Candida Infection in Surgical Patients

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Candida infections have become a common and serious problem in non-neutropenic general surgical patients. This paper reviews the etiologic factors, pathogenesis of systemic candidiasis, and the more common syndromes of infection in surgical patients. Prophylactic and systemic therapy is detailed. The most significant factor in Candida infections is depression of host immune function. Significant abnormalities of T-cells, monocytes, and neutrophils have been described in patients with systemic Candida infection and in patients shown to be at high risk of such infection (burned, malnourished, or septic patients). Systemic infection is a consequence of high density colonization at 1 or more sites. Topical therapy with nystatin, amphotericin B, or the imidazole derivatives is usually effective in terminating local colonization of skin lesions, the gastrointestinal tract, or the bladder. If local colonization is not controlled, the patient may progress to systemic infection. The primary diagnostic difficulty is determining whether conversion to systemic infection has occurred. Serologic testing and blood culture techniques appear to be of value only late in the course of infection. For this reason, the assessment of culture results from multiple sites appears to be of value. Treatment is begun with systemic amphotericin if the patient is immunodepressed or has > 3 sites positive for Candida. In nonneutropenic patients, relatively short therapy appears effective. Treatment of endocarditis requires several (4–6) weeks of therapy, and current evidence suggests that early surgery with valve replacement may improve survival.

Candida infections pose major diagnostic problems which begin rather than end with isolation of the organism in the laboratory. Most organisms of clinical importance cause well-defined infections. If a known pathogen is cultured from an organ system that is clearly diseased, the presumptive diagnosis is clear and specific antibiotic therapy should be curative. By contrast, Candida can be isolated from skin, urine, sputum, pharynx, vagina, stool, and even blood, and may be regarded as a commensal [1, 2]. Even when isolated from areas of clear-cut infection, i.e., peritonitis fluid or lung biopsy, it is habitually disregarded as a pathogen.

Candida colonization is of little consequence in otherwise healthy persons, and 25–50% of nonhospitalized persons have mucous membrane colonization with Candida [2–5]. Under these circumstances, the organism is present in small numbers and is demonstrable only by culture of the oral cavity, stool, or vagina. The density of Candida may increase temporarily with antibiotic therapy without causing evidence of infection. For this reason, isolation of the organism from mucous membranes is not diagnostic of invasive infection.

Recent developments in blood product therapy, total parenteral nutrition, and antineoplastic therapy, however, have permitted an increased aggressiveness in the operative treatment of patients with serious chronic diseases. Such patients are immunocompromised to a significant extent. Immuno-depressed patients developing Candida infections do not exhibit the classic signs of inflammation either locally or systemically, and specific therapy does not generally result in rapid or clear-cut clinical improvement. The problem facing the physician caring for such a patient found to have Candida in sputum, urine, blood, or wound drainage is to review all of the microbiology and other laboratory
Table 1. Factors influencing the development of Candida infection.

Factors increasing the incidence of Candida colonization
- Antibiotic therapy
- Prolonged hospitalization
- Local radiation therapy
- Tube gastrostomy/jejunostomy sites
- Antacid/cimetidine therapy or gastric achlorhydria

Factors diminishing host resistance to Candida infection in general surgical patients
- Malignancy
- Corticosteroid therapy
- Antineoplastic chemotherapy
- Radiation therapy
- Malnutrition
- Uremia
- ? Advanced age
- Severe burns
- Other serious infections

Data available, and correlate these with the risk to the particular patient of developing a serious mycotic infection. The problem is greatly compounded by the lack of definitive laboratory tests for infection, and by the toxicity of systemic therapy with the agent of choice, amphotericin B. Therefore, the differentiation of invasive infection, as opposed to colonization, is the central theme of the problem [6-8].

Pathogenesis of Candida Infections

Defects in Systemic Host Defense

The appearance of fungal septicemia was initially noted in leukemic and other cancer patients, and led to a conceptual model of infection based on the "compromised host" [9]. This model suggests that acquired immune deficiency states act permissively to allow fungal tissue invasion, fungemia, and metastatic abscess formation. The original definition of compromised host was restricted to patients with advanced neoplasia and leukemia and to transplant recipients. More recent studies have shown that patients suffering from malnutrition, multiple trauma, ongoing sepsis [6], and burns are severely immunodepressed and also at risk of developing systemic fungal infections [10-12].

The specific defects in host resistance responsible for infection are incompletely understood. Abnormalities in immunoglobulin response have been described, but the apparent ability of severely compromised patients to generate opsonic responses has been demonstrated [13]. Most compromised patients suffering from Candida infection are able to generate agglutinating and precipitin antibody responses, and hyperglobulinemia has been reported in 90% of patients with candidiasis [14]. Recently, attention has been focused on monocyte/macrophage cellular elements in experimental model systems [15, 16]. Because of the difficulty in isolating such cellular elements from humans, little work has been done in a clinical setting [17]. Additionally, abnormalities in T-cells and in neutrophils have been identified in patients at risk of fungal infections [10, 18, 19]. The defects noted in these patients involve all effector cells, and it is unlikely that a single causative factor will be identified.

Environmental Factors in Infection

An important element in the appearance of Candida infections has been the increased incidence of colonization of hospitalized patients. A major reason for this has been the increased use of broad spectrum antibiotics as prophylaxis for operations involving transection of the gastrointestinal tract and for cardiovascular surgery [20, 21]. The use of antibiotics in some way allows for the growth of Candida species on mucosal surfaces. The most commonly cited explanation is that the elimination of bacterial colonization increases substrates available for fungal overgrowth [22], although recent evidence suggests that more subtle alterations in the nature of the mucus covering the intestinal epithelium might be involved [14]. Prolonged preoperative hospitalization for time-consuming diagnostic workups also has been correlated with an increased incidence of fungal colonization of the oropharynx [5, 23].

At the same time that Candida colonization of skin and mucosal surfaces has increased, a number of procedures have been adopted that break down the local defenses to invasion. These include use of central venous catheterization for parenteral nutrition, insertion of Swan-Ganz catheters for monitoring, long-term urinary catheterization, and use of indwelling endotracheal tubes for prolonged ventilatory support. Furthermore, these modalities that break down external defenses in colonized patients are seldom necessary in patients without depressed immune responses.

A listing of factors increasing the incidence of colonization and of factors depressing host immune responsiveness is presented in Table 1.

Conversion from High Density Colonization to Systemic Infection

Acute disseminated candidiasis (ADC) is the term used to describe a systemic infection with Candida characterized by repetitively positive blood cul-