Cutaneous geotrichosis due to *Geotrichum candidum* in a burn patient

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INTRODUCTION

- The genus *Geotrichum* is composed of 22 species [1, 2], the best known of which is ***Geotrichum candidum* (teleomorph: *Galactomyces candidus*)**. It is a ubiquitous, dimorphic, ascomycetous yeast of the *Saccharomycetes* class primarily seen in the agricultural and cheesemaking industries [3].
- On Sabouraud agar, it appears as rapidly growing, white to cream, hairy colonies (**Figure 1**) [1, 5]. It grows optimally at 25°C and appears pink on chromogenic culture media [6].
- Forms hyaline, septate true hyphae with irregular branching which segment to form arthroconidia of variable lengths (4-10 µm) (**Figure 2**) [4-5, 7]. Blastoconidia are absent.
- Assimilates glucose, galactose and xylose but not lactose, maltose or sucrose [8].
- There have been 16 previous case reports of *G. candidum* infection in humans.
- Most of these cases have involved immunocompromised hosts. Disseminated cases, usually with fungemia and localized disease involving the skin, brain, eye, oral mucosa, GI tract, lung and kidney have been reported [11-13].
- Trauma may be the only predisposing factor in an immunocompetent patient [14].
- Prompt and accurate diagnosis is the greatest challenge in cases of suspected invasive fungal infection.
- Histopathologic or microscopic examination may be indeterminate since the hyphae of young *G. candidum* may be indistinguishable from other fungi including *Candida*, *Trichosporon*, and *Aspergillus* spp. (**Table 1**) [6, 10-11].
- **Here we report the first case, to our knowledge, of cutaneous geotrichosis due to *G. candidum* in a patient with severe thermal burns.**

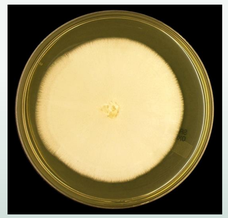

Figure 1: G. candidum grown on Sabouraud agar at 30°C for five days

Table 1: Comparison of the morphology, biochemical characteristics, diagnostic testing and treatment of *G. candidum*, *Candida*, *Trichosporon* and *Aspergillus* spp.

		G. candidum	*Candida* spp.	*Trichosporon* spp.	*Aspergillus* spp.
Colony appearance (Sabouraud agar)		White to cream, hairy, rapid growth	White to cream, smooth, rapid growth	White to cream, farinose, often with cerebriform features or radial furrows	Velvety, powdery or wooly. Pigment varies by species. *A. fumigatus*: white to blue-green, *A. niger*: black, *A. flavus*: yellow to green, *A. terreus*: brown.
Staining	Hematoxylin-eosin	Stains poorly	Stains well	Stains well	Stains well
	Methenamine-silver	Deep staining of hyphal wall, empty-appearing core	Uniform hyphal staining	Uniform hyphal staining	Uniform hyphal staining
Morphology		Hyaline, septate true hyphae with irregular branching, which segment to form arthroconidia of variable lengths (4-10 µm)	Blastoconidia, pseudohyphae or septate true hyphae	Septate true hyphae, pseudohyphae, arthroconidia and blastoconidia	Uniform septate hyphae, dichotomous acute angle branching (45°), terminal conidiophores
Arthronidia		+	–	+	Conidiophores
Blastoconidia		–	+	+	
Carbohydrate assimilation		Glucose, galactose, xylose. Not lactose, maltose or sucrose.	Variable. All assimilate glucose. Most assimilate maltose, sucrose, galactose and trehalose.	Glucose, galactose, sucrose, maltose, lactose	Glucose, sucrose, maltose, fructose, lactose (not *A. niger*)
Urease		–	–	+	+
Diagnostic testing		Insufficient evidence	β-D-glucan T2Candida panel	Dual *Cryptococcus* antigen and galactomannan positivity is suggestive, sensitivity unknown	Galactomannan, PCR
Treatment		Amphotericin B ± flucytosine or voriconazole alone	Echinocandin or triazole	Superficial: shaving + topical triazole or selenium sulfide Invasive: voriconazole ± amphotericin B	Amphotericin B, voriconazole or isavuconazole

CASE

Patient:

- 27-year-old woman with cognitive impairment due to cerebral palsy; no other past medical history
- Brought to the ED approximately 16 hours after sustaining flame burns while reaching over a stove
- 28% total body surface area (TBSA) third-degree burns to the right external ear, neck, anterior and lateral trunk, and bilateral upper arms; 2% TBSA second-degree burn to left anterior thigh

Vitals on presentation: Temp 37.1°C, BP 124/86 mmHg, HR 151 BPM, RR 14, SpO_2 96% on room air

Day	Event	Cultures	Antimicrobials
1	Debridement & grafting		Vancomycin, cefepime, fluconazole
9	Debridement & grafting	Tissue (R face): MRSA, *Candida orthopsilosis*, *Acinetobacter baumannii* (R gentamicin, ertapenem)	
12	SIRS 4/4 Pneumonia	Respiratory: *A. baumannii* (R cefepime, AMGs; S amp/sulbactam, carbapenems)	
14		Blood: *C. orthopsilosis* (SDD FCZ, VCZ; S MFG, AMB)	Cefepime → amp/sulbactam Fluconazole → micafungin
15	Debridement & grafting	Tissue (R flank): *C. orthopsilosis*, ***Geotrichum candidum***	
18	SIRS 4/4 Pneumonia	Respiratory: MRSA, *E. coli* (R amp/sulbactam, cefepime)	Amp/sulbactam → meropenem Micafungin → voriconazole
26	Most grafts fail (**Figure 3**), Remains septic		Voriconazole → liposomal amphotericin B
29	No new CVC site available	Blood: *C. orthopsilosis*	Meropenem → amp/sulbactam
30	*G. candidum* susceptibilities result (**Table 2**)		Amphotericin B (high MIC of 2) → voriconazole + micafungin
33	Febrile, New CVC placed	Blood (from new line): MRSA	Amp/sulbactam → ceftaroline
36	Grafts healing well. CVC replaced w/ midline. Course complicated by CAUTI and another line-related episode of MRSA bacteremia.		
64	Completed 6 weeks of antifungals while inpatient. Discharged to rehabilitation facility.		

Figure 2: Chains of arthroconidia and separate arthroconidia (1000x + 10% digital magnification). Lactophenol cotton blue (LPCB) wet mount.

DISCUSSION

Burn Patients:

- Can be considered immunocompromised due to extensive skin disruption.
- Measures such as heat and moisturized dressings may promote fungal growth [15].
- Broad spectrum antibiotics also facilitate fungal overgrowth [12].
- Pathogens can be introduced nosocomially or by pre-hospital water exposure [15].
- TBSA burns ≥40%, inhalational injury, presence of CVCs and advanced age are associated with risk of fungal infection.

Figure 2: Failed skin graft on hospital day 26.

***Geotrichum candidum*:**

- Variable susceptibility patterns mean susceptibility testing is essential, though there are no CLSI established breakpoints [10].
- Voriconazole consistently has the lowest MICs among the azoles [5, 8, 13].
- Generally susceptible to amphotericin B, itraconazole, posaconazole, and flucytosine. Elevated fluconazole MICs [8, 16]. Reported flucytosine resistance [11] and breakthrough disease while on posaconazole prophylaxis [16].
- Variable echinocandin MICs [13, 16-17]. Not recommended despite possible *in vitro* activity.
- Prolonged PO nystatin has been successful in superficial oral mucosal infection.
- Fungemia has responded to CVC removal without antifungal therapy [12].
- Currently recommended first line treatment: **amphotericin B ± flucytosine or voriconazole alone** [9, 16].

Antifungal medication	MIC in µg/mL
Fluconazole	32
Itraconazole	1.0
Posaconazole	1.0
Voriconazole	0.5
Isavuconazole	0.125
Amphotericin B	2.0
Flucytosine	0.25
Micafungin	0.5
Caspofungin	1.0
Anidulafungin	2.0

Table 2: Antifungal susceptibilities of the patient's *G. candidum* isolate

Our Patient:

- Two fungi (*C. orthopsilosis* and *G. candidum*) with different susceptibility profiles.
- Amphotericin B was used to treat both until *G. candidum* susceptibilities resulted, showing a high MIC for this agent (**Table 2**).
- Liposomal amphotericin B may achieve sufficient tissue concentrations to overcome relative *in vitro* resistance [17]. Extremely high MFCs highlight the importance of host defenses.
- Voriconazole and micafungin were combined for potential additive/synergistic activity of the echinocandin against *G. candidum*.
- VCZ could have been used alone (*C. orthopsilosis* SDD). Isavuconazole would also be appropriate for the *G. candidum* isolate but is not approved for candidemia [18].
- The patient's skin grafts healed well on this regimen. She received 6 weeks of antifungals.

***Geotrichum* spp. are rare emerging fungi which, despite adequate antifungal therapy, are associated with a mortality rate approaching 50% [16]. Clinicians should be aware of geotrichosis as a clinical entity in burn patients as well as the immunocompromised. Antifungal resistance and breakthrough disease are a concern due to the increasing number of at-risk patients and use of routine mold prophylaxis.**

Microbiological Images courtesy of Yuri Amatnieks. Fun With Microbiology (What's Buggin' You?). http://bit.ly/2goAR4a

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