Fungal Pathogens – The Changing Scene

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Fungal Pathogens – The Changing Scene

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Objectives
1. Discuss the epidemiological changes in fungal pathogens in cancer patients
2. Discuss newer therapeutic options and prevention strategies

Epidemiologic surveillance studies and autopsy data from the late 1950’s and early 1960’s demonstrated that invasive fungal infections were extremely rare, even in immunocompromised cancer patients (1, 2). Advances in the treatment of neoplastic disorders (e.g., myelosuppressive chemotherapy, bone marrow/hematopoietic stem cell transplantation) created a group of patients that survived their underlying neoplasm long enough to develop infectious complications, including invasive fungal infections. Consequently, invasive fungal infections in cancer patients are thought to be “diseases of medical progress” (3). Fungal infections have also become more common in the general population. The immunocompromised patients (17).

Other species are much less common. They all resemble Fusarium species being recognized with increasing frequency as opportunistic pathogens in immunosuppressed patients. The most important agents of hyalohyphomycosis are the following:
- Aspergillus terreus
- Scedosporium prolificans
- Trichoderma species

Infections caused by Candida species
Several studies have documented a decline in the proportion of infections caused by Candida albicans and a corresponding increase in infections caused by other Candida species (5, 6). The widespread use of fluconazole has been associated with an increase in infections caused by Candida krusei (which are resistant to this agent) and probably Candida glabrata (which have reduced susceptibility/resistance to it) (7, 8). Central venous catheters have been associated with bloodstream infections caused by Candida parapsilosis, more so than other Candida species (9). Similar epidemiological shifts, however, have also been seen in “azole naïve” patients indicating that other, less obvious factors, may also be responsible for some of these changes (10). There are reports of nystatin-resistant Candida rugosa, and amphotericin B-resistant Candida lusitaniae causing infections in patients receiving these agents (11, 12).

These data serve to remind us that epidemiological shifts are often related to therapeutic maneuvers (prophylaxis, pre-emptive or empiric therapy, specific or targeted therapy).

Other emerging yeast or yeast-like organisms include Blastoschizomyces capitatus, Malassezia furfur, and Trichosporon beigeli (13-15). Susceptibility to standard and newer antifungal agents among these organisms can be quite varied, and so can the response rates to antifungal therapy.

Infections caused by Aspergillus species
Aspergillus fumigatus is the most common species associated with infection in cancer patients. Data from The University of Texas M. D. Anderson Cancer Center suggest that among hospital acquired cases of invasive aspergillosis, Aspergillus terreus is far more common than A. fumigatus (44% vs 18%) (16). Prior exposure to amphotericin B appears to favor the emergence of A. terreus. Environmental factors might also contribute to this shift, as evidenced by culturing this species from potted plants in the vicinity of a hematology ward, at an institution with a high proportion of invasive aspergillus due to A. terreus.

Hyalohyphomycosis
These organisms are ubiquitous soil saprophytes that cause localized infections in immunocompetent persons, but are being recognized with increasing frequency as opportunistic pathogens in immunosuppressed patients. The most important agents of hyalohyphomycosis are the following:

- Fusarium species
- Scedosporium apiospermum (P. boydii)
- Scedosporium prolificans
- Acremonium species

Fusarium species have now been well described as causing invasive pulmonary or disseminated infections in immunocompromised patients (17). Other species are much less common. They all resemble Aspergillus species in tissue (biopsy) specimens, with the potential for misidentification. Accurate identification can be critical since most of these organisms are resistant or have reduced susceptibilities to existing antifungal agents. Response to therapy is generally very poor (unless immunological recovery occurs) and attributable mortality can be as high as 85-90%.

Zygomycosis
Zygomycosis is a rare infection caused by fungi of the order Mucoralis (class Zygomycetes) with the most common species being Mucor, Rhizopus, Absidia, and Rhizomucor (18). There is recent evidence that this infection is becoming more common in severely compromised patients, and might be related to the increasing use of voriconazole (prophylaxis/therapy), to which these organisms are resistant (19). Susceptibility to amphotericin B is also suboptimal, and newer agents, such as posaconazole which is active against the Zygomycetes, are eagerly awaited.
SUMMARY

The epidemiology of invasive fungal infections is changing with a large number of yeasts, yeast-like organisms, and molds emerging as significant opportunistic pathogens in the past decade or so. Many factors including environmental factors, the increasing use of intravascular devices, total parenteral nutrition, increasing use of antifungal agents for prophylaxis, empiric or pre-emptive therapy, and for long-term maintenance therapy of documented fungal infections, are responsible for these changes. Many of the newly emerging fungal pathogens cause infections identical to standard pathogens. They can, however, be difficult to identify, and are often resistant or have reduced susceptibilities to many antifungal agents. For these reasons, they will continue to challenge us for the foreseeable future.

References