Clinical epidemiology and outcomes of invasive pulmonary aspergillosis as a complication of respiratory viral infection in hospitalized patients

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Purpose: Invasive pulmonary aspergillosis (IPA) infections are difficult to diagnose, treat, and are associated with a high risk of death. This infection has been previously associated with immunosuppressive treatments in those undergoing stem cell or solid organ transplantation. Invasive pulmonary aspergillosis is becoming increasingly recognized as a complication of severe influenza infection, although the association between IPA and other respiratory viral infections (RVI) is unclear. Therefore, the purpose of this study is to investigate the risk of developing IPA following RVI involving a variety of respiratory viral pathogens, identify associated risk factors, and evaluate the impact of RVI-associated IPA on patient outcomes and mortality.

Methods: This in-progress study uses a retrospective cohort design conducted at a single academic medical center evaluating inpatient medical records among those admitted between September 30, 2018 and October 5, 2019. Inclusion criteria are patients ages 18 and above who were admitted to the University of Kansas Hospital with a confirmed RVI through a positive multiplex PCR for respiratory virus using a nasopharyngeal swab, nasal wash, or bronchoalveolar lavage specimen. Chart reviews of eligible patients identified the incidence of IPA following RVI and its associated risk factors. Statistical analysis was completed using chi-square tests for nominal data, t-tests for continuous data, and non-parametric alternatives for those variables that violated test assumptions. Additionally, time-to-death was evaluated using Kaplan-Meier curves, hazard ratios, and log-rank testing.

Results: Following the screening of 194 patients, 137 were identified as eligible for study inclusion. Among those, 8% (11 of 137) with RVI went on to experience IPA and 92% (126 of 137) did not. The average age of those with IPA (64+/-11.6 years old) versus those without IPA (57+/- 18 years old) did not significantly differ (P=0.235). Severity of illness (using SOFA and APACHE II scores) and comorbidities (using the Charlson Comorbidity Index) were similar between the study groups. Notably, we found that IPA occurred in 18% (2 of 11) of those infected with influenza but the remaining IPA cases involved RVIs caused by rhinovirus/enterovirus (45%, 5 of 11), (non-COVID-19) coronavirus (18%, 2 of 11), parainfluenza (9%, 1 of 11), and human metapneumovirus (9%, 1 of 11). IPA was not experienced in those with RVIs associated with adenovirus or respiratory syncytial virus. Baseline clinical characteristics that differed significantly between the two groups (+IPA vs -IPA) respectively

included a prior history of leukemia (55% vs 8%, P<0.001), prior corticosteroid use (91% vs 27%, P<0,001), and prophylactic antifungal use (64% vs 13%, P<0.001). Mechanical ventilation was reported in 45% (5 of 11) of those who developed IPA patients and 12% (15 of 126) of those without IPA (P=0.01). Survival analysis indicated those with IPA are significantly more likely to experience mortality when compared to those without IPA (log-rank P=0.016).

Conclusions: Within this interim analysis, 8% of those with RVI went on to develop IPA. We found that IPA more commonly occurred in patients with non-influenza RVIs, suggesting that this complication is not limited to influenza. Leukemia, prior corticosteroid use, and antifungal prophylaxis were associated with IPA development following RVI. We also identified an increased need for mechanical ventilation and increased mortality among those experiencing IPA following RVI. Clinicians should be aware of this potential complication of severe RVI. Future research into appropriate prophylaxis and treatment of post-RVI IPA is needed.