Management of invasive fungal infections (IFIs) in immunocompromised patients

HOT SPOT

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The last few years have seen the appearance of a number of new antifungal therapies for the treatment of immunocompromised patients. These patients are at risk for developing severe infections that would not normally be problems for most people with cancer or those who do not have their immune systems suppressed because of hematological stem cell or organ allografts.

Who is at risk?

- patients with acute leukemia undergoing induction or consolidation therapy
- allogeneic blood and marrow stem cell transplant patients
- patients undergoing lymphoma salvage therapy
- patients receiving organ allografts, such as kidney, heart, liver or lung

Who is not at risk?

- patients undergoing cancer chemotherapy or radiation therapy for solid tumours
- patients undergoing autologous blood and marrow stem cell transplants

Why are these patients at risk?

- chemotherapy and/or radiation therapy breaks down mucosal barriers that protect against such infections
- the use of broad-spectrum antibacterial antibiotics kills off normal host flora that populate skin and gut allowing growth of more virulent pathogens
- long-term neutropenia from therapy leaves the patient devoid of cells that fight infections
- immunosuppressive medications interfere with host mechanisms for fighting infections
- in-dwelling catheters, such as central venous or urinary tract act as portals for entry of these pathogens
- prophylaxis with some antifungals may allow selection of resistant organisms
- some patients with comorbid conditions such as diabetes, renal failure, auto-immune diseases have increased risk

From where do these pathogens arise?

- in general, yeasts come from the host skin or gut although, in some areas, certain ones are endemic in soil
- molds come from the environment for the most part, but patients who have had therapy over very long periods of time may be colonized

Are there environmental issues that may make some patients more susceptible?

- older buildings
- nearby construction
- absence of hepa-filtration or lamellar flow
- turning on of air-conditioning in the summer and heating in the winter may distribute spores into the air
- certain parts of the country may have endemic organisms such as blastomycosis or coccidiomycosis

What organisms are the problems?

- candida albicans is still the most common
- non-albicans candida such as glabrata or kruseii are becoming more common
- molds such as aspergillus and, more recently, fusarium or zygomycetes are being seen more often

How do I diagnosis an IFI?

- high index of suspicion in a patient at risk
- understand that symptoms are often different in an immunocompromised patient—e.g., fever may not be a symptom in someone on corticosteroid
- use imaging appropriately—CT chest instead of CXR, CT abdomen to look at liver/spleen
- aggressive attempts at mycological confirmation—blood cultures for yeasts, tissue biopsies
- fungal marker screening if appropriate

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What types of therapy can be used?

From most widespread to more targeted these can include:

- prophylaxis—where antifungals are used in everyone in an attempt to prevent infections in some
- secondary prophylaxis—where specific antifungals are used in patients who have had previous infections and are now again at risk for developing a repeat infection because of new therapy
- empiric—where a set of symptoms such as fevers that do not respond to antibacterials triggers therapy with a broad spectrum antifungal
- pre-emptive—where a test such as a fungal marker or a chest CT scan finding triggers therapy
- targeted—where a proven or probable infection that includes positive mycology dictates a specific organism-directed therapy

Why not use the best broad-spectrum agents for prophylaxis in everyone who may be at risk?

- resistant organisms can break through
- these drugs can be toxic
- these drugs can often interact with other drugs these patients may have to take
- these drugs are sometimes inconvenient to take—IV formulations only
- these drugs are expensive

What drugs are available?

Basically there are three main classes of broad-spectrum antifungals

- polyenes—such as amphotericin B and lipid formulations
- azoles—such as fluconazole and newer broad-spectrum products such as itraconazole, voriconazole or posaconazole
- echinocandins—such as caspofungin, micafungin and anidulofungin
- other earlier agents are no longer of much value in this type of patient
- combination therapy is theoretically good, but not well proven

Do I need to do anything else other than use antifungal drugs? You bet.

- discontinue or decrease immunosuppression if at all possible
- discontinue unnecessary antibiotics
- help your patient regain white cells/neutrophils—the drugs will not work on their own for long
- treat co-morbid conditions such as high blood sugars
- to remove lines or other foreign materials that are sites for fungal growth and into whose biofilm antifungals may not permeate
- surgery to remove fungal accumulation—drain abscesses, debride tissue

How do I choose what to use and when?

- know your patient
- know your risks
- know your local organisms
- know your environment
- know your symptoms, especially the subtle ones
- know your drugs and know their interactions
- know your infectious disease consultant and consult appropriately

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