Bronchoscopy as an indicator of tracheobronchial fungal infection in non-neutropenic intensive-care unit patients

Ö. Yazıcıoğlu Moçin[1], Z. Karakurt[1], F. Aksoy[2], G. Güngör[1], M. Partal[3], N. Adıgüzel[1], E. Acartürk[1], S. Batı Kutlu[4], R. Baran[5] and H. Erdem[6]

1) *Pulmonology and Respiratory Intensive Care Unit, Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey,* 2) *Department of Pathology, Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey,* 3) *Department of Microbiology, Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey,* 4) *Department of Infectious Diseases and Clinical Microbiology, Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey,* 5) *Department of pulmonology , Acibadem Fulya Hospital, Istanbul, Turkey and* 6) *Department of Infectious Diseases and Clinical Microbiology, GATA Haydarpasa Training Hospital, Istanbul, Turkey*

Abstract

We aimed to establish that a bronchoscopic view can be as reliable as microbiology, and support an empirical tracheobronchial fungal infection (TBFI) treatment decision. We retrospectively studied 95 respiratory failure patients with suspected TBFI admitted to the intensive-care unit (ICU) in 2008 with sticky secretions, hyperaemic mucosa, and whitish plaques on bronchoscopic view. Patients not suspected of having TBFI were chosen as a control group (n = 151). Broncheoalveolar lavage (BAL) fluid was cultured, and biopsy samples were taken from the lesions. Biopsy samples positive for fungi were defined as 'proven', only BAL-positive (+ fungi) cases were 'probable TBFI', and BAL-negative (– fungi) cases were 'possible TBFI'. BAL (+ fungi) and BAL (– fungi) in the control group were defined as 'colonization' and 'no TBFI', respectively. The sensitivity, specificity and positive and negative predictive values of BAL (+ fungi) were 85.1% (63/74), 81.4% (140/172), 66.3% (63/95), and 92.7% (140/151), respectively. Biopsies were performed in 78 of 95 patients, and 28 were proven TBFI with fungal elements, and 100% were BAL (+ fungi). Probable TBFI was seen in 30 of 95 patients with BAL (+ fungi), and possible TBFI (BAL(– fungi)) in 25 of 95. Among the 95 patients, microbiology revealed fungi (90.5% *Candida* species; 9.5% *Aspergillus*) in 63 (66.3%). In the controls, the colonization and no TBFI rates were 11 of 151 and 140 of 151, respectively. Observing sticky secretions, hyperaemic mucosa and whitish plaques by bronchoscopy is faster than and may be as reliable as microbiology for diagnosing TBFI. These findings are relevant for empirical antifungal therapy in suspected TBFI patients in the ICU.

Keywords: Bronchoscopy, fungal infection, intensive-care unit, respiratory failure
Original Submission: 3 February 2012; **Revised Submission:** 26 September 2012; **Accepted:** 14 November 2012
Editor: E. Roilides
Article published online: 22 November 2012
Clin Microbiol Infect 2013; **19:** E136–E141
10.1111/1469-0691.12112

Corresponding author: H. Erdem, Department of Infectious Diseases and Clinical Microbiology, GATA Haydarpasa Training Hospital, Istanbul, Turkey
E-mail: **hakanerdem1969@yahoo.com**

Introduction

Flexible bronchoscopy (FB) is an extremely crucial method in the intensive-care unit (ICU) and an important diagnostic tool for the pulmonologist [1,2]. Endobronchial lesions can be observed and diagnostic specimens, lavage and brush materials can be easily obtained by FB [3]. Accordingly, FB has a considerable place in the management of tracheobronchial fungal infections (TBFIs). However, the diagnosis of TBFI by microbiology and pathology analysis takes 2–3 days at a minimum. Combined with the high rate of colonization [4], this means that, particularly in mechanically ventilated patients [5], a rational therapeutic approach may be delayed or obscured. Only a few studies have documented fungal disease in critically ill, non-neutropenic patients [4,6,7]. To

the best of our knowledge, no one has yet assessed the value of the bronchoscopic inspection in TBFIs to provide clues for rational antifungal treatment. In our respiratory ICU, patients in whom we observed sticky secretions accompanied by hyperaemic and irregular mucosa, followed by whitish plaques and subsequent nodules, were frequently confirmed by microbiology and histopathology to have TBFI. It is already known that fungal disease may manifest as mucosal plaques in infants, older adults who wear dentures, patients being treated with antibiotics, chemotherapy, or radiation therapy, and those with cellular immunodeficiency [8–11]. Recently, bronchoscopy TBFI findings in immunocompromised patients were summarized in a review [12]. We hypothesized that patients with these bronchoscopic findings could alert us to suspect TBFI in critically ill patients in the ICU.

In this study, which is the first and the largest of its kind, we evaluated the detection of whitish plaques by bronchoscopic examination of the tracheobronchial tree, relative to the clinical and laboratory data, in non-neutropenic ICU patients with acute respiratory failure (ARF), to provide evidence for empirical antifungal treatment.

Materials and Methods

This retrospective, observational, case–control study was conducted in the respiratory ICU of Sureyyapasa Chest Diseases and Thoracic Surgery Training and Research Hospital, Istanbul, Turkey. Our unit is labelled as a level III ICU, and has a 20-bed capacity. The criterion for inclusion of patients in the study was clinical suspicion of TBFI [12] during FB in a patient with ARF [13]. The study was carried out between 1 January and 31 December 2008. All invasive procedures, including FB, were performed as a result of clinical indications, and all patients provided signed informed consent. We obtained hospital approval from the Institutional Review Board for this study.

FB (Olympus)

FB was performed for aspiration of secretions and for diagnostic analyses in eligible intubated patients. The nasal route was used for observing the upper level of the vocal cords in all non-intubated patients.

The bronchoscopic view for suspected TBFI

TBFI was suspected when whitish, sticky secretions, oedematous hyperaemic mucosa and/or mucosal plaque formation were observed. When TBFI was suspected, a bronchial mucosal biopsy was performed in all eligible cases.

Modified definitions of TBFI

We prepared a flow chart (Fig. 1) for definitions of 'proven', 'probable' and 'possible' TBFIs, and 'colonization' or 'no TBFI', with the aid of guidelines [5]. Proven TBFI: in the case of suspected TBFI, tissue biopsy and tracheobronchial washing reveal fungi. Probable TBFI: in the case of suspected TBFI, the pathology findings are negative, but the microbiology results of tracheobronchial washing reveal fungi. Possible TBFI: TBFI is suspected, but pathology and microbiology findings are negative for fungi. Colonization: tracheobronchial washing reveals fungi without bronchoscopic suspicion of TBFI. No TBFI: patients have no bronchoscopic findings of TBFI, and have negative histology or microbiology findings for fungi.

Data collection

Patient demographics, APACHE II scores [14] on admission to the ICU, reasons for ARF [13], pneumonia [1,2], chronic obstructive pulmonary disease exacerbation, infections following thoracic surgery, chronic parenchymal diseases, pre-ICU locations, mechanical ventilation, day of bronchoscopic sampling, length of pre-ICU stay, tracheostomy, diabetes mellitus, steroid use, tracheal complications and laboratory data were recorded.

Pathology

Biopsy samples were examined after staining with Grocot and periodic acid–Schiff reagent. TBFI was characterized by disintegration of the surface epithelium, acute inflammatory cell infiltration and fibrin in the bronchial and tracheal mucosa, and yeast-like pseudohyphae among the necrotic cells [15,16]. The type of fungus was not determined. Patients were further separated into two groups according to whether the histopathology findings were positive or negative for fungi.

Microbiology

Bronchial and tracheal washings were cultured onto Sabouraud's dextrose agar, and a microbiological culture analyser (mini API; Biomerieux, Marcy l'Etoile, France) was used for mould and yeast identification. *Candida* was classified into *albicans* and non-*albicans*; further differentiation of *Candida* could not be performed, owing to inadequate laboratory resources. *Aspergillus* was identified by inoculating bronchial and tracheal washings onto Sabouraud's dextrose agar; colonies that were fast-growing and white, yellow, yellow–brown, brown to black or green in colour were accepted as positive.

Bacterial cultures were quantified and microorganisms with $>10^4$ CFUs/mL were assessed as indicative of an infection requiring bronchial washing. Urine, blood, tracheal aspirate and other examples were also examined when needed.