Introduction

The area of intensive care, skin substitution and fluid balance has shown great progress. Simultaneously, the occurrence of nosocomial fungal infections has increased noticeably over the last decade as a main, and often absolute, complication in burn injury, representing substantial morbidity, mortality and healthcare costs. Difficulty of diagnosis is the principal reason for their severity, leading to late treatment and absence of consensus procedures for prophylaxis and empirical therapy. Mainly wound form is what defines burn wound infections, while fungal infections are extremely difficult to diagnose uniquely upon clinical indication. We performed this study to define frequency and predictive factors in fungal infections,
and to describe the epidemiology of nosocomial fungal infections in the National Center for Burns and Plastic Surgery in Casablanca, Morocco.

Materials and methods

From July 2011 to December 2014, 180 patients out of a total of 1812 people admitted to the National Center for Burns and Plastic Surgery (NCB) in Casablanca, Morocco had cultures positive for a fungal species.

Admission, demographic data, medical records and percentage of total body surface area burned (% TBSA) were collected. Inhalation injury was confirmed in half of the cases by bronchoscopy. Burn injuries were managed within NCB by applying silver sulfadiazine cream with a wet wound dressing. Surgical excision was usually performed as soon as possible. Empirical antibiotic therapy for burn patients consisted of cephetazidim and amkacin for minor sepsis occurring within 1 week of admission, and vancomycin and imipenem for severe sepsis.

Microbiological surveillance screening was routinely carried out, and swabs were taken daily. Each positive culture was described microbiologically, specifying the number, site and organism. We also provided supplementary information on morbidity and mortality. Criteria for nosocomial fungal infections were those of the Center for Disease Control in Atlanta (1988, revised 1992 and 2004). We inserted each patient’s data in an Excel™ spreadsheet, processed subsequently by SPSS™ program. Approval was obtained from our hospital’s ethics committee.

Results

Patient demographics and characteristics

During the study period, 1812 people were admitted to the National Center for Burns. Fungi were isolated at wound sites in 180 patients. Mean age of patients was 24.5 +/- 27.3 years, and 63% were female. All patients had risk factors. 85% of the cases were on systemic antibiotics, and 90% received parenteral nutrition; 6% were diabetics. The majority had multiple risk factors (Table I).

Mean % TBSA was 30.7 +/- 23.4%, and % full-thickness surface area (FTSA) was 21.7 +/- 20.1%. Injury due to flame was most common (82%), followed by scald (10%), contact (4%), electrical (3%) and chemical (1%). A third of the study population suffered from inhalation injury (n=60; 30%). Burns were located on the hands (23% of patients), lower limb (20%), upper limb (8%), neck and head (25%), trunk (21%) and perineum (3%).

Descriptive analysis of mycological aspects

The frequency of fungal species in culture results is listed in Table II. The Candida species was the most frequently isolated pathogen from any site (n=164; 91.1%) (Fig. 1). 89 patients were simultaneously overwhelmed by two different Candida species, and 45 patients (27.6%) had fungal cultures positive for more than one type of fungal organism. Seven patients had both Candida and Aspergillus. However, no isolation of Mucor or other more resilient fungi was recorded.

Most of the fungal cultures were obtained from the burn wound (n=125, 69.4%), followed by sputum (n=76, 42.2%), then urine (n=41, 22.7%). Central venous catheter (CVC) site colonization occurred in 26 patients (14.4%). Patients with bloodstream infections who had a CVC were over three times

### Table I - Patient characteristics by fungi positive/complete group

<table>
<thead>
<tr>
<th></th>
<th>Fungi group (N=180)</th>
<th>Complete group (N=1632)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age (yrs)</td>
<td>24.3 +/- 21.5</td>
<td>26 +/- 21.7</td>
</tr>
<tr>
<td>Mean TBSA (%)</td>
<td>30.7% +/- 23.4</td>
<td>25.8% +/- 17.2</td>
</tr>
<tr>
<td>Etiology</td>
<td></td>
<td></td>
</tr>
<tr>
<td>flame</td>
<td>82%</td>
<td>73%</td>
</tr>
<tr>
<td>scald</td>
<td>10%</td>
<td>19%</td>
</tr>
<tr>
<td>Inhalation injury (%)</td>
<td>30%</td>
<td>20.8%</td>
</tr>
<tr>
<td>Risk factors</td>
<td></td>
<td></td>
</tr>
<tr>
<td>diabetes (%)</td>
<td>6%</td>
<td>2.5%</td>
</tr>
<tr>
<td>nutrition(%)</td>
<td>90%</td>
<td>75%</td>
</tr>
<tr>
<td>artificial</td>
<td>22.3%</td>
<td>13%</td>
</tr>
<tr>
<td>ventilation (%)</td>
<td>92%</td>
<td>62.4%</td>
</tr>
<tr>
<td>central venous</td>
<td></td>
<td></td>
</tr>
<tr>
<td>access (%)</td>
<td>85%</td>
<td>41%</td>
</tr>
<tr>
<td>Mortality</td>
<td>21.1%</td>
<td>18.2%</td>
</tr>
</tbody>
</table>

### Table II - Frequency of fungal organisms isolated

<table>
<thead>
<tr>
<th>Fungi species</th>
<th>Number (n)</th>
<th>Rate (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Candida spp</td>
<td>164</td>
<td>91.1%</td>
</tr>
<tr>
<td>Aspergillus spp</td>
<td>7</td>
<td>3.9%</td>
</tr>
<tr>
<td>Unspecified yeast</td>
<td>9</td>
<td>5%</td>
</tr>
</tbody>
</table>

Fig. 1 - Percentage of Candida spp isolated.

Fig. 2 - Incidence of fungal organisms isolated from any site.
more likely to have a fungal pathogen isolated (11.3%) than patients with bloodstream infections who did not have a central venous catheter (3.1%) (Fig. 2). Sixty-eight patients (37.7%) had positive cultures from more than one site. Patients with fungemia had a longer hospital stay, 212.4 days (+/-59.2). Patients with fungal cultures positive for yeast stayed in hospital for only 124.3 days, less than patients who had Aspergillus cultures only. The average time from burn to fungemia was 39 days: 29 days from burn to colonization and 13 days from colonization to fungemia. Not all fungi were vulnerable to amphotericin B, the conventionally used antifungal agent. Antifungal therapy was administered, once infection was confirmed, to 109 patients (60.5%), mostly with enteral and parenteral antifungal agents such as fluconazole. Voriconazole was indicated for the treatment of Aspergillus fungal infection in particular.

**Outcomes**

Mortality rate in the study population due to fungal infections was 21.1% (n=38). Statistically, Aspergillus spp were connected with mortality (3.2%) and morbidity. Fungal pneumonias were seen in 5 patients, and another 5 patients had systemic bloodstream sepsis due to highly immunocompromised state.

In our study, patients with fungal cultures positive for Candida spp stayed in hospital for only 34.3 days, less than patients who had Aspergillus spp (67.8 days). Time from drawing the first positive blood culture to commencement of appropriate treatment was 5.2 days. Treatment for the patients who died of candidaemia lasted 4.5 days (range 3–6 days) while those who survived were treated for 1.9 days. The reason for the delay in treatment was a delay in receiving the results of microbiological tests.

**Discussion**

Although burn patients are at higher risk of infectious complications, improvements in managing them have extended survival in extremely burned patients. Fifty to 75% of nosocomial fungal infections are caused by the candida genus of yeasts. The fatality rate for aspergillosis is also disturbing, at 38%. These are the most common infections in the burns unit. The causal factors for the presence of fungi and mortality included % TBSA burn injury and length of stay. Percentage of surface area (TBSA) burned defines the frequency of skin infection occurrence, with a clear rise in infection rate from 30% of TBSA. Bowser-Wallace et al. recorded 10% of invasive skin infection in children burned on less than 30% surface area: frequency of skin infection was 40% if the body surface area burned was between 30 and 60%, and 80% in children with a TBSA burned of 60% or more. In our study and in several series, an extensive ICU stay was especially connected with an amplified risk of nosocomial infection. A more recent publication by Murray et al. pointed out that expansion of fungal infection and sepsis was linked to hospital length of stay. Several studies on growth properties of fungi in parenteral nutrition solutions have recognized that these solutions differently support the evolution of several Candida species.

Exposure to broad-spectrum antibiotics, either early or accompanying, is a risk factor for infection. The risk of fungal complication increases with broader spectrum and prolonged antibiotic therapy. In the study by Wey and al., the number of different antibiotics was the most significant prognostic risk factor for the expansion of candidiasis: 94% of patients who developed candidiasis had been previously exposed to antibiotics, and 62% had received more than four different agents before developing candidiasis, as observed in the recent study.

Skin colonizers, particularly C. albicans, can also have direct access to the bloodstream during extended central catheterization used for parenteral nutrition, which most likely explains the pathogenesis of catheter-related endemic bloodstream infection. This analysis has identified trends toward increased use of central catheterization and other interventions that appear to increase the risk of fungemia. In addition to these trends, increased survival and use of broad-spectrum antimicrobial therapy (imipenem, vancomycin, and amikacin) in hospitalized patients were conducive to the development of fungi as nosocomial pathogens. In several studies, colonization by Candida yeasts was identified as an independent risk factor for the acquisition of candidemia. Moreover, the survey proved that urinary candiduria added extra potential risk factors in other studies.

Indications for prophylaxis and early empirical therapy in burns are unclear despite an increasing range of effective antifungal treatments. Our unit has no protocol for prophylactic antifungals. Pelz et al. and Garbino et al. selected risk populations where antifungal prophylaxis would be helpful. Still, their studies lacked statistical significance due to a smaller patient number, and they did not achieve any particular results regarding complications in the long term, mortality and cost. While candidaemia in burns patients has a high overall mortality rate, most of these deaths are not caused by candidaemia. Vinsonneau et al. advocated that candidaemia is linked to increased length of stay and mechanical ventilation, but does not affect mortality directly. Late diagnosis might be the reason behind this increased mortality (18.3%) and difficulty in treating fungemia. This study has revealed that the National Center for Burns frequently encounters severe burns with high TBSA (32%). Yet other studies in the literature include much higher mortality rates of up to 75%.

**Conclusion**

According to our findings, early or accompanying exposure to broad-spectrum antibiotics is a definite risk factor for infection. The more the spectrum was expanded and antibiotic therapy prolonged, the greater the risk of fungal complication. The most common pathogen in our burn unit was Candida. Fluconazole and voriconazole remain the most effective antifungal agents against Candida spp and Aspergillus spp. These findings are essential for warranting an accurate antifungal therapy against microorganisms in burn patients.

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**BIBLIOGRAPHY**


Conflict of Interest: None