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Comparison of Bronchial Lavage Cultures Taken During Endobronchial Ultrasonography in Patients with Malignant and Non-malignant Lung Diseases

Kanser ve Kanser Dışı Akciğer Hastalıkları Olan Hastalarda Endobronşiyal Ultrasonografi Sırasında Alınan Bronşiyal Lavaj Kültürlerinin Karşılaştırılması

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Abstract

Aim Airway pathogens have become an increasingly important concern in patients with lung diseases owing to the widespread use of immunosuppressive therapies. However, limited data are available regarding airway pathogens and antibiotic resistance in bronchial lavage (BL) cultures obtained during endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA).

Materials and Methods This single-center, retrospective, cross-sectional study included 347 consecutive patients who underwent microbiological analysis of BL specimens obtained during EBUS-TBNA for the evaluation of suspected malignant or non-malignant lung disease. Clinical and microbiological characteristics were analyzed.

Results The culture positivity rate of BL specimens obtained during EBUS-TBNA was significantly higher in patients with malignant lung disease than in those with non-malignant lung disease (19.2% vs. 5.4%, p=0.001). In patients with non-malignant disease, culture positivity was 0%, 12.5%, and 15.9% in those with lymphadenopathy (LAP), a pulmonary mass/nodule, and both a mass/nodule and LAP on chest computed tomography (CT), respectively (p=0.01, p=0.192, and p=0.01). In patients with malignant disease, the corresponding culture positivity rates were 12.5%, 46.2%, and 18.6%, respectively (p=0.22, p=0.01, and p=0.738). The proportion of isolates resistant to more than one antibiotic was significantly higher in patients with malignant disease than in those with non-malignant disease (80% vs. 20%, p=0.01), whereas resistance to at least two antibiotics was observed only in patients with malignant disease (56% vs. 0%).

Conclusions These findings may help clinicians identify patients in whom microbiological examination of BL samples obtained during EBUS-TBNA should be considered.

Keywords Airway pathogens, bronchial lavage, endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA), lung diseases, microbiological examination

Öz

Amaç *İmmünsüpresif tedavilerin yaygınlaşmasıyla birlikte, hava yolu patojenleri akciğer hastalıklarında giderek daha önemli bir klinik sorun haline gelmiştir. Bununla birlikte, endobronşiyal ultrasonografi eşliğinde transbronşiyal iğne aspirasyonu (EBUS-TBNA) sırasında alınan bronşiyal lavaj (BL) örneklerinden elde edilen kültürlerde hava yolu patojenleri ve antibiyotik direnci hakkında sınırlı sayıda çalışma bulunmaktadır. Bu çalışmada, malign ve malign olmayan akciğer hastalıklarında EBUS-TBNA sırasında alınan BL kültürlerinin mikrobiyolojik özelliklerinin değerlendirilmesi amaçlandı.*

Gereç ve Yöntem *Bu tek merkezli, retrospektif, kesitsel çalışmaya, malign veya malign olmayan akciğer hastalığı ön tanısıyla EBUS-TBNA sırasında alınan BL örneklerinin mikrobiyolojik incelemesi yapılan ardışık 347 hasta dahil edildi. Hastaların klinik ve mikrobiyolojik özellikleri değerlendirildi.*

Bulgular *EBUS-TBNA sırasında alınan BL örneklerinde kültür pozitifliği, malign akciğer hastalığı bulunan hastalarda malign olmayan akciğer hastalığı bulunan hastalara göre anlamlı derecede daha yüksekti (%19,2'ye karşı %5,4, p=0.001). Malign olmayan hastalarda toraks bilgisayarlı tomografisinde (BT) yalnızca lenfadenopati (LAP), kitle/nodül ve kitle/nodül ile birlikte LAP saptanan olgularda kültür pozitifliği sırasıyla %0, %12,5 ve %15,9 olarak bulundu (sırasıyla p=0,01, p=0,192 ve p=0,01). Malign hastalarda ise aynı gruplarda kültür pozitifliği sırasıyla %12,5, %46,2 ve %18,6 olarak saptandı (sırasıyla p=0,22, p=0,01 ve p=0,738). Birden fazla antibiyotiğe dirençli mikroorganizma saptanma oranı malign hastalarda malign olmayan hastalara göre anlamlı olarak daha yüksekti (%80'e karşı %20; p=0,01). En az iki antibiyotiğe direnç ise yalnızca malign hastalarda gözlendi (%56'ya karşı %0).*

Sonuç *Bu bulgular, klinisyenlerin EBUS-TBNA sırasında elde edilen BL örneklerinin mikrobiyolojik incelemesinin düşünülmesi gereken hastaları belirlemelerine yardımcı olabilir.*

Anahtar Kelimeler *Hava yolu patojenleri, bronşiyal lavaj, endobronşiyal ultrasonografi eşliğinde transbronşiyal iğne aspirasyonu (EBUS-TBNA), akciğer hastalıkları, mikrobiyolojik inceleme.*

INTRODUCTION

Airway pathogens have emerged as an important clinical concern in patients with lung diseases, particularly with the increasing use of immunosuppressive therapies. Airway colonization by potentially pathogenic microorganisms has been reported in approximately 1–15% of individuals in developed countries and up to 50% of those in developing countries.[1,2] These microorganisms may persist in the airways for prolonged periods and contribute to neutrophil-mediated inflammation, serve as reservoirs for pathogen transmission, and increase the risk of mortality.[3,5]

Despite substantial advances in the diagnosis and treatment of lung cancer, infectious complications remain a major cause of morbidity and mortality in these patients.[6] Impaired mucociliary clearance and a weakened cough reflex increase susceptibility to respiratory infections during primary cancer treatment.[7,8] Therefore, identifying airway pathogens before lung cancer surgery or the initiation of immunosuppressive therapy may facilitate appropriate antimicrobial management and reduce the risk of infectious complications.[9,10] In addition, airway pathogens have been associated with adverse clinical outcomes, including cardiovascular events and increased mortality, in patients with non-malignant lung diseases.[11,12]

Bronchial lavage (BL) is a simple and widely used bronchoscopic sampling technique for evaluating airway microorganisms. It is performed by instilling sterile saline into the bronchial tree through a bronchoscope and subsequently aspirating the recovered fluid mixed with bronchial secretions.[13,14] BL specimens can be obtained during both flexible bronchoscopy and endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). EBUS-TBNA is a minimally invasive procedure widely used for the diagnosis and staging of mediastinal and hilar lymphadenopathy as well as the diagnosis of peripheral and central lung lesions.[13] Although BL can be readily performed during EBUS-TBNA, current guidelines do not provide recommendations regarding the routine microbiological evaluation of BL specimens obtained during this procedure. Consequently, further evidence is needed to identify the patient populations that may benefit from BL culture during EBUS-TBNA.

Recent advances in microbiome analysis have improved our understanding of the airway microbiota. However, these molecular techniques remain expensive and are not routinely available in many healthcare centers.[15,16] Therefore, conventional microbiological culture continues to represent a practical, accessible, and clinically relevant method for detecting airway pathogens.

The present study aimed to investigate the clinical factors associated with culture positivity and antibiotic resistance in BL specimens obtained during EBUS-TBNA in patients with malignant and non-malignant lung diseases.

MATERIALS and METHODS

Study Design and Setting

This single-center, retrospective, cross-sectional study was conducted at the Department of Chest Diseases, Gaziantep University Faculty of Medicine. For this study, all consecutive patients who underwent both EBUS-TBNA and bronchial lavage, depending on the bronchoscopist's preference, were included.

Participants

A total of 347 consecutive patients who underwent BL sampling during EBUS-TBNA were included in the study.

Inclusion criteria

Patients aged ≥18 years who underwent EBUS-TBNA with BL sampling were eligible for inclusion.

Exclusion criteria

Patients were excluded if they had: (1) no definitive diagnosis following EBUS-TBNA; (2) clinical or radiological evidence of active respiratory infection, defined as new or

progressive pulmonary infiltration on chest radiography or computed tomography accompanied by fever (≥38°C) or purulent sputum; or (3) inadequate BL specimens, defined as samples containing more than 25 epithelial cells per low-power field or fewer than 10 leukocytes per low-power field on microscopic examination.

Sample Size

Sample size was calculated using G*Power version 3.1. Assuming an alpha level of 0.05 and a statistical power of 80%, the minimum required sample size was calculated as 128 participants (64 patients in each group).

Data Collection

Demographic and clinical data, including age, sex, smoking status, comorbidities, histopathological diagnosis, presence of metastasis, thoracic computed tomography (CT) findings (pulmonary mass or nodule, lymphadenopathy [LAP], or both), BL culture and antimicrobial susceptibility results, complications following EBUS-TBNA (death, intensive care unit admission, or hospitalization), and antibiotic use within one month after the procedure, were retrieved from the hospital information management system and recorded using a data collection form.

EBUS-TBNA Procedure and Microbiological Evaluation

EBUS-TBNA was performed using a convex-probe endobronchial ultrasound bronchoscope (BF-UC160F-OL8; Olympus Medical Systems, Tokyo, Japan). Bronchial lavage specimens were obtained by instilling sterile isotonic saline into the bronchial segment corresponding to the radiologically dominant lesion, followed by immediate aspiration.

Each BL specimen underwent Gram staining, aerobic bacterial culture, fungal culture, acid-fast bacilli (AFB) staining, and mycobacterial culture according to routine microbiological protocols.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 25.0 (IBM Corp., Armonk, NY, USA). Descriptive data are presented as mean ± standard deviation or frequency (percentage), as appropriate. The normality of continuous variables was assessed using the Shapiro–Wilk test. Comparisons between two independent groups were performed using the Mann–Whitney U test, whereas comparisons among more than two groups were conducted using the Kruskal–Wallis test. Associations between categorical variables were evaluated using the chi-square test or Fisher's exact test, as appropriate. A two-sided p value of <0.05 was considered statistically significant.

RESULTS

The mean age of the study population was 58.73 ± 12.95 years. Of the patients, 34.6% were female, 38.9% were current smokers, 24.5% had diabetes mellitus, 25.1% had hypertension, and 8.1% had chronic obstructive pulmonary disease (COPD).

According to the EBUS-TBNA findings, 52.4% of the patients were diagnosed with malignant disease. The most common histopathological subtypes were squamous cell carcinoma (12.1%) and adenocarcinoma (10.4%). Gram staining demonstrated Gram-positive cocci in 70.6% of specimens, Gram-negative cocci in 5.1%, and Gram-negative bacilli in 24.3%.

Overall, culture positivity was detected in 12.7% of the patients. The most frequently isolated microorganisms were Acinetobacter spp. (27.3%) and Pseudomonas aeruginosa (20.5%). The culture positivity rate was significantly higher in patients with malignant disease than in those with non-malignant disease (19.2% vs. 5.4%, p=0.001). Although similar microorganisms were isolated in both groups, the distribution of microorganisms did not differ significantly between patients with malignant and non-malignant disease (p=0.67). The microbiological cul-

ture results are summarized in Table 1.

Table 1. Comparison of microorganisms in bronchial lavage culture in patients with non malignant and malignant lung disease

Microorganisms growing in culture	All patients		Patients with non malignant lung pathology		Patients with malignant lung pathology	
	Count	%	Count	%	Count	%
Staphylococcus aureus	5	1.4	1	11.1%	4	11.4%
Acinetobacter spp.	12	3.5	2	22.2%	10	28.6%
Pseudomonas aeruginosa	9	2.6	3	33.3%	6	17.1%
Candidiasis	3	0.9	1	11.1%	2	5.7%
Escherichia coli	2	0.6	0	0.0%	2	5.7%
Aspergillus subtypes	1	0.3	0	0.0%	1	2.9%
Serratia subtypes	2	0.6	1	11.1%	1	2.9%
Klebsiella Pneumoniae	2	0.6	0	0.0%	2	5.7%
Klebsiella oxytoca	3	0.9	0	0.0%	3	8.6%
Stenotrophomonas maltophilia	1	0.3	1	11.1%	0	0.0%
Enterobacter aerogenes	2	0.6	0	0.0%	2	5.7%
Pantoea agglomerans	1	0.3	0	0.0%	1	2.9%
Enterococcus faecalis	1	0.3	0	0.0%	1	2.9%

There was no significant difference in the mean age of patients with positive culture results between the malignant and non-malignant groups (63.51 ± 10.01 vs. 64.67 ± 15.02 years, respectively; p=0.83).

According to chest computed tomography (CT) findings, culture positivity in patients with non-malignant disease was observed in 0% of patients with lymphadenopathy (LAP), 12.5% of those with a pulmonary mass or nodule, and 15.9% of those presenting with both a pulmonary mass or nodule and LAP (p=0.01, p=0.192, and p=0.01, respectively). The corresponding rates in patients with malignant disease were 12.5%, 46.2%, and 18.6%, respectively (p=0.22, p=0.01, and p=0.738, respectively). The associations between culture positivity and clinical characteristics are presented in Table 2.

When analyzed according to histopathological subtype, culture positivity was observed in 26.7% of patients with adenocarcinoma, 26.7% of those with squamous cell carcinoma, 10.0% of those with small cell lung carcinoma, 6.7% of those with large cell carcinoma, 3.3% of those with extrapulmonary metastatic carcinoma, and 30.0% of those with other malignant histopathological diagnoses. No significant association was observed between histopathological subtype and culture positivity (p=0.28).

Among culture-positive patients, 68.2% harbored microorganisms resistant to at least one antibiotic. The proportion of isolates resistant to more than one antibiotic was significantly higher in patients with malignant disease than in those with non-malignant disease (80% vs. 20%, p=0.01). Resistance to at least two antibiotics was observed only in patients with malignant disease (56% vs. 0%, p=0.02).

No significant associations were identified between antibiotic resistance and other clinical characteristics in either group (Table 3).

When stratified by histopathological subtype, antibiotic-resistant microorganisms were isolated in 33.3% of patients with adenocarcinoma, 23.8% of those with squamous cell carcinoma, 23.8% of those with other malignant histopathological diagnoses, 9.5% of those with small cell lung carcinoma, and 4.8% of those with both large cell carcinoma and extrapulmonary metastatic carcinoma. The prevalence of antibiotic-resistant microorganisms did not differ significantly among histopathological subtypes (p=0.71). Among patients with malignant disease, culture positivity was observed in 56.7% of those with metastatic disease and in 44.0% of those without metastasis (p=0.438). Antibiotic-resistant microorganisms were iso-

Table 2. The relationship between bronchial lavage culture positivity and clinical variables patients with non malignant and malignant lung diseases

Variables		**Patients with non malignant lung pathology**					**Patients with malignant lung pathology**				
		No culture positivity in bronchial lavage		**Culture positivity in bronchial lavage**		**p**	**No culture positivity in bronchial lavage**		**Culture positivity in bronchial lavage**		**p**
		n	**%**	**n**	**%**		**n**	**%**	**n**	**%**	
Complications	No	150	94.9%	8	5,1%	0.293	134	80.7%	32	19.3%	0.959
	Yes	6	85.7%	1	14.3%		13	81.3%	3	18.8%	
Sex	Female	74	96.1%	3	3.9%	0.410	39	90.7%	4	9.3%	0.059
	Male	82	93.2%	6	6.8%		108	77.7%	31	22.3%	
Cigarette use	No	105	94.6%	6	5.4%	0.968	87	86.1%	14	13.9%	**0.058**
	Yes	51	94.4%	3	5.6%		60	74.1%	21	25.9%	
Diabetes mellitus	No	114	94.2%	7	5.8%	0.756	111	79.3%	29	20.7%	0.386
	Yes	42	95.5%	2	4.5%		35	85.4%	6	14.6%	
Hypertension	No	113	93.4%	8	6.6%	0.278	112	81.2%	26	18.8%	0.762
	Yes	43	97.7%	1	2.3%		34	79.1%	9	20.9%	
COPD	No	152	94.4%	9	5.6%	0.627	127	80.9%	30	19.1%	0.623
	Yes	4	100%	0	0.0%			79.2%	5	20.8%	
Heart failure	No	156	94.5%	9	5.5%		145	80.6%	35	19.4%	
	Yes	0	0.0%	0	0.0%		1	100%	0	0.0%	
History of tuberculosis	No	153	95.0%	8	5.0%	**<0.01**	146	80.7%	35	19.3%	NA
	Yes	0	0.0%	1	100.0%		0	0.0%	0	0.0%	
Thorax CT findings	Mass	14	87.5%	2	12.5%	**<0.01**	7	53.8%	6	46.2%	**0.026**
	LAP	105	100%	0	0.0%		35	87.5%	5	12.5%	
	Mass and LAP	37	84.1%	7	15.9%		105	81.4%	24	18.6%	

COPD:Chronic obstructive pulmonary disease, CT:Computed tomography LAP:Lymphadenopathy

Table 3. The relationship between clinical variables and antibiotic resistance patients with non malignant and malignant lung diseases

Variables		Patients with non malignant lung pathology		Patients with malignant lung pathology		p
		n	%	n	%	
Age (Mean±SD)		62.52 ± 11.16		60.20 ±19.46		0.80
Sex	Female	2	40.0%	4	16.0%	0.221
	Male	3	60.0%	21	84.0%	
Smoking	No	4	80.0%	12	48.0%	0.190
	Yes	1	20.0%	13	52.0%	
Diabetes mellitus	No	4	80.0%	20	80.0%	NA
	Yes	1	20.0%	5	20.0%	
Hypertension	No	4	80.0%	18	72.0%	0.712
	Yes	1	20.0%	7	28.0%	
COPD	No	5	100%	20	80.0%	0.273
	Yes	0	0.0%	5	20.0%	
Heart failure	No	5	100%	25	100%	NA
	Yes	0	0.0%	0	0.0%	
History of tuberculosis	No	4	80.0%	25	100%	**0.023**
	Yes	1	20.0%	0	0.0%	
Thorax CT findings	No mass	4	80.0%	21	84.0%	0.827
	Mass	1	20.0%	4	16.0%	
	No LAP	5	100%	21	84.0%	0.337
	LAP	0	0.0%	4	16.0%	
	No mass or LAP	1	20.0%	8	32.0%	0.593
	Mass or LAP	4	80.0%	17	68.0%	
More than one antibiotic resistance	No	4	80.0%	5	20.0%	**<0.01**
	Yes	1	20.0%	20	80.0%	
More than two antibiotic resistance	No	5	100%	11	44.0%	**0.022**
	Yes	0	0.0%	14	56.0%	
Post-procedure complication	No	4	80.0%	22	88.0%	0.631
	Yes	1	20.0%	3	12.0%	

SD: Standard deviation, COPD:Chronic obstructive pulmonary disease, CT: Computed tomography LAP: Lymphadenopathy

lated in 77.8% of patients with metastasis and in 64.7% of those without metastasis (p=0.471).

Based on the histopathological diagnosis established by EBUS-TBNA, 52.4% of the patients had malignant disease. Among those who received antibiotic therapy, 75% had malignant disease and 25% had non-malignant disease (p=0.49). Similarly, among patients with antibiotic-resistant microorganisms, 85.7% had malignant disease and 14.3% had non-malignant disease; however, this difference was not statistically significant (p=0.74).

DISCUSSION

In the present study, both culture positivity and the prevalence of microorganisms resistant to at least one antibiotic were higher in BL specimens obtained during EBUS-TBNA from patients with malignant disease than from those with non-malignant disease. To the best of our knowledge, this is the first study to compare the microbiological characteristics of BL specimens obtained during EBUS-TBNA between patients with malignant and non-malignant lung diseases.

In malignant and some non-malignant diseases of the lung, it is important to detect microbiologic factors before systemic treatment. In the current study, patients with malignant disease in BL taken during EBUS-TBNA had approximately three times higher positivity rates in cultures than those with non-malignant disease (19.2% vs. 5.4%, respectively). There are a limited number of studies in this field in the literature.[13] Carmen et al. identified positivity in culture in 6.7% of patients in BL taken during EBUS-TBNA, but only patients with a pre-malignant diagnoses were included in this study.[13] Previous studies have reported culture positivity rates ranging from 10.5% to 41% in patients with lung cancer undergoing bronchoscopic brushing or bronchoalveolar lavage, whereas reported rates in non-malignant lung diseases range from 22.7% to 51.4%.8, 12-15 The lower culture positivity observed in our non-malignant group may be explained by differences in patient selection and sampling techniques. Although patients with active respiratory infection were excluded, this does not fully rule out the possibility that some positive cultures reflected airway colonization rather than true infection, a distinction that remains inherently difficult in bronchoscopic microbiology, particularly in the presence of malignancy-related airway changes. Nevertheless, regardless of the underlying mechanism, culture positivity may carry clinical significance. Identification of airway pathogens prior to lung cancer surgery or initiation of immunosuppressive therapy may facilitate appropriate antimicrobial management and reduce infectious complications.[9,10] Airway pathogens have also been associated with adverse outcomes—including cardiovascular events and increased mortality—in patients with non-malignant lung disease.[11,12] These findings therefore warrant further prospective evaluation to clarify their impact on patient management.

In this study, culture positivity in patients with non-malignant disease was associated with a history of tuberculosis and the presence of a mass on chest CT. In malignant patients, on the other hand, culture positivity was associated with the presence of a mass on chest CT. This association may be related to impaired regional airway clearance and secretion retention associated with pulmonary mass lesions, thereby facilitating bacterial colonization. No significant associations were observed for the remaining clinical variables. Similarly, a previous study evaluating BL specimens obtained during flexible bronchoscopy in patients with lung cancer reported that age, sex, smoking status, histopathological subtype, and tumor stage were not associated with culture positivity.[16] In the literature, the presence of calcification in the lesion on radiologic imaging has been reported to be associated with culture positivity.[17] Another study, using analysis of samples obtained by protected specimen brush and lung tissue, reported that central tumor location was an independent risk factor for bronchial colonization (OR: 9.2).[18] These findings suggest that clinical history together with chest CT findings may

help identify patients who are more likely to benefit from microbiological analysis of BL specimens obtained during EBUS-TBNA.

In this study, BL cultures taken during EBUS-TBNA procedures grew Pseudomonas spp., Acinetobacter spp., and S. aureus most frequently in both patient groups. These factors often cause infectious complications in patients receiving treatment for malignant and non-malignant lung disease.[19,20] Therefore, in both patient groups, physicians performing BL cultures to determine microbiologic factors during EBUS-TBNA procedures may contribute to patient follow-up.

Antimicrobial resistance is an important challenge when selecting empirical antibiotic therapy in critically ill patients.[21] In our study the proportion of isolates resistance to more than one antibiotics were significantly higher in patients with malignant disease than in those with non-malignant disease (80% vs. 20%, respectively). The development of antibiotic resistance in this context may be attributable to frequent contact with healthcare settings, including factors such as prior hospitalization, prolonged hospitalization, long-term antibiotic use, a history of colonization with resistant organisms, immunosuppressive therapies, and invasive procedures.[22-26] These findings support the potential value of microbiological analysis of bronchial lavage (BL) specimens obtained during EBUS-TBNA for guiding empirical antibiotic therapy. However, larger prospective studies are required to validate these findings. Among patients with culture-positive bronchial lavage (BL) specimens, post-procedural complications occurred at similar rates in those with malignant and non-malignant disease (12% vs. 20%, respectively). Previous studies have reported conflicting findings regarding the clinical significance of bronchial colonization. Kang et al. reported that bronchial colonization was not associated with an increased incidence of pneumonia or reduced survival among patients with lung cancer receiving chemotherapy.[27] In contrast, other studies have demonstrated that preoperative bronchial colonization is associated with postoperative pneumonia and increased mortality in patients undergoing surgical resection for lung cancer.[28] Consistent with these findings, another study demonstrated that bronchial colonization has been associated with a higher incidence of postoperative pneumonia, an increased need for mechanical ventilation, and prolonged hospitalization following lung cancer surgery.[9] The absence of a significant difference in post-procedural complication rates in our study may be explained by several factors. First, the relatively small number of culture-positive patients likely limited the statistical power to detect clinically meaningful differences. Second, our study population differed substantially from those evaluated in previous reports. Whereas the aforementioned studies primarily investigated patients undergoing lung cancer surgery, our cohort consisted of patients undergoing EBUS-TBNA, a minimally invasive bronchoscopic procedure associated with a considerably lower risk of infectious complications than surgical resection. Therefore, direct comparisons between these studies should be interpreted with caution. Nevertheless, microbiological evaluation of BL specimens may still provide clinically relevant information by identifying potentially pathogenic microorganisms in selected patients. Prospective multicenter studies with larger sample sizes are needed to determine whether incorporating BL microbiological analysis into routine EBUS-TBNA practice improves patient management and clinical outcomes.

Limitations

This study has some limitations. The study was conducted in only one center and tertiary health care institution in Turkey, so the results cannot be generalized to the entire population. Although the overall sample size was adequate according to the a priori power analysis, the relatively low number of patients with culture positivity (n=44) limited the feasibility of further sub-analyses, including multivariable modeling. In particular, given the small number of patients with a history of tuberculosis, the findings pertaining to this subgroup should be interpreted with caution. Future

prospective studies with larger cohorts of culture-positive patients are warranted to employ multivariable analysis for the identification of independent predictors of culture positivity in this population. Another limitation is that, although patients who underwent bronchial lavage (BL) sampling during EBUS-TBNA were included in the study consecutively, this sampling was performed at the discretion of the bronchoscopist. Therefore, considering that the decision to obtain samples may have been influenced by unmeasured factors, this approach may have introduced selection bias. In the BL sampling method, there is a risk of sample contamination. Therefore, taking BL with a protected catheter during EBUS-TBNA procedures may provide more reliable results. An additional limitation of this study is that the clinical implications of the observed differences in culture positivity and antimicrobial resistance between patients with malignant and non-malignant lung disease could not be assessed. Because of the retrospective study design, data regarding changes in antibiotic therapy, postponement of oncologic treatment, infectious complications, and other clinically relevant outcomes were not consistently available. Therefore, prospective longitudinal studies are warranted to determine the clinical significance of these microbiological findings and their impact on patient management and long-term clinical outcomes.

CONCLUSION

Patients with malignant lung disease had higher rates of both culture positivity and microorganisms resistant to more than one antibiotic in BL specimens obtained during EBUS-TBNA than patients with non-malignant lung disease. However, given the retrospective, single-center design of this study, the findings should be interpreted as demonstrating an association rather than providing evidence of clinical benefit. Prospective, multicenter studies are warranted to validate these findings and to determine whether selective microbiological analysis of bronchial lavage (BL) specimens, guided by clinical and radiological risk factors, provides meaningful diagnostic or therapeutic benefit. Such evidence is required before this approach can be recommended as a routine component of EBUS-TBNA procedures.

Ethical Approval

The study was conducted in accordance with the Declaration of Helsinki. Permission for the study was obtained from the Gaziantep University Non-Intervention Clinical Research Ethics Committee (Approval no: 393/2024, date: October 23rd, 2024).

Peer-review

Externally and internally peer-reviewed.

Authorship Contributions

Concept: S.D., S.G.A., Design: S.D., S.G.A., Data Collection or Processing: S.D., Analysis or Interpretation: S.G.A., Literature Search: S.D., S.G.A., Writing: S.D., S.G.A.

Conflicts of Interest

The authors declare that they have no conflict of interest.

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