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Endobronchial Ultrasonographic Practices with Rapid Onset Pathological Evaluation

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ABSTRACT

Endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA) is a standard procedure to evaluate suspicious mediastinal lesions. The utility of rapid on-site evaluation (ROSE) during EBUS-TBNA is still controversial. The aim of this study is to assess the role of ROSE during EBUS-TBNA on the last pathologic diagnosis.

597 EBUS cases were included in the study. The records were analyzed retrospectively according to demographic characteristics, indications of the procedure, number of stations, ROSE diagnosis and final diagnosis.

455 (76.2%) of EBUS procedures were accompanied by the pathologist (ROSE), while ROSE procedure could not be applied in 142 (23.8%) cases. In 43 (7.2%) cases, the result of sampling was not diagnostic. The rate of non-diagnostic patients was 3.7% in 455 cases with ROSE, whereas the rate was 18.3% for no-ROSE group. There is a statistical difference between these two rates ($p<0.001$).

We think that ROSE of EBUS-TBNA improves efficiency of the biopsy and yield of the procedure if performed by an experienced cytopathologist or cytotechnologist. Our diagnosis rate increased when our pathologist guided us about the adequacy of the sample during the procedure and influenced our decision to terminate or continue accordingly.

Key Words: Endobronchial ultrasound, rapid on-site evaluation, pathologic diagnosis

Introduction

With the use of endobronchial ultrasound (EBUS) since the beginning of the 2000s, bronchoscopy has allowed examination and biopsy of not only the airways but also the mediastinum and peribronchial area, when necessary. This process has taken its place especially in the management algorithm for the diagnosis, staging, and genetic analysis of Non-small Cell Lung Cancer (NSCLC), which has recently played a major role in the treatment. According to World Association Bronchology and Interventional Pulmonology (WABIP) guide on needle aspiration for diagnosis and molecular tests in lung cancer; using needle diameter or mini-forceps for the diagnostic value is not recommended for lung cancer, but for lymphoma and sarcoidosis (1).

One of the many advantages of this procedure is that it eliminates the need for a surgical procedure such as mediastinoscopy and it can give simultaneous diagnosis (rapid onsite evaluation = ROSE) if feasible. There are different remarks in the literature regarding the need for EBUS-ROSE. In particular, the duration of the procedure, the pathological result, the rate of diagnosis, and its adequacy for molecular analysis have been examined in different studies, but no consensus has been achieved (2).

In this study; because of different comments about need of ROSE, we aimed to evaluate the diagnostic contribution of ROSE to our own EBUS applications. For this purpose, 2-years of EBUS procedure records were retrospectively analyzed and the contribution of ROSE to the last diagnosis was researched.

Materials and Methods

All cases whose pathological specimens could be acquired by EBUS between 2016 and 2018 were included in the study. Procedures terminated without biopsy were excluded. A convex probe endobronchial ultrasound (Fujifilm's EB-530US) and 21 Gauge needle were used for these procedures. General anesthesia with controlled ventilation was applied.

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The ethical approval statement was taken from Samsun Education and Research Hospital Ethic Committee (Protocholno: GOKA 2020/7/7, Date: 27/05/20). The records of procedures were analyzed retrospectively according to demographic characteristics, indications of the procedure, number of stations on which biopsies were conducted, ROSE diagnosis and final diagnosis. Pathological evaluation was performed by the same pathologist. Smears were dried by the pathologist in the operating room and examined by Diff-Quick method, the blocks were kept in 10% formaldehyde.

The data were analyzed with IBM SPSS V23. Fisher's Exact Chi Square test was used to compare the rates of non-diagnostics with regard to having ROSE. All categorical data were expressed as frequency and percentage. The significance level was taken as $p < 0.05$.

Results

619 cases were included in study, but 22 of them were excluded because no biopsy was taken. EBUS was performed to 597 patients and 455 of them were evaluated with ROSE. Of the 597 cases; 395 (66.2%) were male and 202 (33.8%) were female. The average age was 59.78 (Min 18 - max 86). The indications for EBUS that we made for diagnostic and staging purposes are given in Table 1. EBUS procedure was performed constantly due to mediastinal lymphadenopathy, and secondly mass lesion. The maximum number of targeted samples was 2 stations (339 cases, 56.8%). In two cases, sampling was performed from 4 different stations in terms of surgical margins (Table2). Through different assignments of the pathologist, ROSE procedure could not be performed in 142 (23.8%) cases.

According to ROSE, the diagnoses of the cases are shown in Table 3. Diagnosis according to cell block evaluation; 247 cases (41.4%) were malignant, 307 (51.4%) cases were benign with diagnosis of benign lymph node tissue, granulomatous reaction, anthracosis and thyroid tissue. By inclusion of 4 cases with pathologic result of necrosis, 43 (7.2%) samples were non-diagnostic (Table 4). 554 (92.8%) of 597 cases were diagnosed as well.

When the non-diagnostic results are compared between the cases with ROSE and with no ROSE, it was detected that the rate of non-diagnostic diagnosis is statistically significantly higher in the group with no ROSE. The rate of non-diagnostic patients was 3.7% in 455 cases with ROSE, whereas the rate was 18.3% for no-ROSE group. There is a statistical difference between these two rates ($p < 0.001$). In 395 (86.8%) of 455 cases with ROSE, onsite and last diagnosis were compatible.

Discussion

This study is one of the studies supporting the fact that while performing EBUS-TBNA, the presence of a pathologist increases the diagnostic rate. There was a statistically significant difference between ROSE and no-ROSE group according to non-diagnostic results ($p < 0.001$). There are different views on the need of ROSE during EBUS-TBNA. While some studies argue that ROSE does not contribute to the diagnostic adequacy of EBUS-TBNA (2), some indicate that it increases diagnostic utility by 30%, preventing extra biopsy and bronchoscopy, repetition of diagnostic procedures, and risk of bronchoscopy complications (3). According to a study designed at 2018 for similar purpose, it was detected that EBUS-TBNA combined with C-ROSE can improve the specimen qualified rate and diagnostic rate and reduce the complications as well (4).

While examining ROSE slides, the first goal is to make differential diagnosis by using immunohistochemical and mutational analysis, flow cytometry for hematological malignancy suspect, or microbiological sampling. One of the recommendations of the World Health Organization for pathologists related to the classification of lung cancers with small tissues is (5) that ROSE should be done in cases of molecular test requirement. Pulmonary Pathology Society has published a review suggesting that ROSE can minimize repeating of the procedures for additional desired testing and reduce the number of additional invasive procedure (6).

It has been mentioned that preparation of sample by the experienced cytopathologist provides benefits for direct macroscopic examination, optimal smear technique and molecular tests and adequate tissue separation for auxiliary techniques (7). Consumption of materials while the cell blocks are being examined and inadequacy of tissue for further examinations may be the reasons of non-diagnostic results. ROSE also gives information about the need for taking samples from all other stations in multiple PET positive lymph node after sampling first station. We think that our diagnosis rate increased when our pathologist guided us about the adequacy of the sample during the procedure and influenced our

Table 1. EBUS Indications

	n	Percentage %
Mediastinal LAP	189	31,7
Mass	140	23,5
Mass and LAP	112	18,8
Lung cancer and PET(+) LAP	35	5,8
Cancer and Mediastinal LAP	76	12,7
Pulmonary cosolidation and LAP	45	7,5
TOTAL	597	100

LAP Lymphadenopaty, PET Positron Emulsion Tomography, NSCL Cnonsmall Cell Lung Cancer

Table 2. Number of Targets Sampled

Sampling center number	*n*	*Percentage %*
1	157	26,3
2	339	56,8
3	99	16,6
4	2	,3
total	597	100

decision to terminate or continue accordingly.When our pathologist detected images indicating malignancy, the next biopsies were taken in terms of surgical range or prospect. If the first smear was compatible with granulomatous or anthracosis, we collected subsequent samples for microbiologic research. During the procedure, informing the pathologist about the presumption of metastatic malignancy, infectious process, or a primary tumor also contributed the pathological evaluation. Therefore, we believe that the presence of a pathologist on-site increases the efficiency of the biopsy and the effectiveness of the procedure.

In most of the studies; there is a 90-98% compliance between the diagnosis of ROSE and the final diagnosis (6). In a retrospective study analyzing "adequate" aspirates on ROSE, but inconclusive upon final cytologic interpretation, ROSE and final cytology discrepant cases formed a very small fraction of total number of 606 ROSE-EBUS cases (8). In our study, there is a high compliance of 86.8%. There were 12 cases (2.6%) which were reported as benign on ROSE but had malign cell blocks. The reasons for this situation could be inadequate material aspiration despite multiple biopsies, separating the majority of aspirate for the block, or the restriction of the slides examined as ROSE and the lack of cellularity.

There are some limitations of ROSE-TBNA. These are as follows: the necessity of an experienced cytopathologist or cytotechnician, the probability of prolongation of the procedure, the cost and utilization of scarce resources, the lack of sufficient data about number of aspirations, duration of the procedure and risk of complications supporting ROSE. In retrospective analysis of 141 cases (4), according to the message of puncture and complication of EBUS-TBNA with or without C-ROSE, there were no statistical difference of the needle passes between C-ROSE group and No C-ROSE group; however incidence of complications in the C-ROSE group was significantly lower than that in the no C-ROSE group. According to a meta-analysis (9), use of ROSE neither improved the diagnostic yield nor reduced the procedure time during TBNA, but related with fewer number of needle passes during EBUS-TBNA.

One of the limitations of our study was that the procedure duration was not recorded since the first case, and the group with and without ROSE could not be compared in this respect. Also, when EBUS procedures were started in our clinic, since pathologist support had not started yet, number of biopsies taken from each target was not recorded by the first case, so this data could not be compared between ROSE and non-ROSE groups.

When performed with ROSE, EBUS-TBNA both increases the comfort of the physician and speeds up the diagnosis and treatment process for the patient and keeps it in a safer range. In these last periods with rapid developments related to

Table 3. Diagnosis According to ROSE

	n	Percentage %
Benignlymphadenopaty	137	22.9
Granulomatous reaction	72	12,1
NSCLC	79	13,2
SCLC	10	1,7
Adeno cancer	10	1,7
Malignancy	73	12,2
Anthracosis	22	3,7
Thyroid	1	,2
Neuroendocrine tumor	4	,7
Necrosis	5	,8
Lymphoma	3	,5
Nondiagnostic	39	6,5
TOTAL	455	76.2

NSCLCnonsmall cell lung cancer, SCLC small cell lung cancer

Table 4. Final Diagnosis According To Cell Blocks

	n	Percentage %
Beninglymphadenopaty	150	25,1
Granulomatous lymphadenopaty	115	19,3
NSCLC	91	15,2
SCLC	29	4,9
Adeno cancer	77	12,9
Malignity	18	3,0
Anthracosis	41	6,9
Neuroendocrin tumor	13	2,2
Necrosis	4	0,7
thyroid	1	,2
Mixed cell tumor	3	,5
Lymphoma	6	1,0
Breast cancer	5	,8
Clear cell sarcoma	1	,2
Ovary cancer	1	,2
Thyroid cancer	1	,2
Renal cell cancer	1	,2
Prostat cancer	1	,2
Nondiagnostic	39	6,5
TOTAL	597	100,0

NSCLCnonsmall cell lung cancer, SCLC small cell lung cancer

targeted therapy, obtaining a sufficient amount of sample in a short time provides a great advantage for patients. Our study results support other literature arguing that ROSE increases the rate of diagnosis. However, we think that different studies should be conducted, in which the effect of the processing time and the adequacy of the samples taken in terms of molecular evaluation are evaluated.

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