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Incidence of bacteraemia following endobronchial ultrasound-guided transbronchial needle aspiration.

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ABSTRACT

BACKGROUND: Little data exists concerning possible infectious complications associated with endobronchial ultrasound-guided transbronchial needle aspiration (EBUS-TBNA). This prospective evaluation was undertaken to determine the incidence of bacteremia and infectious complications associated with EBUS-TBNA.

METHOD: Consecutive patients undergoing EBUS-TBNA for evaluation of mediastinal or hilar lymph node lesions were studied. Venisection within 60 seconds of TBNA was performed for aerobic and anaerobic blood culture. Sterile saline washings of TBNA needles was also performed. Patients with positive blood cultures were reviewed immediately and all patients underwent clinical review within a week of EBUS-TBNA.

RESULTS: Forty-three patients underwent EBUS-TBNA with bacteraemia demonstrated in 3 patients (7%). All bacterial isolates were typical oropharyngeal commensal organisms. TBNA needle washings culture was positive in 15 patients (35%). None of the three bacteraemic patients had clinical features suggestive of infection, and no complications were seen among our cohort.

CONCLUSION: Incidence of bacteraemia following EBUS-TBNA is comparable to that following routine flexible bronchoscopy. Performance of TBNA does not appear to measurably increase the risk of bacteraemia over that associated with insertion of the bronchoscope into the airway. Contamination of TBNA needle by oropharyngeal commensal bacteria is common however clinically significant infection following EBUS-TBNA appears rare.

KEYWORDS

Complications

Endobronchial ultrasound

Infection

Lung cancer

INTRODUCTION

The recent introduction of endobronchial ultrasound-guided TBNA (EBUS-TBNA) has revolutionized the evaluation of intrathoracic lymph nodes and other paratracheal structures. Since its description in 2004,[1] this minimally invasive bronchoscopic technique has achieved widespread popularity among respiratory physicians and thoracic surgeons and in centres where it is available is now the procedure of choice for mediastinal staging of lung cancer. Its popularity is based in part on its excellent performance characteristics, but equally on its excellent safety profile. Diagnostic accuracy is at least equivalent to mediastinoscopy and significantly higher for certain lymph node (LN) stations,[2] while a recently published meta-analysis noted no important complications among over 1,500 completed procedures.[3]

Infective complications following conventional (Wang needle) TBNA have been reported but prospective studies suggested bacteraemia following conventional TBNA is extremely rare.[4] Two recent reports have illustrated that EBUS-TBNA may be associated with clinically significant infection, due to direct inoculation of oropharyngeal flora into mediastinal tissue by the TBNA needle.[5, 6] We conducted a prospective study to determine the incidence of bacteraemia following EBUS-TBNA in order to inform clinicians regarding the risk of complicating infection. We also performed culture of needles following TBNA in order to identify microbial pathogens responsible for clinical infection following inoculation by TBNA. We demonstrate for the first time that bacteraemia rates following EBUS-TBNA were consistent with rates reported following routine bronchoscopy. Culture of the needles post TBNA identified organisms that routinely colonise the oropharanyx (15/43, 35%). No local infections or complications related to bacteraemia were identified.

MATERIALS AND METHODS

Institutional review board approval was granted for the performance of this study. All patients provided informed written consent.

All patients undergoing EBUS-TBNA for evaluation of mediastinal lesions were considered for inclusion in the study. We applied the following exclusion criteria; current febrile illness; antibiotic therapy in previous fortnight; current respiratory infection, and; indication for prophylactic antibiotics.

EBUS-TBNA was performed under conscious sedation using a dedicated linear array bronchoscope (BF-UC180F-OL8, Olympus, Tokyo, Japan) by a single operator (DPS). Topical anaesthetic using lignocaine 2% was introduced via the working channel of the linear array bronchoscope. A single use TBNA needle (NA-201SX-4022, Olympus, Tokyo, Japan) was used for each patient. To ensure assessment of bacteraemia pertained specifically to EBUS-TBNA, TBNA was performed as the first diagnostic procedure and blood cultures drawn prior to any further diagnostic procedures being performed.

Venipuncture of an antecubital vein was performed within sixty seconds of completion of the final TBNA. 20mL blood was drawn and then divided equally into both aerobic (BD BACTEC Plus Aerobic/F 442192. Becton Dickinson. Maryland, USA) and anaerobic (BD BACTEC Plus Anaerobic/F 442193. Becton Dickinson.

Maryland, USA) culture bottles. Specimens were incubated at 35°C in an instrumented blood culture system (BD BACTEC 9240. Maryland, USA). Positive blood culture vials were processed according to the manufacturers instructions.

Following completion of the procedure, 10mL sterile Normal Saline was washed through the TBNA needle lumen into a sterile container and sent for microbial culture. Following centrifugation, material was inoculated onto both horse blood agar and chocolate agar and incubated in CO2 at 35°C for 48 hours. Patients whose blood cultures were positive were immediately contacted by phone to review any symptoms that might suggest clinical infection. All patients underwent detailed clinical review at the time of scheduled post-procedure review at three to seven days following EBUS-TBNA.

Statistics

Comparison between patient groups was made using Fisher's exact test. This test, and confidence intervals, were calculated using online software available at http://www.graphpad.com/quickcalcs (GraphPad Software, La Jolla, CA. USA).

RESULTS

Forty-five consecutive patients undergoing EBUS-TBNA between March 19th and August 21st 2009 consented to involvement in this study. Two patients met exclusion criteria (one required prophylactic antibiotics, and one had a concurrent febrile

illness) therefore 43 patients had samples taken for analysis. Clinical indication for performance of EBUS-TBNA, and final diagnosis, is recorded in table 1.

EBUS-TBNA was performed for evaluation of mediastinal lesions at a number of lymph node stations (see table 2). Median lesion size was 2.6±0.9cm (range 0.9 – 3.5cm). Median number of needle passes performed prior to venisection was 2.3 (range 1 – 4). Sufficient material for pathologic analysis was obtained in 41 patients (95%) and demonstrated a definitive diagnosis in 33 patients, with TBNA from eight patients demonstrating normal lymphoid tissue.

Peripheral blood cultures taken within sixty seconds of TBNA were positive in 3 patients (7.0% 95%CI 1.7–19.3%). All organisms identified typically colonise the oropharnyx. Bacteria isolated and clinical features of these three patients are recorded in table 3. No statistically significant relationship was seen between presence of bacteraemia and lesion size, number of needle aspirations performed, or underlying pathology. Bacteraemia was even noted for one patient, undergoing EBUS-TBNA for evaluation of suspected mediastinal recurrence of breast carcinoma, in whom inadequate samples were obtained. None of the three bacteraemic patients had clinical features suggestive of infection, and no complications were seen among our cohort.

Culture of needles following TBNA was negative in 28 patients (65%), Cultures were positive in 15 patients (35%) with growth of multiple anaerobic and aerobic organisms, typical of upper respiratory tract flora, in fourteen patients and a pure growth of Streptococcus *mitis* in one patient. Needle culture was negative in all three patients in whom bacteraemia was identified.

DISCUSSION

This is the first report to describe the frequency of bacteraemia following EBUS-TBNA, which appears comparable to the rate of bacteraemia associated with routine flexible bronchoscopy. We have recorded a bacteraemia rate of 7% among patients undergoing EBUS-TBNA for evaluation of mediastinal and hilar lesions, though importantly none of our patients experienced any clinically significant infective complications. The risk of bacteraemia did not appear to depend on lesion size, or the underlying pathology being sampled. It is also interesting to observe that bacteraemia may even occur despite an inadequate sample being retrieved by the procedure. The exact cause of bacteraemia following EBUS-TBNA remains unclear.

The rate of bacteraemia following routine flexible bronchoscopy varies between reports from 0% to 6%.[7-11] Yigla and co-workers previously observed bacteraemia in 6% of patients undergoing bronchoscopy – comparable to our observed bacteraemia rate – and noted no association between bacteraemia and performance of procedures (eg. brushings, biopsy) and suggested that bacteraemia may result from bacterial mucosal penetration above the vocal cords, or alternately due to bronchial mucosal trauma following introduction of the bronchoscope.[8] This is supported by the observation in both human and animal studies that bacteraemia may be seen in over 30% of patients undergoing rigid bronchoscopy, in which mucosal trauma is significantly greater than that seen for flexible bronchoscopy.[12, 13]

It is of interest to observe that bacterial culture of the TBNA needle washings was negative in all three patients in whom bacteraemia was demonstrated. This may be a result of the reduced sensivity of the agar culture method used for the needle washing compared with the bactec system used for detecting bacteraemia. It is also possible that bacteraemia in our patients was a result of introduction of the bronchoscope *per se* and that performance of TBNA did not measurably increase the risk of bacteraemia. This is also consistent with the observation that, while infections at the site of needle puncture following conventional TBNA have been reported,[14] the only study to examine bacteraemia rates following conventional TBNA observed no bacteraemia in 50 procedures.[4] In comparison to a routine bronchoscope (through which conventional TBNA is performed), the EBUS-TBNA bronchoscope is larger, less manoeuvrable, and has poorer video optics (including a 30 degree viewing camera). This increases the likelihood of pharyngeal and glottic contact during introduction of the bronchoscope through the upper airway and may explain the higher bacteraemia rate we observed in comparison to those undergoing conventional TBNA.[4]

Similarly, bacteraemia rates following upper gastrointestinal endoscopic ultrasound (EUS) are similar whether FNA is performed or not.[15] Observed incidence of bacteramia following EUS is equal to that seen in routine gastroscopy (6%),[16, 17] and for both procedures, biopsy or other endoscopic operation does not appear to increase the likelihood of bacteremia.[16, 17]

Epstein and co-workers previously reported polymicrobial contamination of conventional TBNA needle contents in all patients examined.[14] Our findings also

indicate that contamination of the TBNA needle by oropharyngeal flora is common. We also observe that the majority of reports describing clinically significant infection following either TBNA or EUS-FNA describe infection of relatively avascular tissue.[5, 6, 14, 18, 19] During insertion of the bronchoscope through the oropharynx suctioning is very difficult to avoid while establishing a view of the larynx. Contamination of the bronchoscope channel lumen should be assumed for all EBUS-TBNA procedures. While insertion of the bronchoscope through an endotracheal tube (under general anaesthetic) may avoid this, intubation itself is associated with a bacteraemia rate of over 10%,[20] and the very low observed incidence of infection complicating EBUS-TBNA should not influence sedation practice.

Guidelines from the American Heart Association for the prevention of infective endocarditis acknowledge that respiratory tract procedures may cause transient bacteremia with a wide array of microorganisms, but that the risk of antibiotic-associated adverse events exceeds the benefit, if any, from prophylactic antibiotic therapy.[21] Our findings suggest that, given a comparable bacteraemia rate to routine flexible bronchoscopy, recommendations for use of prophylactic antibiotics for the prevention of infective endocarditis in patients undergoing EBUS -TBNA should not differ from those for routine bronchoscopy. Current guidelines recommend antibiotic prophylaxis for bronchoscopic procedures only in patients with cardiac conditions associated with the highest risk of adverse outcome from endocarditis.[21]

We identify some limitations of our study. Blood cultures were taken at only one time-point. However, rates of bacteraemia following dental procedures are highest immediately after the procedure, and fall dramatically after just two to five

minutes.[22] Therefore, the likelihood we have missed bacteraemic events occuring after our venisection seems very low. We excluded patients with fever, and no patients were immunocompromised at the time of EBUS-TBNA. Such patients may be at higher risk of bacteraemia, or infective complications. Finally, culture of needle washings was performed by inoculation onto agar plates. The sensitivity of this method is less than 100% and it is likely our finding under-estimates the true rate of needle contamination by oropharyngeal bacteria.

This study cannot inform comment on the exact risk of local infections. Although bacterial contamination of the TBNA needle was demonstrated in 35% of patients, none developed evidence of clinically significant infection. Oropharyngeal commensal bacterial contamination of the TBNA needle is almost certainly a common event in EBUS-TBNA. Despite this, only two reports describe clinically significant infections complicating EBUS-TBNA,[5, 6] suggesting local infection at the site of TBNA is either extremely rare, or potentially under-recognized and/or under-reported.

Given the assumed needle contamination, we believe patient factors influence the risk of local infection during EBUS-TBNA more so than procedural factors. Future larger prospective studies are required to determine which lesions pose the highest risk of local infection. Further evaluation of the cause of bacteraemia in EBUS-TBNA is also warranted, comparing bacteraemia rates following TBNA with rates following bronchoscope insertion, prior to performance of TBNA.

In conclusion, we observe a low rate of bacteraemia following performance of EBUS-TBNA, comparable to that previously reported following routine flexible bronchoscopy. Bacteraemia appears likely to be due to insertion of the bronchscope itself rather than due to performance of TBNA. Contamination of the TBNA needle by oropharyngeal flora is common and may predispose patients to clinically significant infection at the site of TBNA puncture, though this appears rare.

Table 1. Indication for performance of EBUS-TBNA, and final diagnoses

Indication	Final diagnosis	(n)
Staging of known NSCLC*	Adenocarcinoma	6
	Squamous cell carcinoma	3
	NSCLC*	2
	Large cell carcinoma	2
	Sarcoidal granulomas	1
	Normal lymph node	6
Mediastinal evaluation of suspected locally advanced NSCLC*	Small cell lung carcinoma	4
	Squamous cell carcinoma	3
	Adenocarcinoma	1
	Granulomatous inflammation	1
	Normal lymph node	2
Suspected sarcoidosis	Sarcoidosis	5
	Normal lymph node	1
Isolated mediastinal/hilar lymphadenopathy	Hodgkin's disease	2
	Breast carcinoma metastases	2
	Metastatic melanoma	1
	Carcinoid tumour	1

*NSCLC – non-small cell lung cancer

Table 2. Lymph node stations sampled.

Lymph node station*	Number of patients
7	21
4R/4L	13
10R/L	7
2R	1
1L	1

*Mountain & Dresler lymph node station classification.[23]

Table 3. Clinical features of patients with confirmed bacteraemia following TBNA.

Gender	Age (years)	Location of lesion*	Size (cm)	Number of needle aspirates performed	Final diagnosis	Bacterial isolate	Cl sig in
F	62	7	2.4	2	Insufficient material#	Actinomyces *spp*.	No
M	77	10L	3.1	1	Metastatic melanoma	Streptococcus *salivarius*	No
M	26	7	1.9	2	Granulomatous inflammation	Streptococcus *mitis*	No

*Mountain & Dresler lymph node station classification.[23]

#confirmed metastatic adenocarcinoma of breast by subsequent surgical biopsy.

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