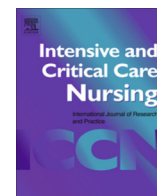




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Candida tropicalis burn wound sepsis: A series of histopathology-confirmed cases

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ABSTRACT

Fungal infection in severely burned patients is a serious problem due to various factors, such as the extensive application of antibiotics. In this study, we report on the course of severely burned patients with *Candida tropicalis* burn wound sepsis. Five such cases were reviewed. The patients were treated with itraconazole intravenously and simultaneous antibiotics to prevent bacterial infections. In addition, dermabrasion was used to excise the eschar and the wound surface was covered immediately with dermatoplasty. Meanwhile, the skin necrosis related to the fungal infection was removed. The wound surfaces of all five patients were healed well and the parameters of laboratory examination went back to normal. We assume that prompt diagnosis and timely treatment including extensive debridement of necrosis, antifungal drugs, and antibiotics were the key points leading to favourable outcome.

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Implications for Clinical Practice

- *Candida* burn wound sepsis is a relatively rare but potentially life-threatening complication of severe burn injury.
- Based on our limited case series we assume that early diagnosis, excision of the necrosis, and antifungal therapy are crucial to optimise the chances for survival.

Introduction

Fungal infection in severely burned patients is a serious problem partly related to the excessive use of antibiotics (Struck and Gille, 2013). Mortality among burn patients with fungal infections is high (Ballard et al., 2008; Horvath et al., 2007). Therapeutic approaches to burn wounds has been changed dramatically in the past decades and the prognosis of these patients is improved, but nevertheless, there are still many drawbacks in the current treatment (Belgian Outcome in Burn Injury Study, 2009; Brusselaers et al., 2010a; Sarabahi et al., 2012). In order to counter the deleterious effect of *Candida* infections, four antifungal-based

therapeutic options have been described: prophylaxis, pre-emptive, empiric and definite antifungal therapy (Blot and Vandewoude, 2004). Prophylaxis is a preventive approach for the patients based on primary diagnosis instead of individual risk factors. Pre-emptive antifungal therapy is justified in the presence of *Candida* colonisation and multiple risk factors for invasive candidiasis. Generally, at least two major or three minor risk factors should be present when applying pre-emptive therapy. Major risk factors include extensive burns covering more than 50% of the total body surface area, immunosuppression, neutropenia, prolonged antibacterial therapy, intestinal perforation, diarrhoea or ileus, major abdominal surgery, total parenteral nutrition and renal replacement therapy. Minor risk factors include length of intensive care unit (ICU) stay of more than 10 days, renal insufficiency, older age (or neonates), multilumen central venous catheters, the presence of a urinary bladder catheter, diabetes mellitus and candiduria ($>10^5$ cfu/mL). In clinical practice, several of these risk factors are often present in severely burned patients thereby justifying either pre-emptive or empiric antifungal therapy in case of an

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Table 1
Characteristics of burn patients with *Candida tropicalis* burn wound sepsis.

	Year of admission	Gender	Age (years)	Cause of burn	%TBSA	Length of burn unit stay before onset of <i>Candida</i> sepsis (days)	Length of burn unit stay (days)	Survival
Case 1	2012	Male	36	Flame	95%	9	60	Yes
Case 2	2013	Male	23	Electric	50%	7	58	Yes
Case 3	2013	Male	46	Flame	58%	14	55	Yes
Case 4	2014	Female	38	Flame	55%	24	50	Yes
Case 5	2014	Male	40	Flame	62%	11	55	Yes

TBSA, total burned surface area

overt risk profile. In this paper we reported on the course of five severely burned patients whose burn unit stay was complicated by *Candida tropicalis* wound sepsis.

Case series

This study was approved by the local ethics committee at Jinan Central Hospital Affiliated to Shandong University. The ethics permission (No. 2017-024-01) was obtained from the Institutional Review Board (IRB) of Jinan Central Hospital Affiliated to Shandong University. Five cases of severely burned patients (4 males, 1 female) were reviewed in this study. Basic characteristics of the patients are summarised in Table 1. The patients were admitted to the Department of Burn and Plastic Surgery, Jinan Central Hospital Affiliated to Shandong University from 2012 to 2014. The age of the patients ranged from 23 to 46 years. Four had flame burns and one suffered from an electrical burn injury. The total burn surface area (TBSA) ranged 50%–95% with an average of 64%. Third degree burn area was 23%–60% with an average of 37%. The burn wound infection was suspected based on clinical observation of the affected skin area and an increased systemic inflammatory response leading to the diagnosis of burn wound sepsis.

Treatments and outcomes

Initial burn wound treatments: meropenem (Dainippon Sumitomo Pharm Co., LTD, Oita Plant, Japan) (0.5 g/q12h) was used as a preventive anti-infective therapy. Wound surfaces were covered by sulfadiazine silver (Shandong Health Pharmaceutical Co., LTD, China) and oiled gauzes (Baotou Huahai Chemical Group Co., LTD, China) after the debridement. At 48–72 hours after injury, operations including tangential excision, autologous small autografts transplantation, and biological dressing A (Weihai Walt Health Products Co., LTD, China) coverage were completed successfully under general anaesthesia (Brusselaers et al., 2010b). Conventional post-operational measurements including restrictive antimicrobial therapy and continue the nutritional support were used to improve general conditions. The patients were cared with contact isolation precautions (Raes et al., 2017).

Fungal complications: In all cases the initial burn injury management led to hemodynamic stabilisation and decreasing of inflammatory parameters. Body temperature ranged 38.0 °C to 38.7 °C but this was interpreted as a post-burn or post-surgery inflammatory response.

On an average of 13 days post-burn (range 7–24 days), the patients' condition worsened with core temperatures of 39.0–40.0 °C. Upon physical examination, some visible mildew spots were found on the wound surface. Three patients showed obvious caseous necrosis, remittent fever and substantial mental disorders including exciting, depression, dysphoria and confusion. Two patients had diarrhoea and the stool microscopic examination showed a great number of mould spores. The results of fungal culture showed the growth of *Candida tropicalis* in all of the five

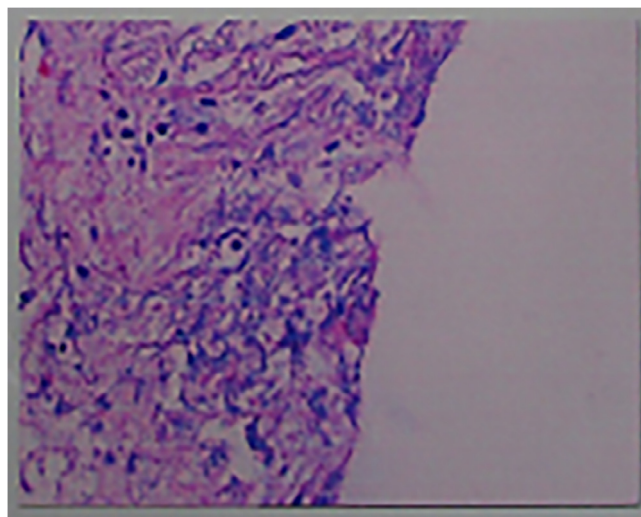


Fig. 1. Histopathologic examination report of case 1. The results of fungal culture showed the growth of *Candida tropicalis*, and hyphae and spores were found after histopathologic examination of the focal necrosis.

patients, and hyphae and spores were found after histopathologic examination of the focal necrosis (Fig. 1).

Debridements of the wound surface and dressings change were then performed all over the body. Treatment was administered as follows. 1) Itraconazole (Janssen Pharmaceutical LTD, Belgium) was given intravenously and continuously with a dosage of 0.25 g/12 hours. 2) Empiric antibiotics (ticarcillin disodium and clavulanate potassium, Shandong Anti-Lu Pharmaceutical Co., LTD, China) were used in patients with associated bacterial infections. 3) The fungal infection focal necrosis was removed promptly. In addition, dermabrasion was employed to excise the eschar and dermatoplasty was used to cover the wound surface.

After 3–5 days administration of itraconazole, the symptoms of patients were obviously improved. Administration of itraconazole was stopped 7–12 days later when the results of laboratory examination became negative. Only nutritional support therapy and regular dressings change were performed consecutively. The dressing change was performed once every other day. In case of excessive exudate dressing changes were performed daily. After 50–60 days, the vast majority of wound healed and all of the five patients were dismissed from the hospital (Table 2). A typical wound case is shown in Fig. 2.

Discussion

Patients with extensive burns have a high risk of *Candida* sepsis because of the destroyed defence barrier of the skin and mucous membrane, malnutrition caused by hypermetabolism, and decreased immunity (Murray et al., 2008). In addition, the broad-spectrum antibiotic therapy adds another risk factor for concomitant fungal infection (Sarabahi et al., 2012). While multiple risk

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