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Research Article
Transbronchial

Conventional transbronchial needle aspiration cytology as a diagnostic tool in patients with suspected lung cancer - Our experience at a tertiary care center.

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Background: Conventional transbronchial needle aspiration (c-TBNA) is a minimally invasive bronchoscopic technique used to obtain cytological samples from peribronchial lesions and mediastinal lymph nodes. However, the concern about its efficacy and the advent of newer techniques have led to the underutilization of this time tested and cost-effective modality. **Objective:** The present study was aimed to assess the diagnostic yield of c-TBNA in suspected cases of lung cancer. **Method:** c-TBNA smears received from January 2017 to February 2020, with clinical-radiological suspicion of lung malignancy were retrospectively analyzed. **Result:** A total of 22 cases were reviewed. The mean age of the study population was 57.54 years, with a male-female ratio of ~2:1. The adequate aspirate was obtained in 19/22 (86%) cases. The overall diagnostic yield of c-TBNA was 82%. 14/19 (74%) cases were positive for malignancy, non-small cell lung carcinoma being the most common malignancy diagnosed (11 cases). 4/19 (21%) cases were diagnosed with granulomatous pathology, while smears in 1 case were non-diagnostic. **Conclusion:** Conventional transbronchial needle aspiration cytology is an efficacious method used for the diagnosis of lung carcinoma. Especially in resource-limited settings, it remains irreplaceable as a diagnostic tool and should be routinely utilized.

Keywords: Bronchoscopy, Lung cancer, Transbronchial needle aspiration

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Introduction

According to GLOBOCAN 2018, lung cancer is the most common malignancy as well as the leading cause of cancer mortality worldwide [1]. It is the 4th most commonly detected cancer in India, with 67795 new cases reported in 2018 [2]. The prevalence and mortality in India appear to be rising due to an increase in cigarette smoking, changes in lifestyle, and environmental pollution [3].

A myriad of diagnostic modalities is available to diagnose lung malignancy at the earliest possible. Though radiological investigations like CT/PET can indicate the presence of a lesion in the lung and mediastinum, cell and tissue samples are needed in most cases to reach a more confirmatory diagnosis [4]. These samples can be collected through bronchoalveolar lavage, bronchial brushing, transbronchial needle aspiration cytology, and bronchial biopsy, that can be performed during bronchoscopy [5].

Cytology is a powerful tool in the diagnosis of lung malignancies as it is minimally invasive, less time-consuming, and can provide a clear distinction between non-small cell and small cell lung carcinoma [6,7]. Transbronchial needle aspiration (TBNA) is one such minimally invasive technique used to obtain cytological samples from pulmonary lesions present in a peribronchial location (adjacent to a tracheobronchial tree), as well as from hilar and mediastinal lymph nodes [8]. TBNA provides a diagnosis even in the absence of endobronchial disease [9].

TBNA was first developed in 1949, to be used with rigid bronchoscopy [10]. In 1983, the use of TBNA with a flexible bronchoscope was described in detail by Wang et al [11] TBNA can be performed with or without real-time endobronchial ultrasound guidance (EBUS-TBNA). TBNA without EBUS is called conventional TBNA (c-TBNA), which utilizes chest computed tomography to locate the lesion and is dependent on a thorough understanding of thoracic anatomy [12,13]. The present study aimed to assess the utility of conventional transbronchial needle aspiration cytology in terms of diagnostic yield, in patients with suspected lung cancer.

Material and Methods

Setting: This study was conducted in the Department of Pathology, in collaboration with the Department of Medicine, Teerthanker Mahaveer Medical College and Research Center, Moradabad, Uttar Pradesh, India.

Duration and type of study: It was a retrospective analysis of conventional transbronchial needle aspiration smears submitted in the Department of Pathology from January 2017 to February 2020.

Sample size: A total of 22 cases were studied.

Inclusion Criteria: Patients who underwent flexible bronchoscopy along with c-TBNA for clinical and radiological suspicion of lung malignancy were included in the study.

Exclusion criteria: Patients in whom c-TBNA could not be performed with bronchoscopy due to any contraindication were excluded.

Data collection: Complete history, clinical examination, and radiological details of the patients were recorded. c-TBNA smears received in the cytopathology lab were retrieved and reviewed.

Procedure: Flexible bronchoscopy was performed by the pulmonologist on a daycare basis, under local anesthesia. 22 gauge needle was used for the TBNA procedure that was done in a conventional fashion, without any real-time sonographic guidance. 2-3 pricks were taken from the area of interest and the aspirate was smeared on 6-7 clean glass slides. 2 slides were immediately fixed in 95% ethanol and the rest were air-dried. Rapid on-site evaluation (ROSE) of smears was not done. The smears were then submitted to the cytopathology lab where these smears were stained by Giemsa, H and E and Ziehl- Neelsen stains and cytopathological analysis was performed.

Ethical consideration and permission: Informed written consent was obtained from the patients before the bronchoscopy procedure and they were aware that data could be used anonymously for scientific research purposes. No ethical issues were involved.

Statistical Analysis: Data obtained were compiled in the MS Excel sheet and were then analyzed using mean (SD), percentage, and graphic representation.

Results

Out of the total 22 cases included in the study, 15 (68%) cases were males and 7 (32%) cases were females, with a male to female ratio of ~ 2:1. The age range of the study population was from 32 to

85 years, mean age being 57.54 years. The majority of cases (7/22, 32%) belonged to the age group of 51-60 years. Figure 1 shows the distribution of the study population based on age and gender.

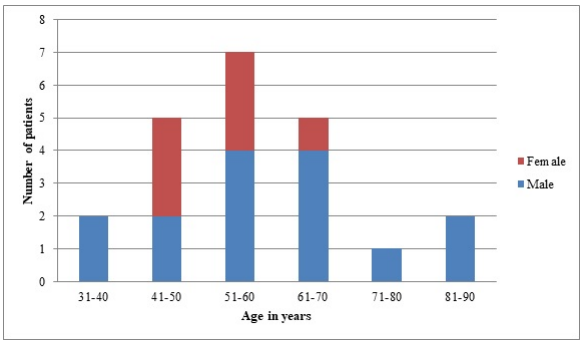

Fig-1: Age and sex distribution of cases.

The clinical profile of the patients showed cough as the most common clinical presentation (15/22, 68%), followed by weight loss (12/22, 54%) and shortness of breath (8/22, 36%). Additional clinical features included hemoptysis and fever (Table 1).

Table-1: Clinical profile of the study population.

Clinical presentation	Number of cases (n)	(%)
Cough	15	68%
Weight loss	12	54%
Breathlessness	08	36%
Hemoptysis	04	18%
Fever	05	22%

Microscopic examination of the received smears showed adequate material for cytopathological analysis in 19/22 cases (86%). 3 cases were found unsatisfactory due to inadequate yield (Figure 2). 1 case had scant aspirate and the other 2 showed only blood as the aspirated material. Cytopathology of the c-TBNA smears was diagnostic in 18 out of 19 adequately aspirated cases.

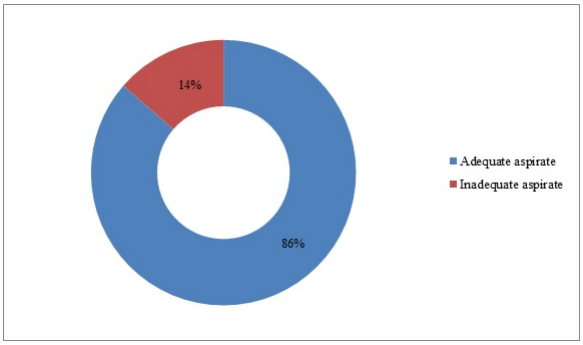

Fig-2: Adequacy of c-TBNA aspirate.

TBNA cytology was positive for malignancy in 14/19 (74%) cases. Cytological features in 4/19 (21%) cases led to a benign diagnosis, with no evidence of malignancy. No definite diagnosis could be made in 1 case because of dense non-specific inflammatory infiltrate as the only cytological finding (Figure 3). The overall diagnostic yield of c-TBNA was found to be 82%.

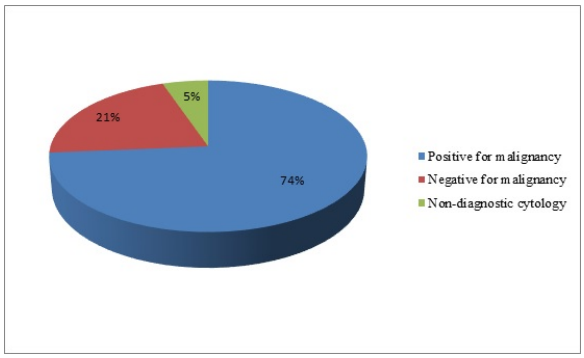

Fig-3: Cytology of adequate c-TBNA smears.

Non-small cell lung carcinoma was the most common malignancy diagnosed (11 cases). Out of these 11 cases, 6 cases showed cytomorphological features consistent with squamous cell carcinoma and 5 cases were consistent with adenocarcinoma. 2 cases were diagnosed as small cell carcinoma. In 1 case, definite typing of malignancy could not be done on the basis of cytological findings only (Table 2).

Table-2: Final diagnosis reached on c-TBNA cytopathological analysis.

Patients with adequate aspirate on c-TBNA		19/22
c-TBNA positive for malignancy		14/19
1. Non-small cell lung carcinoma		11
	Adenocarcinoma	5
	Squamous cell carcinoma	6
2. Small cell carcinoma		2
3. Malignant, typing not possible		1
c-TBNA negative for malignancy		4/19
1. Confirmed Tuberculosis	AFB - Positive	1
2. Probable Tuberculosis	A necrotizing granulomatous lesion, AFB-negative	2
3. Sarcoid like granulomatous lesion		1
c-TBNA with adequate aspirate but non-diagnostic cytology		1/19

Amongst the c-TBNA smears- negative for malignancy, 1 case showed necrotizing epithelioid cell granulomas and was found positive for acid-fast bacilli (AFB) on Ziehl- Neelsen staining. This was confirmed as a case of tuberculosis.

2 cases showing necrotizing granulomas, but with negative AFB, were diagnosed as probable tuberculosis. Smears in 1 case revealed non-necrotizing, compact, sarcoid like granulomas, negative for AFB and fungal stains, and a presumptive diagnosis of sarcoidosis was given, taking clinical and radiological features, tuberculin negativity, and ACE levels into consideration.

Discussion

Bronchoscopic evaluation is amongst the primary standard of care diagnostic procedures for patients with pulmonary and mediastinal pathologies. Conventional transbronchial needle aspiration can be easily combined with routine flexible bronchoscopy if the pulmonologist is aware of the radiological location of the lesion and has a good understanding of anatomical landmarks of the lungs and tracheobronchial tree. Hence, c-TBNA does not exactly remain a 'blind' procedure, in hands of a skilled and experienced pulmonologist, as is generally considered [13]. Despite this, c-TBNA remains an underutilized diagnostic technique, owing to concerns about its diagnostic yield [8,14].

The current study analyzed the data of 22 conventional TBNA cases received in our department. Previous studies have had a variable mean age of presentation of the study population, ranging from as low as 39 years [15] to 65 years [16,17]. The mean age in the present study was 57.54 years, which was similar to studies of Kupeli et al [18], Walia et al [19], Darjani et al [20], and Farrag et al [21]. This variation in mean age can be due to the marked difference in the number of cases in various studies.

Sample adequacy of 80-90% was observed in various studies [20,22-24] similar to 86% in the present study. Cetinkaya et al [15] and Farrag et al [21] showed higher adequacy rates of 98% and 96.6% respectively, while those in studies of Walia et al [19] and Ramieri et al [16] were less than 60%. The overall diagnostic yield of c-TBNA in the present study was found to be 82 % which was either comparable to or higher than many other studies (Table-3).

Table-3: Diagnostic yield of c-TBNA in various studies.

Study	Diagnostic yield
Present study	82%
Cetinkaya et al [15]	75%
Kupeli et al [18]	44.4%
Walia et al [19]	42.3%
Darjani et al [20]	55.26%
Farrag et al [21]	88.3%
Madan et al [23]	78%
Shah et al [24]	83%
Soja et al [25]	41.5%
Chokhani R [26]	88.2%
Khan et al [27]	40.5%
Kumari et al [28]	54.38%

Wide variation in diagnostic yield observed in different studies has been attributed to difference in the prevalence of nodal metastasis in the study group, [29] size of the involved lymph nodes, [21,30,31] selective aspiration of subcarinal and paratracheal lymph nodes [32], and use of different bore needles to obtain the specimen [17,27,33]. The skill and experience of the bronchoscopist performing the procedure also play an important role. c-TBNA has a short and steep learning curve [34] and its diagnostic yield is noticed to improve over time with practice [18,19,22,35].

The presence of a pathologist on-site to perform rapid on-site cytopathological evaluation (ROSE) of the smears has been shown to improve the diagnostic yield of c-TBNA [23,34,36,37]. But some studies failed to detect this improvement with ROSE as significant [38]. ROSE was not performed in current study, but the diagnostic yield was still comparable to other studies in which c-TBNA was done along with the onsite evaluation of the aspirate [16,23]. Farrag et al [21] also observed the findings similar to the present study. Therefore, the emphasis is laid on performing c-TBNA even if ROSE is not possible because of the unavailability of a cytopathologist.

Some studies have compared conventional versus EBUS-guided TBNA and showed that ultrasound guidance increases the yield of TBNA [30,39,40]. However, the diagnostic yields obtained by c-TBNA were found similar to ultrasound-guided TBNA in the subcarinal and lower paratracheal lymph nodes [40,41]. Bonifazi et al also did not find the sensitivity of EBUS-TBNA as significantly superior to that of c-TBNA [17]. So, there is no reason to undermine the importance of c-TBNA as a diagnostic test, especially in absence of newer modalities. Studies have shown that TBNA cytology can be used in pathological diagnosis and typing of pulmonary and mediastinal neoplasms, diagnosis of unknown hilar/mediastinal lymphadenopathy, and in the staging of lung cancer patients [8,16,30,32,33].

In the present study, 74% of cases were found positive for malignancy, while in 21% of cases a benign diagnosis was made.

Cytological typing of malignancy was possible in 13/14 cases, the majority being non-small cell lung carcinoma, similar to most other studies [19,21,27]. Darjani et al reported small cell carcinoma as the most common malignancy [20].

It was found that squamous cell carcinoma was the most common subtype diagnosed, similar to the studies of Walia et al [19] and Kumari et al [28] whereas adenocarcinoma was more commonly reported in studies of Ramieri et al [16] and Bonifazi et al [17]. This variation in a pathological profile can be explained by the prevalence of different types of lung malignancies in different geographical regions [42].

The present study also showed a possibility of obtaining non- malignant diagnosis on c-TBNA done in face of initial suspicion of malignancy, similar to the study of Walia et al [19]. The present study, 4 cases with granulomatous pathology were diagnosed, out of which 3 were tuberculosis and 1 was sarcoidosis.

Granulomas can be identified on TBNA cytology in a reliable manner [43]. However, higher TBNA yield has been noted for carcinoma when compared to benign lesions [15,30]. Still, TBNA can be considered a valuable method to obtain a cytological specimen for diagnosing malignancy as well as tuberculosis and sarcoidosis in intrathoracic lymph nodes [15,44].

Limitation

The limitation of this study is that the sample size was small. So, it is recommended that the same study should be conducted on a large number of cases so that concrete evidence could be derived on the efficacy of c-TBNA as an early diagnostic tool.

Conclusion

Conventional transbronchial needle aspiration cytology is an efficacious technique used for the diagnosis of lung carcinoma. It can provide good results in hands of a skilled bronchoscopist and cytopathologist. In developing countries like India, where resources are limited and affordability of medical facilities is a major concern, c-TBNA remains irreplaceable as a diagnostic tool.

Therefore, it is emphasized that the more enthusiastic use of this technique is necessary so that no patient misses the opportunity to early diagnosis due to the unavailability of more advanced technologies.

What does this study add to the existing knowledge

The current study highlights c-TBNA as a promising, simple, and easy diagnostic modality for early diagnosis of lung cancer, even in this era of new advances in bronchoscopic procedures.

Authors' contribution

Dr. Rashmi Chauhan: Concept and design of the study, manuscript preparation, analysis, and interpretation of data.

Dr. Seema Awasthi: Data analysis, manuscript review, final approval of the version to be published.

Dr. Deepti Arora, Dr. Faiyaz Ahmed, Dr. Himanshu Joshi, Dr. Ina Garg: Data acquisition, literature search, manuscript editing, and review.

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