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Major article

Surveillance of patients identified with fungal mold at a public academic medical center

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Background: This study describes the epidemiology of patients with fungal mold infection or colonization at a large academic medical center during a period of ongoing construction of a new hospital building.

Methods: This is an observational retrospective cohort study performed at a public academic hospital. We performed focused medical record review of all patients with fungal mold isolated on microbiologic culture over a 3-year period from May 2009 through April 2012. We established case definitions by modifying criteria used in previously published studies. We established 4 categories for invasiveness: proven invasive fungal disease (IFD), probable IFD, clinical infection not meeting IFD criteria, or colonization/contamination. We also established 3 categories for association with our health care facilities: health care–associated hospital onset (HO), health care–associated community onset (HACO), or community associated (CA).

Results: Of the 188 cases included in the study, 15 (7.9%) and 23 (12.2%) met criteria for proven and probable IFD, respectively. Of the cases, 114 (60.6%) represented contamination or colonization, and 36 (19.1%) had clinical infection not meeting IFD criteria. Epidemiologically, 46 (24.5%) cases were HO, 42 (22.3%) cases were HACO, and 100 (53.2%) cases were CA.

Conclusion: The surveillance methods we established were helpful for characterizing and monitoring fungal mold infections at the study institution.

INTRODUCTION

Opportunistic fungal infections are a rising threat in increasingly immunocompromised and critically ill patients.[1] Although invasive fungal disease (IFD) attributed to *Candida* or *Aspergillus* species predominates, the incidence of infections from dematiaceous molds and zygomycetes is increasing.[1,2] Because these molds are ubiquitous in the environment, there is concern during construction activities for infection or colonization in immunocompromised hosts, including patients with hematologic malignancies, hematopoietic stem cell and solid organ transplants, human immunodeficiency virus, and burns.[3] Fungal infections can lead to increased long-term sequelae and mortality in these vulnerable populations.[4] Data on the incidence of fungal mold infections outside of the context of outbreaks or immunocompromised patients are scant. The objective of this study was to describe the epidemiology of patients identified with fungal mold on microbiologic cultures at a large academic medical center. The context in which this study was undertaken was massive ongoing construction activity across the street from where our hospital facilities are located. Additional information regarding the construction is available on the Parkland Memorial Hospital website (http://newparkland.parklandhospital.com/).

METHODS

We performed a retrospective observational cohort study at Parkland Memorial Hospital, Dallas, TX. It is an 809-bed public academic tertiary hospital with services, including a level I trauma center, level III neonatal intensive care unit, regional burn unit, renal transplantation, and high-risk obstetrics. Physician services

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are largely provided by the University of Texas Southwestern Medical Center. The study period was May 2009 through April 2012. We obtained a line list of all patients with any culture positive for a fungus during the study period from the microbiology laboratory. In the Parkland microbiology laboratory, fungal molds may be recovered on bacterial and mycobacterial cultures and fungal cultures. In the study, we excluded yeasts, dermatophytes, and endemic dimorphic fungi. We also excluded duplicate isolates. Culture negative mold infections were not included because data extraction was not feasible. We established surveillance case definitions, which are subsequently described. We performed a focused medical record review to collect demographic, clinical, and laboratory data. The study was approved and considered exempt from full review by the institutional review board.

The current hospital facility was built in the 1950s. In November 2010, construction of a new 2.5-million-sq-ft building began across the street from the current building. During the years 2008 to 2010, a considerable amount of demolition occurred at the new hospital site. Several buildings, including 2 warehouses, parking garage, bridge, and some houses, were demolished to clear the construction site. No special dust suppression measures were implemented at the site itself, other than watering down after demolition. In the current hospital building, the dust suppression measures used were monitoring of the air ventilation system throughout the hospital at least once every 2 weeks, particularly the performance of air handlers and preintake and postintake filters on the intake side of the building. In May 2011, oversight of air handler maintenance processes was enhanced throughout the hospital building by weekly inspection of preintake and postintake filters and replacement if dirty. Because of changes in the facilities team and leadership in the summer of 2011, policies related to dust control on the floors and dust containment during repairs and remodeling within the hospital building were strictly implemented. The construction is ongoing at the time of submitting this article, and it is expected to be completed in August 2014.

Case definitions

The clinical criteria from the European Organization for Research and Treatment of Cancer/Invasive Fungal Infections Cooperative Group/Mycoses Study Group (EORTC/MSG)[5] were modified to develop the following case definitions. These criteria needed to be modified because they were originally established for use in clinical trials of antifungal drugs in immunocompromised patients with invasive fungal infections. We adapted the definitions to make them applicable to the entire spectrum of patients seen in our institution, including immunocompetent patients and burn patients.

We established the following 4 categories based on invasiveness.

1. Proven IFD: isolation or evidence of a mold on histopathology or culture of sterile material or blood (except *Aspergillus spp*).
2. Probable IFD: isolation of fungal mold from any specimen source, 1 host factor criterion [criteria were recent history of neutropenia <500 neutrophils/mm^3 for >10 days temporally related to onset of fungal disease; receipt of allogeneic stem cell transplant; prolonged use of corticosteroids (>0.3 mg/kg/d prednisone or equivalent for >3 weeks); treatment with other recognized T-cell suppressants in the past 90 days; inherited severe immunodeficiency; presence of burn injuries], and clinical features suggestive of infection.

The patient was considered to have clinical evidence of infection if there were clinical signs and symptoms that could be associated with the positive culture and they were treated for the mold infection by the primary physician.

3. Clinical infection not meeting IFD criteria: presence of signs and symptoms of infection and treated for mold infection, without any host factor criteria.
4. Colonization/contamination: positive culture in the absence of clinical symptoms. We categorized colonization and contamination together because it is not always feasible to differentiate colonization vs contamination of the specimen, particularly when multiple cultures are not sent per patient.

We established the following 3 categories based on association with our health care facilities:

- Health care–associated hospital onset (HO): symptom-onset or positive culture $\geq$7 days after hospital admission.
- Health care–associated community onset (HACO): symptom onset or positive culture $<$7 days after hospital admission, in the setting of patient contact with our institutional facilities within 1 month prior to symptom onset or date of culture.
- Community associated (CA): symptom onset or positive culture $<$7 days after hospital admission, and no prior contact with our institutional facilities.

RESULTS

During the 3-year study period from May 2009 through April 2012, 200 nonduplicate patients had a positive microbiologic culture for fungal mold. The volume of cultures performed in the Parkland microbiology laboratory did not change significantly from month to month during the study period. Ten patients with known infection under treatment and 2 patients with incomplete medical records were excluded from further review, leaving 188 patients in the study. The age range was 0-91 years (median, 50 years), including 1 newborn infant and 1 five-year-old burn victim. Of the patients, 114 (60.6%) patients were men. The admitting services were general medicine (n = 113, 60.1%), surgery/trauma (n = 47, 25%), burn (n = 18, 9.6%), medicine-hematology/oncology (n = 5, 2.7%), transplant (n = 4, 2.1%), and neonatology (n = 1, 0.5%).

Of the 188 patients, 173 (92%) had a single mold isolated, and the remaining 8% had $\geq$2 fungal molds isolated in the same culture. The distribution of fungal isolates is shown in Figure 1. *Aspergillus* is the most predominant isolate (102, 47.9%) followed by *Penicillium* (37, 17.4%) and *Cladosporium* (16, 7.5%). Of the 102 *Aspergillus* isolates, 81 were speciated. The species were *fumigatus* (29, 35.8%), *niger* (24, 29.6%), *terreus* (14, 17.3%), *flavus* (11, 13.6%), and *versicolor* (3, 3.7%).

Of the 188 cases included in the study, 15 (7.9%) and 23 (12.2%) met criteria for proven and probable IFD, respectively. There were 114 (60.6%) cases representing contamination or colonization, and 36 (19.1%) cases had clinical infection not meeting IFD criteria. Epidemiologically, 46 (24.5%) cases were HO, 42 (22.3%) cases were HACO, and 100 (53.2%) cases were CA. The temporal trends in these cases are shown in Figures 2 and 3. The average monthly volume of cultures performed has not changed at Parkland during this time period. On review of the line list for clustering of $\geq$2 patients with fungal mold of the same species in the same clinical area within the same month, we identified 13 small clusters of 2 patients each: 4 in 2009, 7 in 2010, and 2 in 2011. Eighteen of these 26 patients were identified with colonization/contamination, 5 patients with a CA clinical infection that was not IFD, 1 patient was categorized as proven IFD that was CA, 2 patients had probable IFD that was hospital onset, and the remaining 1 patient had probable IFD that was CA. All but 2 of these clusters had occurred during the phase when demolitions were undertaken to prepare the site for construction. There was no clustering of HO or HACO cases during the study period.