Prognostic factors in 264 adults with invasive *Scedosporium* and *Lomentospora* infections

Data from the literature and FungiScope®

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Background

A growing number of non-*Aspergillus* mold infections, such as invasive *Scedosporium* and *Lomentospora* infections, are of particular concern because of intrinsic resistance of such pathogens and thus limited treatment options [1].

Medically most relevant pathogens causing scedosporiosis are species of the genus *Scedosporium* (e.g. *S. apiospermum*, *S. boydii*) and *Lomentospora prolificans* (formerly *Scedosporium prolificans*). *Scedosporium* spp. are often resistant to amphotericin B, but susceptible to posaconazole and voriconazole, whereas *L. prolificans* is resistant to all available antifungals [2-5].

Immunocompromised patients are at highest risk for these infections. Primarily those with hematological malignancy with prolonged profound neutropenia, hematopoietic stem cell or solid organ recipients, and patients with inherited or acquired immunodeficiency. Immunocompetent patients are at risk through direct inoculation of the pathogen after traumatic injury, major surgery or aspiration of contaminated water associated with near drowning [6, 7]. Mortality rates of up to 90% despite best available antifungal therapy underline the unmet medical need of an effective treatment option improving clinical management [7].

Methods and Objective

Cases of proven and probable infections according to EORTC/MSG criteria [9] related to *Scedosporium* spp. and *L. prolificans* diagnosed between 2000 and August 2017 were selected from the **FungiScope® registry**. Respective cases were identified from the literature using the **PubMed** search filter "(Scedospori* OR Pseudallescheri* OR Lomentospori*) AND ((invasive OR disseminated OR infection) AND (case OR patient OR report))".

Collected data included: demographics, fungal pathogens, underlying diseases and risk factors for IFD, site of infection, signs and symptoms at time of diagnosis of IFD (imaging findings, fever, cough, dyspnea, neurological signs), antifungal and surgical therapy, susceptibility to antifungals (EUCAST, CLSI), outcome, autopsy findings.

For a comprehensive assessment of the epidemiology and currently used treatments.

Results

- 208 Scedosporium spp.
  - 185 *S. apiospermum*
  - 16 *S. boydii*
  - 7 *S. aurantiacum*
- 56 *L. prolificans*
- Proven 89 %
- Male 60.6 %
- Median age 57 (IQR 40 – 65) years

Results

Risk factors

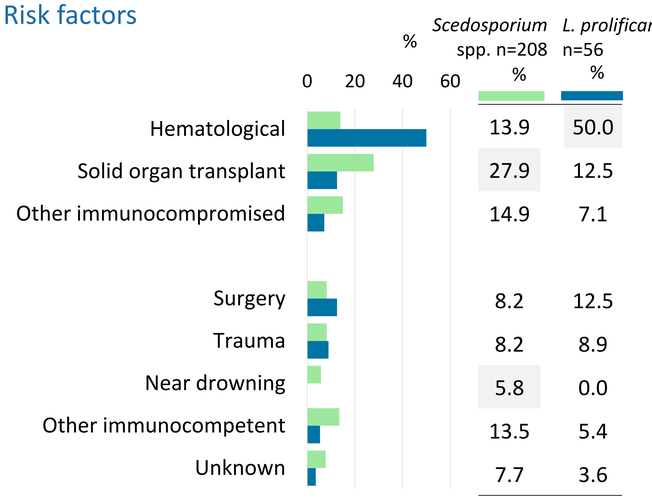


Figure 1. Predisposing factors
Other immunocompromised: asthma, rheumatic arthritis, chronic pulmonary disease, chronic granulomatous disease, HIV/AIDS
Other immunocompetent: Bronchiectasis, cystic fibrosis, chronic kidney disease/Diabetes Mellitus, contact lens, chronic pulmonary disease, dialysis, extracorporeal membrane oxygenation, glaucoma, intravenous drug abuse, tuberculosis , viral pneumonia

Site of Infection

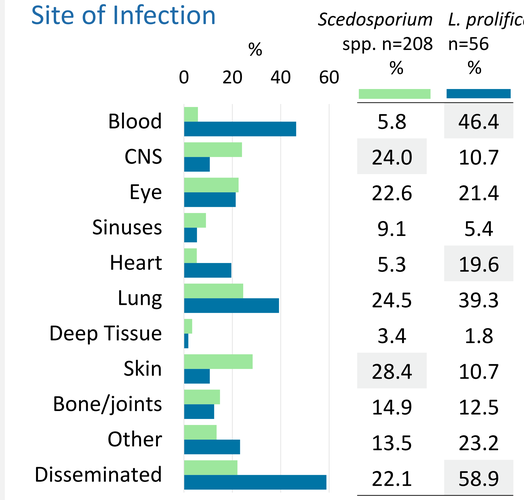


Figure 2. Frequent site of infection
Disseminated: includes bloodstream infections

L. prolificans isolates show high MICs to antifungals

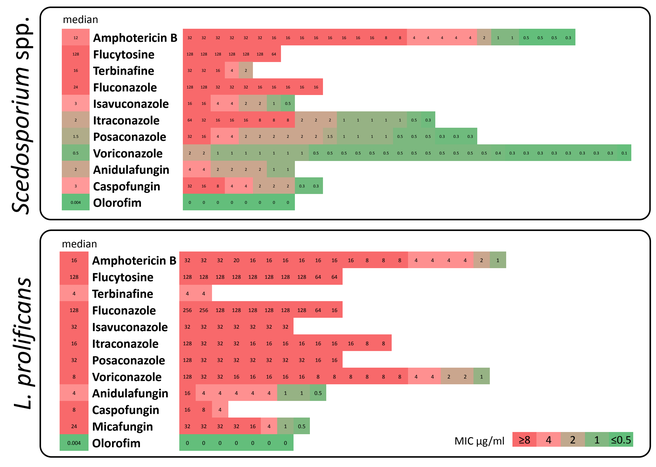


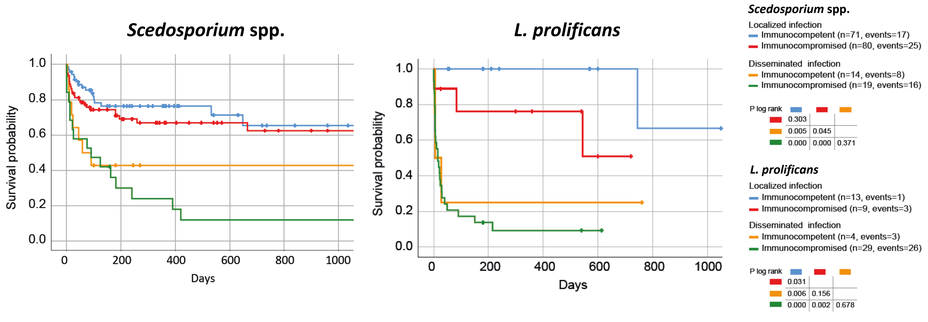
Figure 3. Minimum inhibitory concentration (MIC) against antifungals determined by EUCAST and CLSI methods.

Treatment

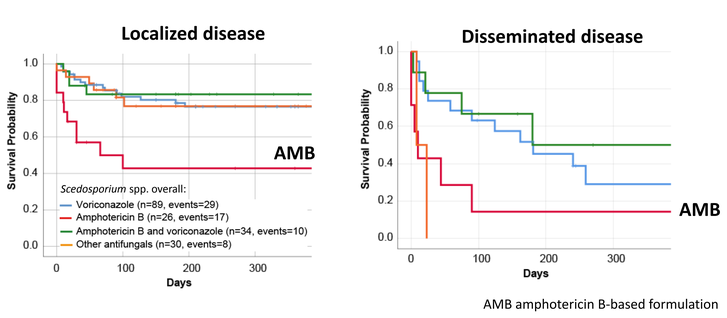
	Scedosporium spp. n=208	*L. prolificans* n=56
Prophylaxis (%)	20 (9.6)	13 (23.2)
POS, VRC	7 (35)	10 (76.9)
Other[a]	13 (65)	3 (23.1)
Antifungal treatment		
Antifungal + surgery	117 (56.3)	24 (42.9)
Antifungal	87 (41.8)	31 (55.4)
Surgery	2 (1)	- -
No treatment	2 (1)	1 (1.8)
Antifungal drugs (%)		
Amphotericin B	63 (30.3)	27 (48.2)
Voriconazole	137 (65.9)	38 (67.9)
Posaconazole	15 (7.2)	8 (14.3)
Itraconazole	57 (27.4)	8 (14.3)
Other azoles	20 (9.6)	4 (7.1)
Terbinafine	26 (12.5)	22 (39.3)
Echinocandin	22 (10.6)	17 (30.4)

Table 1. Treatment
[a]*Scedosporium* spp.: ITRA (5), FLU (4), AMB (3), CASP (1); *L. prolificans*: FLU (2), ITRA (1)

Dissemination of the infection predicts worse outcome



Usage of AMB alone is associated with worse outcome



AMB amphotericin B-based formulation

Conclusion

- *Scedosporium* spp. and *L. prolificans* infections in patients not only with compromised immune status
- Frequently presents as fungemia with devastating outcome
- *Scedosporium* spp. and *L. prolificans* are resistant to most antifungals currently available
- Voriconazole usage is associated with improved outcome compared to amphotericin B formulations alone

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