Twofold point mutations in *Candida albicans* FKS1 gene leading to echinocandin resistance after long-time treatment

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### Objectives

The development of pan-echinocandin resistance of *Candida albicans* isolates with the same MLST (multilocus sequence typing) profile isolated from a candidemic patient prior and after caspofungin treatment is shown.

### Materials and Methods

Two *C. albicans* isolates obtained from the same patient before and after caspofungin treatment were investigated. Antifungal susceptibility tests for echinocandins, amphotericin B, fluconazole and azoles were performed both with Etest® and MICRONAUT susceptibility testing system. The β-1,3-glucan synthase catalytic subunit 1 (FKS1) gene, which is known as a hot spot for mutations leading to reduced susceptibility to echinocandins, was amplified and sequenced. MLST profiles were examined by comparison of the sequences of 7 DNA sites encoding housekeeping genes: AAT1a, ACC1, ADP1, PMI1b, SYA1, VPS13, and ZWF1b.

### Results (1)

The colonizing isolate obtained after caspofungin treatment showed reduced pan-echinocandin susceptibility whereas the pre-treatment invasive isolate was susceptible to all antifungals tested (tab. 1). Both isolates shared the same MLST profile, suggesting a high clonal homology.

### Results (2)

FKS1 sequencing of the pre-treatment strain showed a sequence corresponding to the wild type, whereas the post-treatment strain showed two point mutations in resistance hot spot 1. Both these mutations resulted in amino acid changes: V576G, S654F (fig. 1).

<table>
<thead>
<tr>
<th>Tab. 1</th>
<th>EUCAST breakpoints</th>
<th>pre-treatment isolate</th>
<th>post-treatment isolate</th>
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</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>1</td>
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<td>0.5</td>
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<tr>
<td>Fluconazole</td>
<td>0.12</td>
<td>0.06</td>
<td>0.06</td>
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<tr>
<td>Voriconazole</td>
<td>0.06</td>
<td>0.012</td>
<td>0.016</td>
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<tr>
<td>Caspofungin</td>
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<td>0.032</td>
<td>1.5</td>
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<tr>
<td>Micafungin</td>
<td>0.016</td>
<td>0.032</td>
<td>1.5</td>
</tr>
</tbody>
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### References


