Incidence, Clinical Characteristics, and Risk Factors of Invasive Fungal Infection in Patients with Acute Leukemia Receiving Induction Chemotherapy

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\textbf{Background:} Invasive fungal infection (IFI) is a leading cause of morbidity and mortality in patients with acute leukemia (AL). The standard guidelines have recommended prophylactic antifungal in patients with acute myeloid leukemia and myelodysplastic syndrome receiving induction chemotherapy. However, the epidemiological information in Thailand remains unclear and prophylactic antifungal has not been recommended in Thai treatment guidelines.

\textbf{Objective:} We aimed to review the characteristics, risk factors, and treatment outcomes of IFIs in Thai patients with AL receiving induction chemotherapy.

\textbf{Methods:} Data of patients, aged 18 years or older, with a diagnosis of AL and treated with induction chemotherapies between May 2011 and January 2016 were identified through Thammasat University Hospital database. IFIs were classified as proven, probable, and possible according to the EORTC/MSG definitions.

\textbf{Results:} The analysis included 71 AL patients with a median age of 52 years. Twelve patients (17\%) received antifungal prophylaxis. IFIs was diagnosed in 22 patients (31\%) including 9, 8, 5 patients with possible, probable, and proven IFIs, respectively. A 30-day cumulative incidence of IFIs was 23.1\%. Lower respiratory tract was the most common site of infections (17 patients, 77\%). Four patients had positive fungal cultures from the blood or tissues. Pathogens identified were Aspergillus spp., Candida spp., Exserohilum spp. Chrysonillia silphiophilia, and Penicillium spp. Increased serum galactomannan was found in 9 patients with IFIs (41\%). Whereas, none of the patients without IFI had an increased serum galactomannan. In multivariable analysis, prolonged neutropenia more than 14 days (OR 1.29 (1.08-1.99), p=0.049) and presence of comorbidities (OR 4.176 (1.066-16.353), p=0.04) were independent risk factors for IFI occurrence. The occurrence of IFIs during induction phase was independently associated with an increased treatment-related mortality compared to no IFI with a cumulative incidence at 100 days of 21\% vs 6.1\%, (p=0.02); (HR 1.58 (1.4-1.76), P=0.006); (Figure 1). However, there was no difference in both overall and leukemia-free survival between the 2 groups.

\textbf{Conclusion:} This study confirms high incidence of IFIs in Thailand, which results in an increased risk of death in patients with AL. This epidemiological data help provide useful information on antifungal prophylaxis and treatments for AL patients during induction treatment.

\textbf{Keywords:} Acute leukemia, Invasive fungal infection, Induction chemotherapy.
Figure 1. Treatment-related mortality of acute leukemia patients with and without invasive fungal infections during induction chemotherapy