafter Wang developed the flexible type.[4] Various diagnostic techniques like endobronchial biopsy, bronchial washing and bronchial brushing, endobronchial and transbronchial needle aspiration cytology (EBNA & TBNA) are employed during fiberoptic bronchoscopy. Studies have confirmed that employing various techniques in combinations increases the diagnostic yield of fiberoptic bronchoscopy.[5]

Transbronchial needle aspiration (TBNA) via flexible bronchoscopy is a well-established sampling tool for diagnosis of lung malignancies.[6] TBNA is superior to all other sampling modalities in peribronchial and submucosal lesions and is on par with bronchoscopic forcep biopsy in endobronchial tumour with an average diagnostic yield of 80%.[6] On the other hand the previous studies of bronchoscopy in peripheral lesions have shown a great variability in the diagnostic yield, with sensitivity for cancer between 20% and 86%.[7]

TBNA improves the yield of FOB when added to bronchial washing, brushing and forcep biopsy.[8,9] Despite all these positive aspects, however, TBNA is underutilized.[10] This has been ascribed to lack of formal training, difficulties with needle handling, poor success rate and insufficient cytological laboratory support.[8,11] Although a combination of all these techniques has been shown to increase the diagnostic yield, it is not always possible to perform all these sampling techniques in the same patient.[11]

In this study, we observed the role of TBNA in submucosal and peribronchial lesions as compared to other bronchoscopic techniques such as bronchial wash, bronchial brush and forcep biopsy in confirming diagnosis of lung malignancies, with special emphasis on additional yield of TBNA in comparison to other techniques. We also analyzed sole positive yield of TBNA in peribronchial lesions.

MATERIALS AND METHODS

Prospective, two tertiary care center study conducted between November 2012 and February 2013 at Bronchoscopy unit of MIMSR Medical College Latur, & Venkatesh chest hospital Latur India, to find the role of TBNA in bronchoscopically nonvisible (peribronchial) lesions (PBL) in confirming the diagnosis of lung cancer and to find additive yield over other techniques such as BB, BW and FB, and included 150 patients on the basis of clinical and radiological features of malignancy. Hospital's Ethical committee approval and written informed consent of patient.

Inclusion criteria

1. Unexplained paralysis of vocal cord (hoarseness of voice) or stridor.
2. Chest x-ray with radiological features of malignancy. (Coin lesions, Mass lesions, Mediastinal widening, unilateral high hemidiphragm, Segmental/complete lung collapse, Non-resolving Pneumonia).
3. Normal chest x-ray with high clinical suspicion.
4. Localized monophonic wheeze.
5. Unexplained & recurrent pleural effusion.

Exclusion criteria

1. Coagulopathy which cannot be corrected & Platelets <50,000 per μL**.**
2. Pulmonary hypertension.
3. Uremia & Serum creatinine >3**.**
4. Mechanical ventilation with high PEEP**.**
5. Refractory hypoxemia.
6. Recent myocardial infarction or unstable angina.
7. Significant dysrhythmia and hemodynamic instability**.**
8. Poor ability to cooperate with procedure.

The Fiberoptic Video Bronchoscope FUJINON EPX-201H, fiberoptic video-bronchoscope was used during procedures in all patients enrolled in study by two operators. The upper airway was anaesthetized with 2 ml of 10% lignocaine solution. An additional small quantity of 1% lignocaine is instilled through the bronchoscope for topical bronchial anesthesia, as needed. Patients if he or she was apprehensive were sedated with intravenous midazolam. Bronchoscope was inserted transnasally in about 85% of cases, while in the remaining cases, the transoral route is used. Fluoroscopy facility is also available in our unit.

During bronchoscopy characteristic endoscopic features of Peribronchial Lesions during bronchoscopy documented as narrowing of airway due to extrinsic compression of airways by tumour or Lymphadenopathy, or predominant feature of 'bulge' seen in the lumen.[12,13]

In order to avoid contamination TBNA was performed prior to other procedures such as bronchial brush, forcep biopsy and bronchial wash. TBNA was procedure was done first to avoid false positive and then other techniques were performed. TBNA and forcep biopsy performed in most of the cases and other conventional diagnostic techniques like bronchial wash and bronchial brush decision taken by operator doing bronchoscopy.

TBNA was performed using MW 522 needle catheters (Mill-Rose Laboratories). During bronchoscopy the catheter was passed through the biopsy channel with the needle retracted. Under direct vision the needle was advanced at 90^0 peribronchial lesions or bulge. In peribronchial lesions needle was inserted in to lesion according to pushing technique introduced by Wang. Once the needle was appropriately placed within the lesion, it was minimally advanced, so that the entire length of the needle will be in the tissue. Then the inner 22-gauge needle was retracted and locked in position. The needle was moved to and fro, under applied suction from a 20-mL syringe. The pressure was released before the needle was taken out from the tissue, to avoid false-positive aspirates. The aspirated material was blown in to four or five slides, smeared, fixed with 95% alcohol and sent for cytological examination at Pathology Department.

The statistical analysis was done by using Chi Square test. Significant values of x^2 were seen from probability table for different degree of freedom required. P value was considered significant if it was below 0.05 and highly significant in case <0.001.

OBSERVATION AND ANALYSIS

Total 150 patients, on the basis of clinical and radiological signs of malignancy, between age group 21-87 years with mean age 59.16 years. Males were 81.33% of total, of which 79% were smoker with 57.87% cases were having >40 pack years smoking history. Commoner symptoms were cough (92.33%), Shortness of breath (66.33%) & chest pain (61.33%), while commoner radiological presenting features were hilar mass (51%), parahilar opacity (21%), collapse segmental/lobar (18%).

Table 1: Yield of TBNA, Forcep Biopsy and CDTs in Peribronchial lesions.

Results	TBNA	Forcep Biopsy	CDT
Positive	101 (68.66%)	41 (27.33%)	62 (41.33%)
Negative	49	109	88
Total	150	150	150

($\chi 2$=53.11, *df* =2, p<0.00001).

In peribronchial lesions, TBNA has significant diagnostic yield i.e 68.66% individually as compared to forcep biopsy 27.33% and CDT 41.33%. Additional CDTs like bronchial brush cytology and bronchial wash has additive yield to forcep biopsy from 27.33% to 41.33% in peribronchial lesions (P<0.00001).[Table 1].

Table 2: Sensitivity of TBNA and CDTS (Conventional Diagnostic Techniques) in Peribronchial lesions during bronchoscopy.

Procedure	Positive yield	No yield	Total Diagnosed cases
TBNA	101	4	105
CDT	62	43	105

($\chi 2$=41.69, *df*=1, p< 0.00001).

Sensitivity of TBNA in diagnosing Peribronchial lung malignancy is 96.19% while that of CDTs 59.04%. TBNA has very high sensitivity as compared to CDTs, and is statistically significant in Peribronchial lesions (P<0.00001).[Table 2].

DISCUSSION

1. Yield of TBNA, Forcep biopsy and other conventional diagnostic techniques in Peribronchial Lesions (bulge)

In peribronchial lesions, TBNA has significant diagnostic yield i.e 68.66% individually as compared to forcep biopsy 27.33% and CDT 41.33%. Additional CDTs like bronchial brush cytology and bronchial wash has additive yield to forcep biopsy from 27.33% to 41.33% in peribronchial lesions (P<0.00001). Ladina Joos et al[18] reported yield of TBNA was 43.6% in their study. Harrow EM et al[19] reported success rate of TBNA up to 80% for peribronchial disease.

Additional CDTs like bronchial brush cytology and bronchial wash has additive yield to forcep biopsy from 27.33% to 41.33% in peribronchial Lesions (P<0.0001). Dasgupta et al[6], Govert et al[20] found combination of higher yield of TBNA over CDT and have increased yield CDT over forcep biopsy alone in their studies. Caglayan et al[12] in peribronchial disease reported diagnostic rate was 52% by CDT, 87% by TBNA plus CDT and superiority of combination over CDT was significant (p<0.001).

TBNA was the only diagnostic technique in 31 out of 101 cases of peribronchial lesions in our study. Sole yield of TBNA in our study is 30.69% (31/101) which is significantly higher than any Individual CDTs. Caglayan et al[12] reported 34.3% yield of TBNA as a sole in their study in peribronchial lesions.

In our study Sensitivity of TBNA in diagnosing lung malignancy is 96.19% while that of CDTs 59.04%. TBNA has very high sensitivity as compared to CDTs, and is statistically significant in Peribronchial Lesions. (P<0.01) Khoo et al[17] reported sensitivity of TBNA 89% and Shure and Fedullo et al[13] reported sensitivity of CDTs 71% in their study.

2. Other important observations during study

A. Without TBNA during routine bronchoscopy in Peribronchial lesions overall yield is decreased, & need for repeat procedures are increased

When TBNA cytology was showing malignant cells with no histological type and forcep biopsy report was inconclusive or non-diagnostic. In such cases we performed repeat bronchoscopy procedure for further additional samplings. Repeat bronchoscopy can be prevented by ROSE (rapid on site evaluation) technique, which aids immediate diagnosis and helps in guiding adequacy of samples during bronchoscopy. We have rapid on site evaluation cytology facility which was helped us in decreasing repeat procedure. We require average 9 passes of TBNA in these difficult cases, and routinely we preferred 6 TBNA passes to get adequate yield and final confirmatory diagnosis. A. Diacon et al[26] reported ROSE detected diagnostic material at first site sampled in 50% of all procedures, 64% of bronchoscopy procedures were terminated early because of early diagnosis and in 35% cases only sampling methods other than TBNA is required.

B. TBNA procedure related adverse events documented in present study

Thirteen patients in our study was developed hypoxemia during procedures and was corrected by oxygen supplementation and finally we completed the procedure with supplementation of oxygen. We usually provide oxygen supplementation as a protocol whenever oxygen saturation falls below 90% and terminate the procedure if it is not correctable with oxygen supplementation. C.T.Bollinger et al[4] documented hypoxemia during bronchoscopy procedure and recommended monitoring oxygen saturation with pulse oximetry during procedure.

Other complications like minor bleeding & significant bleeding was documented in 26 & 9 cases respectively of

total 350 in our study, and manifested as post bronchoscopy hemoptysis. We were used instillation of cold saline and topical adrenaline bronchoscopically to manage bleeding. Pneumothorax which is a minor and rare complication of TBNA is observed in 0.014% (5/350) cases. Mortality rate in our study during bronchoscopic procedures was zero percent. C.T.Bollinger et al[4], Jin F et al[27] ACCP Guidelines on Interventional Pulmonology 2003[28] reported mortality rate of 0.01% and complication rate 0.7% in their study. Other potentially life threatening complications like respiratory depression, airway obstruction, arrhythmias and infections were also not observed in our study.

CONCLUSION

Bronchoscopy guided diagnostic techniques has limited diagnostic yield in endoscopically non visible or peribronchial lesions. With the use of conventional TBNA, diagnostic yield has changed significantly to other conventional techniques like Forcep biopsy and bronchial wash. Conventional TBNA is underutilized & less utilized routinely during bronchoscopy in diagnosing peribronchial lesions.

TBNA in Peribronchial lesions is most sensitive modality over conventional techniques and considered as 'gold standard' in these lesions. TBNA is cost effective and it will decrease need for repeat bronchoscopy. TBNA should be considered routinely during bronchoscopy where EBUS TBNA is not available or not affordable in setting like India. More emphasis should be given to TBNA training especially in interventional pulmonology centers.

"Compliance with Ethical Standards"

1. **Funding-nil (no funding or any grant utilized)**
2. **Disclosure of potential conflicts of interest-** "we declare that we have no conflicts of interest.''
3. **Research involving human participants and/or animals-** All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.
4. **Informed consent-** Informed consent was obtained from all individual participants included in the study.

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