1709. Epidemiology of Invasive Fungal Infection (IFI) after Severe Influenza Requiring Intensive Care Unit (ICU) Admission: 10-Year Experience at a Tertiary Care Center in the United States

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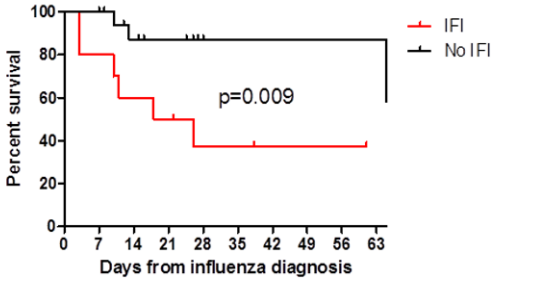
Background. Despite increasing recognition of aspergillosis complicating severe influenza and its associated high fatality in Europe, incidence and features of the disease in the United States are unknown.

Methods. We reviewed all influenza cases requiring ICU admission from 2009 to 2019 at our center.

Results. 262 patients with influenza required ICU admission. 4% (10) developed IFI at median 2d after influenza diagnosis. 80% (8/10) of patients with IFI were infected with influenza A vs. 88% (221/252) without IFI. 20% were on steroids at the time of IFI diagnosis. 70% of IFI required mechanical ventilation. Types of IFI were pneumonia (70%, 6 Aspergillus and 1 Wangiella), endobronchial IFI (20%, 1 each with Aspergillus and Lictheimia), and *Coccidioides fungemia* (10%). 4% (10) of patients were fungal colonized, but did not have IFI (5 *A. fumigatus*, 1 *A. terreus*, 4 Penicillium). CT findings of IFI included nodules (4), cavitation (3), and ground-glass opacities (2). Serum galactomannan (GM) was positive in 3 (43%). Median time to antifungal therapy (AF) was 2 days. Triazoles were prescribed to all 7 patients with aspergillosis. Posaconazole and amphotericin B were AF for patients with Wangiellaand Lichteimia, respectively. Patients with *C. immitis* fungemia died before AF. Median duration of AF was 60 days among survivors. Patients with IFI required acute hemodialysis more frequently than colonized patients (60% vs. 0%, $P = 0.01$). 30-day mortality was 60% (6/10) and 20% 92/10) in patients with IFI and colonization, respectively ($P = 0.2$). Patients with IFI had significantly higher in-hospital and 60-day mortality than those without IFI (Fig 1, $P = 0.009$).

Conclusion. Our rate of post-influenza IFI (4%) was lower than reported in Europe (~15%), which might stem from a lack of systematic BAL GM testing at our center, over-reliance on GM to make diagnoses in Europe, and/or differences in pt populations and clinical practices in treating severe influenza. IFI and fungal colonization rates were similar at our center, highlighting the importance of using well-defined criteria to define disease. Given the high mortality of post-influenza IFI, priority should be given to defining risk factors that might identify patients for targeted AF prophylaxis. In using AF, it is important to recognize that Aspergillus is not the only cause of IFI.

Fig 1. Mortality of patients with severe influenza admitted to ICU



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1710. Profiling Patients with Rare Mucormycosis Infections Using Real-world Data

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Background. Invasive mucormycosis (IM) is universally fatal if untreated and is a challenge to assess due to its rarity. Diagnosis is difficult and can be missed due to a low index for suspicion. IM prevalence may be increasing with medical advances, especially in neutropenia management, leading to improved survival and expansion of the at-risk patient group. Large administrative databases contain patient-level chart information and may offer a way to describe IM patients in a representative sample of the population.

Methods. A retrospective observational study was conducted using US data from the deidentified Optum Electronic Health Record database between January 2007 and June 2018. Patients with any fungal infection and IM specifically were defined by ICD9 (110–119, 117.7) or ICD10 (B35-49, B46) codes. Descriptive statistics were used to assess demographics, comorbidities, and antifungal agents (AF) prescribed among IM patients with an underlying diagnosis of hematologic malignancy (HM). Restricting to an at-risk population minimized possible false IM coding in the sample.

Results. Of the approximately 97 million patients in the database, about 5 million had a fungal infection diagnosis and 5,208 had an IM diagnosis (0.005% overall, 0.11% of fungal infection). Among those with underlying HM ($n = 698,187$), 641 IM cases were observed (0.09%); of whom, 46% were male, 82% were over 40 years of age, and 77% were in the Midwest region of the United States. They were 83% Caucasian, 7% African American, 2% Asian, and 8% other/unknown race or ethnicity. The mean Charlson Comorbidity Index score was 3 ± 2 and the top comorbidities, aside from malignancy, were diabetes (24%, $n = 151$), chronic pulmonary disease (22%, $n = 141$), and renal disease (11%, $n = 69$). Not all IM patients were treated. There were 376 AF prescriptions, of which 35% were for fluconazole, 28% for posaconazole, and 14% for voriconazole, followed by 7–8% each for isavuconazole and amphotericin formulations.

Conclusion. A sizable number of IM patients were identified from a large US electronic medical records database. More work is needed to understand the data. Given the significant challenges in prospectively identifying IM patients, a large database may allow for a broader insight into patients at risk and potential predictors of IM.

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1711. Histoplasmosis-Associated Hemophagocytic Lymphohistiocytosis: A Case Series and Review of the Literature

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Background. Histoplasmosis is an endemic fungal disease with a spectrum of presentations from asymptomatic, mild to disseminated infections. Histoplasmosis-associated hemophagocytic lymphohistiocytosis (HLH) is a rare disorder with limited data regarding treatment and outcome. We described the clinical features, treatment, and outcomes of five patients. This review also summarized the current literature about presentation, treatment, and outcome of this infection-related HLH entity.

Methods. We searched the electronic medical records for patients with histoplasmosis-associated HLH at our institution from January 1, 2006 to September 30, 2017. Diagnosis of HLH was confirmed and by chart review according to HLH-04 criteria. We also searched the current literature for case reports and case series of this entity.

Results. We reported five cases of histoplasmosis-associated HLH during this period. All patients were diagnosed after 2010, this may be explained in part by increased awareness of this entity. The literature review yielded 60 cases of histoplasmosis-associated HLH. Among all patients (65 patients), the most common underlying condition was HIV in 61% of all patients. The majority of histoplasmosis patients were treated with amphotericin B formulation in 81%. The specific treatment for HLH was as follows: nine patients received steroids only, six patients received intravenous immunoglobulin (IVIG) only, three patients received dexamethasone and etoposide, two patients received etoposide, dexamethasone, and cyclosporine, two patients received steroids and IVIG, and one patient received Anakinra and IVIG. The inpatient mortality rate was 31% with most of the deaths occurring within 2 weeks of hospital admission.

Conclusion. Histoplasmosis-associated HLH among adults is an uncommon but aggressive disease with multiorgan involvement. Early antifungal therapy with a lipid formulation amphotericin B is the most important part of the management. Initial HLH-specific immunosuppressive therapy with regimens such as the HLH-94 protocol is usually individualized.

Table 1. Clinical characteristics of histoplasmosis induced HLH patients at our institution (n=5)

Case #	Year	Age	Gender	Race	Comorbid conditions	Immunosuppressive agent	Yeast in BM	Urine Histoplasma Ag	Sites Growing Histoplasma	CXR Findings
1	2011	48	M	White	HIV/CD4 count 50	None	Yes	Above LoQ	Blood	No infiltrates
2	2014	48	F	White	MCTD	HCQ/prednisone 10 mg daily	No	Above LoQ	Blood	LAD without infiltrates
3	2016	75	M	White	? Crohn's	Infliximab/ azathioprine/prednisone	Yes	N/A (serum Ag: Above LoQ)	Blood and BM	No infiltrates
4	2017	46	M	African American	Sarcoid	Prednisone	Yes	Above LoQ	Blood and BM	Diffuse infiltrate
5	2017	41	M	White	HIV/CD4 count 10	None	N/A	Above LoQ	Blood	Diffuse infiltrate

Notes. M: male; F: female; HIV: human immunodeficiency virus; MCTD: mixed connective tissue disease; N/A: not applicable, BM: bone marrow; dexa: dexamethasone; CXR: chest X-ray, Ag: antigen, LAD: lymphadenopathy, LoQ: limit level of quantification, HCQ: hydroxychloroquine.

Table 2. Diagnosis of HLH (n=5)

Case #	Fever	Cytopenia (2 lines)	IL2-receptor (pg/mL)	Peak triglycerides (mg/dl)	BM with hemophagocytosis	Splenomegaly	Peak ferritin (ng/mL)	Nadir fibrinogen (mg/dl)
1	Yes	Yes	5167	258	Yes	No	>15,000	95
2	Yes	Yes	115,900	329	Yes	Yes	4487	265
3	No	Yes	9580	227	Yes	No	> 7500	384
4	Yes	Yes	1648	192	No	Yes	>7500	168
5	No	Yes	15,540	246	N/A	Yes	> 7500	51

Notes. BM: bone marrow, IL: interleukin

Table 3. Treatment and outcome of histoplasmosis associated HLH patients at our institution (n=5)

Case #	Antifungal drug	HLH specific treatment	Outcome (hospital discharge)
1	Liposomal amphotericin B for 2 weeks then Itraconazole for 12 months	None	Survived
2	Liposomal amphotericin B for 4 weeks then oral azoles for 4 years	Dexamethasone 10 mg/m2 for 2 days	Survived
3	Voriconazole	None	Discharged to hospice
4	Liposomal amphotericin B for 2 weeks then Itraconazole for 4 months	Dexamethasone 10 mg/m2	Survived
5	Liposomal amphotericin B for 2 weeks then oral azoles	None	Died (day 43)

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