Prevalence Of Fungal Infections In Immunosuppressed Patients In Lagos University Teaching Hospital - A Preliminary Report

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ABSTRACT

Introduction: There is paucity of data on prevalence of fungal infections in this environment. A prevalence survey was therefore carried out to ascertain the benefit of prophylactic and therapeutic antifungal therapy in immuno suppressed patients.

Methodology: Immunosuppressed patients who had systemic infections were selected based on pre-designed clinical and laboratory criteria. Specimens which included blood, sputum, urine and throat swab were aseptically collected from them and examined by microscopy and culture.

Result: Candida spp was cultured from seven of the 100 patients but only five were confirmed cases of Candidiasis. Four of the isolates were Candida albicans. Of the five cases of candidiasis, two were patients with Diabetes mellitus. One had AIDS, one had a malignancy and the remaining one was a patient who had septicaemia and had been on antibiotics for a long time. The five cases of candidiasis were two urinary tract infections, two blood stream infections and a case of pharyngitis. No other fungus apart from Candida was cultured.

Conclusion: The low prevalence of fungal infection obtained in this study may actually be an under estimate. Isolates were from AIDS and Diabetes mellitus patients. There is need for a future survey of the susceptible population.

INTRODUCTION

The frequency of serious fungal infection is increasing in high-risk patients1-5. These infections range from non-life-threatening mucocutaneous illness to invasive processes that may involve virtually any organ.

Although infection due to candida species are the most common fungal infections, immuno suppressed patients are also at significant risk from invasive aspergillosis, and rare or refractory fungal pathogens like Fusarium spp, Trichosporon spp Paecilomyces lilacinus, Pseudallescheria boydii and Scedosporium spp are becoming increasingly important because they cause life-threatening infections in the severely immunocompromised 6-8.

The broad range of infections caused by these pathogens requires an equally broad range of diagnostic strategies. The traditional microbiological culturing techniques are still useful and new diagnostic techniques are available though these remain limited by lack of sensitivity and specificity. New diagnostic kits, which show promise are also being investigated 9,10.

Treatment options are currently being investigated and practice guidelines for treatment have been developed 11,12. New antifungal agents, which are effective against a wide range of rare or refractory fungal pathogens, are now available. The potential of T-cell vaccination against invasive pulmonary aspergillosis is currently under investigation 13.

Over the years, invasive fungal infections have been difficult to treat and late diagnosis as well as delayed treatment further complicates their management. Emphasis is laid therefore in being on targeted antifungal prophylaxis strategies which can improve survival rates. Antifungals like fluconazole and flucytosine have been investigated and found useful for prophylaxis for Candidiasis in selected patients 14-16. A recently published study, which suggested that flucytosine prophylaxis improves survival rates from Candidiasis in allogeneic but not autologous bone marrow transplant recipients probably underlines the fact that knowledge of epidemiology, pathogenesis and specific host risks might be the key to implementing a successful antifungal prophylaxis policy 17. This study was done to determine the prevalence of fungal infections in the Lagos University Teaching Hospital. Knowledge of epidemiological and risk factors associated with such infections is desirable but could not be done due to peculiar problems of this initial study.

METHODOLOGY

Patients: All immuno suppressed patients admitted into Lagos University Teaching Hospital wards between March and September 2001 that fitted the designed criteria below were admitted into the study. Their demographic data and history of clinical illness were recorded. Findings on full clinical examination were also recorded.

All relevant specimens were collected aseptically from immuno suppressed patients diagnosed clinically to have systemic infections and these were immediately transported to the LUTH Microbiology Laboratory where all procedures were carried out.

Smears were prepared from various specimens and stained by Gram's method for examination for yeast cells by microscopy. CSF samples were examined with India ink for Cryptococcus neoformans. Wet preparations with 10% KOH and lactophenol blue were examined microscopically for yeasts and hyphae. Each specimen was inoculated on
Sabouraud dextrose agar and also on other culture media to rule out bacterial infection.

All isolates were identified by standard laboratory methods.

Inclusion criteria

A. PATIENTS THAT HAVE ONE OR MULTIPLE OF THESE:

1. Disturbance of the epithelial barrier caused by:
   - Broad-spectrum or multiple antibiotic therapy
   - Indwelling catheters
   - Perineal dialysis
   - Burns, ulcers, major trauma
   - Radiotherapy

2. Any of the following:
   - Radiotherapy
   - Chemotherapy
   - Aplastic anaemia
   - Chronic granulomatous disease
   - Diabetes mellitus
   - and so may have defect or dysfunction of neutrophils, mononuclear phagocytes and other granulocytes

3. Any of the following:
   - AIDS
   - Hodgkin’s disease
   - Transplantation
   - Chemotherapy
   - Radiotherapy
   - Leukemia
   - Aplastic anaemia
   - and so may have defect or dysfunction of T-lymphocyte mediated immunity

B. PLUS AT LEAST THREE CRITERIA OF SYSTEMIC INFLAMMATORY RESPONSE (SIRS) OR SEPSIS-INDUCED HYPTENSION AS LISTED BELOW:

   a. Body temperature > 39°C or < 36°C
   b. Heart rate > 90 beats per minutes
   c. Tachypnoea, manifested by a respiratory rabe > 20 breaths per minute, or hyperventilation, as indicated by a Pa Co2 < 32 mmHg
   d. Alteration in the white blood cell count, such as:
      - A count > 12,000/mm3
      - A count < 4,000/mm3
      - Presence of > 10% immature neutrophils (bands)
   e. Systolic blood pressure < 90 mmHg or a reduction in the systolic blood pressure of > 40 mmHg in the absence of other causes of hypotension

Exclusion Criteria

Patients already on prophylactic antifungal treatment
Superficial dermatophytoes not linked to immunosuppression

TO CONFIRM INFECTION RATHER THAN COLONIZATION, THE FOLLOWING CRITERIA WERE USED:

<table>
<thead>
<tr>
<th>Specimen</th>
<th>Total No of patients</th>
<th>No or percentage of specimens with positive culture</th>
<th>No of Negative cultures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Blood</td>
<td>65</td>
<td>1</td>
<td>30</td>
</tr>
<tr>
<td>Urine</td>
<td>17</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>Sputum</td>
<td>4</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Throat swab</td>
<td>8</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>C S F</td>
<td>6</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Total</td>
<td>100</td>
<td>7</td>
<td>33</td>
</tr>
</tbody>
</table>

Table

Culture results of various specimens obtained from immunosuppressed patients
DISCUSSION

Generally, improved survival of the immunocompromised has increased the frequency of opportunistic fungal infections. Candida is now the fourth commonest organism isolated from blood stream infections in the United States.2,3

In this study, the low prevalence rate (5%) is probably underestimated, because the major conditions associated with high incidence of systemic fungal infections were poorly represented. In the hospital, only two cases of Leukaemia and a case of Hodgkin’s lymphoma, fitted our criteria. These cancers among others have been identified as the underlying diseases in systemic fungal infections.4-6 Patients who have cancer especially acute Leukaemia may, as a result of the disease process or chemotherapy, have granulocytopenia, which makes them vulnerable to various infections including fungal infection.5-8 Even when they do not have obvious fungal infections, they have prominent colonization rates have been directly linked with high mortality rates. Further, a causal relationship has been established between colonization of multiple sites and adverse impact on short-term mortality in patients with hematological cancers.7

Risk factors for Candidaemia include Diabetes mellitus, hyperalimentation, surgery, prolonged stay in the ICU and colonisation of multiple sterile sites.8-10 Diabetes mellitus appeared to be the predisposing factor for the bloodstream infection in this study. Candidaemia, which may be the cause or result of other systemic infections, usually presents a management problem and is associated with significant morbidity and mortality but empiric antifungal therapy reduces the frequency of development of clinically invasive fungal infection in high-risk populations and is recommended.9

The two patients with candiduria had Diabetes mellitus, a documented risk factor for development of Candida UTI. Although, in most patients, isolation of candida from the urine represents only colonization and a benign event; it may be the source of subsequent dissemination or a marker of acute hematogenous dissemination especially in neutropenic patients.10-12 Diabetes mellitus is also a risk factor for other invasive candida infections, but only four fitted our criteria in this study. It may however be possible to assess the value of antifungal prophylaxis or therapy in a larger study.

C. albicans was isolated from the sputum samples of two adult AIDS cases in this study. It was not possible to determine their significance as C. albicans may be found as a flora in the mouth, which contaminates sputum. The patients had been on treatment for pulmonary tuberculosis and would need a histological confirmation of co-existing candida pneumonia.13 However, candida pneumonia may occur following aspiration of candida laden oropharyngeal material. More commonly though, it occurs as a result of hematogenous spread especially in patients with malignancy and AIDS in which case it is associated with a high mortality.14-16 It is therefore desirable to identify the risk factors for development of candida pneumonia in Nigeria, which would help in identifying patients that will benefit from prophylaxis and prompt therapy.

Only 8 cases of acquired immunodeficiency syndrome fitted the criteria for inclusion in the study, and though Candida was isolated from three of them, infection was confirmed in only one. Candidiasis is very common in patients with Human immunodeficiency Virus and oropharyngeal candidiasis is actually an AIDS defining illness. Antimycotic prophylaxis for Candida and invasive Aspergillosis infections is often necessary in those with low CD4 counts.2,10

The low number of AIDS cases in this study is probably due to the fact that many patients are lost to follow up after a few initial visits despite the fact that about five new cases are diagnosed every week. However, with the advent of government sponsored awareness campaigns and subsidized antiretroviral therapy, this picture is changing as more patients come for follow up.

Today, the routine laboratory diagnosis of fungal infections rests mainly on microscopy and culture, which were employed in this study. Out of the 100 specimens examined, bacteria were isolated in 33 while 7 grew Candida. As many as 60 cultures were sterile. This may be due to the high level of antibiotic abuse in this environment.11 Fungal culture however has low sensitivity and is accepted as inadequate for diagnosis because it has been shown that up to 50% of candidaemia may not be detected at autopsy.12 In the last twenty years however, there have been some advances in the diagnosis of fungal infections. The lysis centrifugation and Bactec systems have markedly improved the sensitivity of fungal blood cultures.11-13 Diagnostic kits based on detection of substances released by fungi also allow rapid results to be obtained although their precise role in clinical management remains to be defined.14 Commercially available yeast identification systems are also available for rapid species diagnosis. With optimal techniques it may actually be possible to determine the realistic prevalence rates of fungal infections in AIDS and Diabetic patients who appear to be the patient populations likely to benefit from possible prophylaxis and therapy of fungal infections in our environment.

ACKNOWLEDGEMENT

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REFERENCES

6. Munoz P. New antifungal agents active against rare


