Clinical risk factors and bronchoscopic features of invasive aspergillosis in Intensive Care Unit patients

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Key words
Risk factors • Bronchoscopy • Invasive aspergillosis • ICU

Introduction
Invasive aspergillosis (IA) is an important cause of morbidity and mortality in immunocompromised patients. During recent years, a rising incidence of IA in Intensive Care Unit (ICU) patients has been reported. The patterns of IA related infection may differ according to the type of underlying disease. Unfortunately little is known about the characteristics of IA in ICU patients. In the present study we assessed IA related clinical and bronchoscopy findings in ICU patients.

Materials and methods
This study was performed at the ICU units in Sari and Babul, Mazandaran from August 2009 through September 2010. We analysed 43 ICU patients with underlying predisposing conditions for IA. Bronchoalveolar lavage (BAL) samples were collected by bronchoscope twice a weekly. The samples were analyzed by direct microscopic examination, culture and non-culture based diagnostic methods. Patients were assigned a probable or possible diagnosis of IA according to the consensus definition of the EORTC/MSG.

Results
Out of 43 suspected patients to IA, 13 (36.1%) cases showed IA. According to criteria presented by EORTC/MSG, they were categorized as: 4 cases (30.8%) of possible IA and 9 (69.2%) of probable IA. The observed mortality was 69.2%. The main underlying predisposing conditions were neutropenia, hematologic malignancy, and COPD. The macroscopic finding in bronchoscopy included of Prulent secretion (46.6%), Mucosal bleeding (30.7%), Mucosal erythema (23%), Trachobronchomalacia (15.3%).

Conclusion
The diagnosis of IA in patients with critical illness in ICU is even more difficult. The clinical diagnostic process is often dependent on indirect circumstantial data enhancing the probability of IA. Bronchoscopy with inspection of the tracheobronchial tree, sampling of deep airway secretions and BAL can be helpful.
Invasive aspergillosis in ICU

ous studies [11, 12]. Airway IA was considered when the predominant CT findings revealed a tree-in-bud pattern or peribronchial consolidation. During hospitalization, bronchoalveolar lavage (BAL) samples were collected by bronchoscope (Olympus BF20D) twice a week. The bronchus of the lobe in which consolidation was imaged by chest radiograph or chest CT scan was wedged, and 50 mL of 0.9% sterile saline solution at room temperature was instilled with a syringe through the working channel of the bronchoscope. The total volume of saline solution instilled into the lung was typically 150 mL, and 50 to 100 mL of BAL fluid was recovered. The presence of any tracheal or bronchial lesions was recorded by the endoscopist. The BAL samples were analyzed by culture and non-culture based diagnostic methods. BAL galactomannan (GM) antigen levels were measured by ELISA (Platelia Aspergillus GM EIA) assays. An optical density ratio of 1.0 was considered positive for GM in BAL samples [13].

Patients were assigned a probable or possible diagnosis of IA according to the consensus definition of the EORTC/MSG [14], with the modification. Probable IA was diagnosed when culture or cytology analyses of BAL fluid tested for Aspergillus species, and when one major clinical criteria (such as halo sign, air-crescent sign, or cavity within an area of consolidation on CT scan) or 2 minor clinical criteria (such as symptoms of lower respiratory tract infection, pleural rub, or a new infiltrate without an alternative diagnosis) were evident. Possible IA was defined by the presence of a host factor and either a positive culture or 1 major (or 2 minor) criteria. In this present study we were not be able to define a proven IA case (histologic evidence of tissue invasion) because there was an explicit refusal of the family to doing biopsy or autopsy.

Results

During the study period, 43 patients fulfilling the inclusion criteria were enrolled. According to the EORTC/MSG criteria, cases were classified as 9 (69.2%) of probable IA and 4 cases (30.8%) of possible IA. The median patient age was 56.5 years and 58.8% patients were male. The observed mortality in IA patients was 69.2% and 4 (30.7%) had survived. The characteristics of patients are summarized in Table I.

We found that the incidence of fever and rate of respiratory failure requiring mechanical ventilation were significantly higher in neutropenic patients than in patients with Solid organ cancer and COPD (P < 0.001). The macroscopic finding in bronchoscopy included of Prulent secretion (46.6%), Mucosal bleeding (30.7%), Mucosal erythema (23%), Trachobronchomalasia (15.3%). As showed in Table II, mucosal bleeding and prulent secretion were more prevalent in patient with IA. Neutropenic patients were more likely to exhibit peribronchial consolidation, mucosal bleeding, and mass-like consolidation. Hence, the airway-invasive pattern was more commonly observed in neutropenic patients (85.7%) than in other patients with IA.

Conclusions

Although a few studies have focused on the IA in ICU patients [15, 16], evaluation incidence of IA in ICU patients is important. The diagnosis of IA in patients with critical illness in ICU is even more difficult, because of Clinical manifestations are often non-specific, and diagnostic criteria have been adapted from standardized guidelines developed for ICU patients [10]. In addition, critically ill patients with prolonged stays in the ICU often develop pulmonary infiltrates, atelectasis and/or acute respiratory distress syndrome, whereas patients with prior lung disease (e.g. COPD) may present with pre-existing cavi-

<table>
<thead>
<tr>
<th>Bronchoscopic features</th>
<th>IA (n = 13)</th>
<th>Non IA (n = 30)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mucosal bleeding (%)</td>
<td>4 (30.7)</td>
<td>3 (10)</td>
<td>0.0154</td>
</tr>
<tr>
<td>Prulent secretion (%)</td>
<td>6 (46.6)</td>
<td>1 (3.3)</td>
<td>0.0082</td>
</tr>
<tr>
<td>Mucosal erythema (%)</td>
<td>3 (23)</td>
<td>4 (13.3)</td>
<td>0.0599</td>
</tr>
<tr>
<td>Tracheobronchomalasia (%)</td>
<td>2 (15.3)</td>
<td>0</td>
<td>0.0952</td>
</tr>
</tbody>
</table>

Tab. I. Demographic and characteristics of all patients with probable, possible and non-IA.

Tab. II. Macroscopic finding in bronchoscopy of all patients with IA and non-invasive aspergillosis
that the airway-invasive pattern was more commonly observed in neutropenic patients with IA is in agreement with previous reports [9, 17, 18]. Fiberoptic bronchoscopy with inspection of the tracheobronchial tree, sampling of deep airway secretions and BAL can be helpful [16]. This technique is a useful first procedure for the evaluation of IA patients, but a negative result does not exclude aspergillosis. Our study had several limitations. Firstly, we had a relatively small sample size which may have limited our power to detect differences between the groups. Secondly, because the critical condition of many patients did not permit an invasive diagnostic procedure and autopsy after death from patients suspected IA, has not been reported cases of proven IA.

In conclusion, the clinical and radiological features of IA differed between patients with underlying disease in ICU unit. Its occurrence in ICU usually entails a poor prognosis despite major recent improvements in the diagnosis and treatment of IA in patients with haematological diseases. Multicenter studies are warranted to explore the exact incidence and to better delineate clinical risk factors and bronchoscopy findings IA in ICU patients.

References