Characterization of Invasive Mold Infections in Acute Leukemia and Hematopoietic Stem Cell Transplant Recipients and Risk Factors for Mortality - a Single Center Experience

R. Kubat[1], P. Subramanian[2], Y. Li[3], A. Eid[1], A. Dias[4], K. Hammoud[1], W. El Atrouni[1]

[1]Division of Infectious Diseases, Department of Internal Medicine, The University of Kansas Medical Center, Kansas City, KS, [2]Department of Internal Medicine, The University of Kansas Medical Center, Kansas City, KS, [3]Department of Biostatistics and Data Science, The University of Kansas Medical Center, Kansas City, KS, [4]Division of Hematology Oncology, Department of Medicine, Beth Israel Deaconess Medical Center, Boston, MA

Background

- Invasive mold infections (IMIs) are a significant cause of morbidity and mortality in acute leukemia (AL) and hematopoietic stem cell transplant (HSCT) recipients despite antifungal prophylaxis, with 12-week mortality up to 58.6% [1]
- Reported risk factors for IMI: Older age, GVHD, HLA-mismatch, neutropenia, CMV disease [2]
- Reported risk factors for mortality: mechanical ventilation, hemodialysis, platelets <100K, male gender [3]
- Study goal: characterize IMIs and determine risk factors for morality and determine incidence of IMI among patients with acute myelogenous leukemia (AML) undergoing HSCT

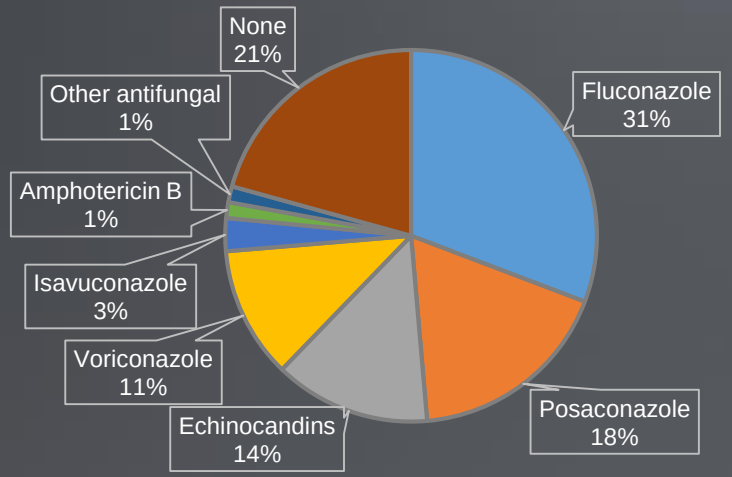
Methods

- Identified patients from 2009-2018 with diagnosis of ALs or HSCT and an IMI diagnosis based on ICD9 and ICD10 codes and microbiology data
- Classified as proven & probable IMI based on 2009 EORTC/MSG consensus guidelines
- Excluded age <18, >1 HSCT, IMI diagnosis prior to AL or HSCT
- Incidence for IMI in AML undergoing HSCT was calculated as IMI cases/100 person-years
- Risk factors for mortality determined using univariate Cox proportional-hazards regression model

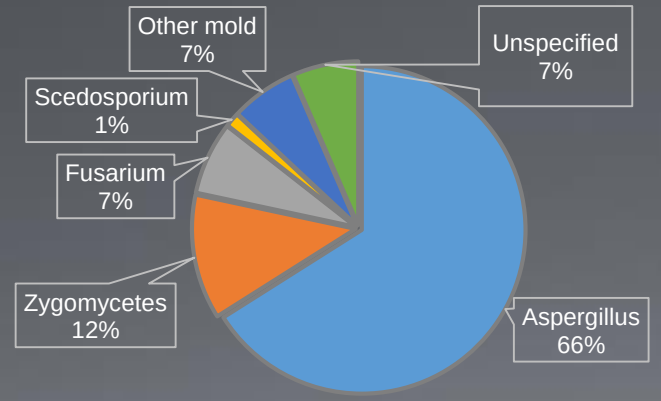
References

1. Kuster, S., Stampf, S., ... & Berger, C. (2018). Incidence and outcome of invasive fungal diseases after allogeneic hematopoietic stem cell transplantation: A Swiss transplant cohort study. Transplant infectious disease, 20(6), e12981.
2. Chien, S. H., Liu, Y. C., ... & Gau, J. P. (2019). Invasive mold infections in acute leukemia patients undergoing allogeneic hematopoietic stem cell transplantation. Journal of Microbiology, Immunology and Infection, 52(6), 973-982.
3. Neofytos, D., Treadway, S., ... & Marr, K. A. (2013). Epidemiology, outcomes, and mortality predictors of invasive mold infections among transplant recipients: a 10-year, single-center experience. Transplant Infectious Disease, 15(3), 233-242.
4. Waitman LR, Warren JJ, Manos EL, Connolly DW. Expressing observations from electronic medical record flowsheets in an i2b2 based clinical data repository to support research and quality improvement. AMIA Annu Symp Proc. 2011;2011:1454-63.
5. Murphy SN, Weber G, Mendis M, Chueh HC, Churchill S, Glaser JP, Kohane IS. Serving the Enterprise and beyond with Informatics for Integrating Biology and the Bedside (i2b2). J Am Med Inform Assoc. 2010;17(2):124-30. PMID:20190053.

Antifungal Prophylaxis at Time of IMI



IMIs by Pathogen in HSCT-Recipients and Acute Leukemia Patients from 2009-2019



Results

- 138 total IMIs - 79 in HSCT recipients, 59 in AL (49 AML)
- IMI incidence in AML undergoing HSCT – 2.35 cases/100 person-years
- Average age at IMI diagnosis was 55y with majority male (69.6%) and non-Hispanic white (80.4%); 49% of patients had neutropenia (ANC <500) at diagnosis, 57% of HSCT patients had active GVHD
- 33% of IMIs were proven by EORTC/MSG criteria, 67% probable
- Site of infection: 76% pulmonary; 11% sino-nasal; 11% skin/soft tissue
- Mortality after IMI diagnosis 23.1% at 6 wks, 34.1% at 12 wks, and 61.2% at 1 year with no statistically significant difference between AL and HSCT groups
- Karnofsky performance status ≥70 was associated with lower 6-wk mortality among HSCT recipients (HR 0.317, 95% CI [0.110, 0.914])
- ICU admission within 7 days prior to IMI diagnosis (HR 6.469, 95% CI [1.779, 23.530]) and each one-point increase in BMI (HR 1.051, CI [1.001, 1.103]) were associated with increased 6-week mortality in the AL group

Conclusions

- Despite lower mortality rate compared to previous studies, IMIs in AL and HSCT are still associated with 34% mortality at 12 weeks; additional research is needed to further delineate risk factors for mortality in this high-risk population

Funding

- This project utilized HERON and REDCap informatics services. This work was supported by a CTSA grant from NCATS awarded to the University of Kansas for Frontiers: University of Kansas Clinical and Translational Science Institute (# UL1TR002366, KL2TR000119, TL1TR00120). The contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH or NCATS.