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Clonal diversity of *Candida albicans* isolates causing candidaemia over a 4-year period: patients located in different departments can be infected by identical genotypes

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UPDATED ABSTRACT

Objectives: Most episodes of fungaemia are caused by *Candida albicans*. Genotyping of *C. albicans* strains isolated from blood may clarify the genotypic diversity of this species, although the technique is rarely performed. We studied the clonal diversity of *C. albicans* isolates using a highly reproducible and discriminatory microsatellite marker panel.

Methods: We studied 224 *C. albicans* strains isolated from the blood cultures of 208 patients with candidaemia (Jan 2007 to Dec 2011). Each isolate corresponded to 1 episode of candidaemia. Multiple episodes were defined as isolation of *C. albicans* in additional blood cultures taken ≥7 days after the last isolation in blood culture. The isolates were identified after amplification and sequencing of the ITS1-5.8S-ITS2 region and further genotyped using a panel of 6 microsatellite markers (Botterel JCM 2001, Sampaio JCM 2003, Sampaio JCM 2005). Patients had 1 episode (n=193), 2 episodes (n=14), or 3 episodes (n=1). Patients with mixed genotypes in the same culture were excluded (n=5). Identical genotypes showed the same alleles for all 6 markers. A similarity dendrogram was constructed using the remaining 218 strains from the 203 patients included.

Results: An intrapatient analysis revealed that the genotypes causing both episodes were identical in most patients with 2 episodes (12/14). In contrast, 2 different genotypes were found in the patient with 3 episodes, one causing the first and second episodes and the other causing the third episode (isolated 6 months later). An interpatient analysis revealed that 154 of the 174 different genotypes found were involved in only 1 episode (n=148 patients); the remaining genotypes grouped in 20 clusters (n=52 patients) including 2-6 patients each. In 12 of the 20 clusters, the patients were infected by the same genotype but had been admitted to different departments. In contrast, each of the remaining 8 clusters grouped isolates from patients infected by the same genotype in the same department. Interestingly, 5 of the clusters had a different genotype and involved patients admitted to the same unit (neonatology).

Conclusion: We showed that patients admitted to hospital could develop candidaemia caused by an identical genotype of *C. albicans*. In up to 65% of cases, patients were not located in the same department at diagnosis. In contrast, in patients with multiple episodes of *C. albicans* candidaemia, the genotype causing the first episode was found in the subsequent episodes.

INTRODUCTION

Although candidaemia can be caused by endogenous strains, horizontal exogenous transmission of *Candida albicans* is possible. Endemic genotypes have been detected in specific units (Ásmundstóttir, CID 2008, Shin, JCM 2011).

We hypothesized that a single *C. albicans* genotype can infect ≥2 patients, suggesting that the infection can be acquired in the same hospital unit.

However, it is unknown whether patients admitted to different areas of the hospital may become infected by the same *C. albicans* genotype.

Furthermore, it is also unknown whether multiple fungaemia episodes are caused by the same genotype.

PURPOSE

To genotype *C. albicans* strains isolated from blood cultures of patients with fungaemia, with emphasis on detecting potential clusters of genotypes involving different patients. We also studied the number of genotypes found in patients with multiple episodes of candidaemia

METHODS

We studied 224 *C. albicans* strains isolated from the blood cultures of 208 patients with candidaemia (Jan 2007 to Dec 2011).

Each isolate represented 1 episode of candidaemia. In patients with ≥2 episodes, subsequent episodes were confirmed by isolation of *C. albicans* in additional blood cultures taken ≥7 days after the last isolation during the previous episode.

The isolates were identified using molecular techniques after amplification and sequencing of the ITS1-5.8S-ITS2 region and further genotyped using a panel of 6 short tandem repeat (STR) markers (Botterel, JCM 2001, Sampaio, JCM 2003, Sampaio, JCM 2005).

Genotypes showing the same alleles for all 6 markers were considered identical.

Clusters were defined as a group of ≥2 patients infected by the same *C. albicans* genotype. The patients involved in each cluster were geographically related regardless of whether they were admitted to the same ward or not.

In the case of patients with the same genotype in different wards at the time of the blood sample collection, we studied whether they had shared a ward in the previous 2 years.

RESULTS

Intra-patient analysis

The 208 patients had 1, 2, or 3 different episodes (Figure 1). A mix of genotypes was found in 6 episodes (2.7%) from 5 patients; these episodes were excluded from the inter-patient analysis.

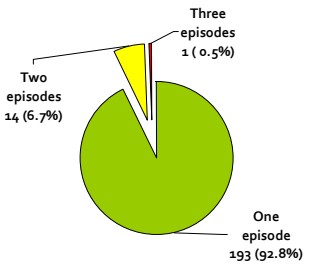

Figure 1. Distribution of the 208 patients with 1, 2, or 3 episodes.

In most of the patients with 2 episodes (12/14; 85.7%), both genotypes were identical.

In contrast, 2 different genotypes were found in the patient with 3 episodes, one causing the first 2 episodes and the other causing the third episode (isolated 6 months later).

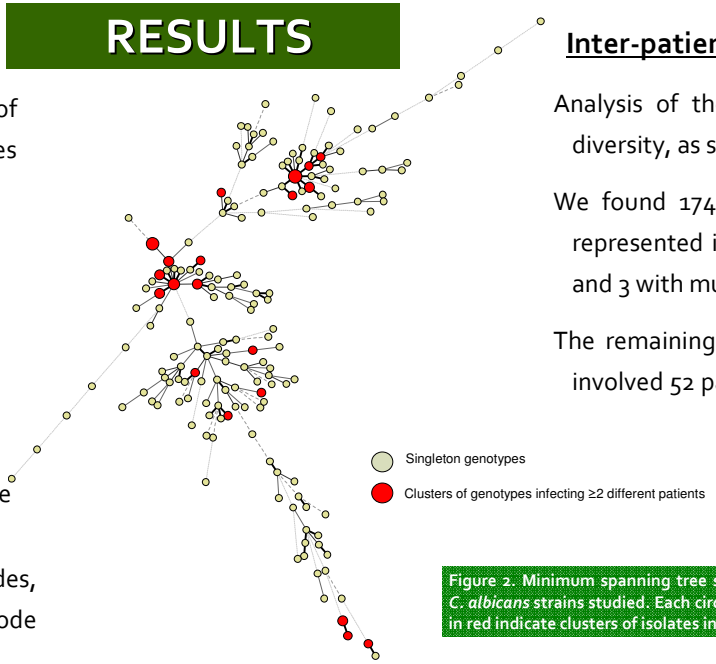

Figure 2. Minimum spanning tree showing the genotypic diversity of the *C. albicans* strains studied. Each circle represents a single genotype. Circles in red indicate clusters of isolates involving ≥2 patients.

Inter-patient analysis

Analysis of the 218 strains (n=203 patients) revealed high genotypic diversity, as shown in the minimum spanning tree (Figure 2).

We found 174 different genotypes; 154/174 were singleton and were represented in only in 1 episode (n=148 patients with a single episode and 3 with multiple episodes) (beige circles, Figure 2).

The remaining genotypes grouped in 20 clusters (named 1 to 20) that involved 52 patients (2-6 patients per cluster) (red circles, Figure 2).

Table 1 summarizes the patients involved in 8/20 clusters (40%) who were admitted to the same ward at the time of blood sample collection.

Table 1. Clusters involving patients admitted to the same ward at the time of blood sample collection

Cluster Code	No. of patients involved	Ward of admission	No. of days*
1	2	Neonatology	367
5	2	Post-surgical ICU	5
6	2	Digestive medicine	142
7	2	Neonatology	44
10	2	General surgery	8
15	4	Neonatology ICU	33
18	3	Neonatology	136
19	2	Neonatology	1

*Number of days from blood sample collection of the first patient to that of the last patient involved in each cluster.

Table 2 summarizes another group of 3/20 clusters (15%) involving patients who were not admitted to the same ward at the time of blood sample collection. However, the patients had previously been on the same ward at the same time.

Table 2. In each of the 3 clusters, the patients shared the ward of admission prior to the diagnosis of fungaemia

Cluster Code	No. of patients involved	Ward of admission	Ward of coincidence	No. of days*
4	2	Paediatric ICU Paediatric haematology	Paediatric haematology	63
9	2	General surgery Internal medicine	General surgery	41
17	2	Internal medicine Digestive medicine	Internal medicine	681

*Number of days from blood sample collection of the first patient to that of the last patient involved in each cluster.

In the remaining 9/20 clusters (45%), we did not find any geographical relationship between the patients involved in each cluster at the time of the blood sample collection or during the previous 3 years (Table 3).

Table 3. Each cluster grouped patients infected by the same genotype but never admitted to the same ward.

Cluster code	No. of patients involved	No. of different wards involved
2	3	3
3	6	5
8	2	2
11	4	4
12	3	2
13	2	2
14	3	3
16	2	2
20	2	2

*Number of days from blood sample collection of the first patient to that of the last patient involved in each cluster.

Interestingly, most of the clusters shown in Table 1 involved patients from the neonatology ward/ICU (Figure 3).

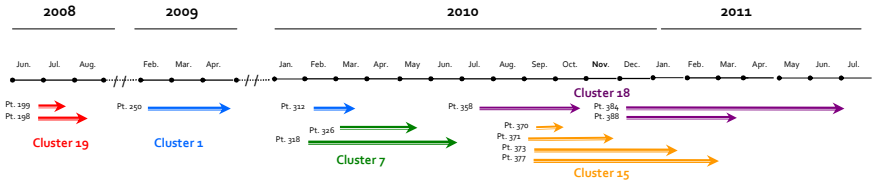

Figure 3. Patients involved in the 5 clusters found in the neonatology ward/ICU. Each patient is represented with a different arrow. Arrows in the same colour include patients grouped in the same cluster. The length of the arrow indicates the length of stay in the unit.

CONCLUSIONS

- We found high genotypic diversity among *C. albicans* isolates causing fungaemia.
- Up to 25% of patients were infected by a genotype found in at least one other patient.
- Patients in clusters are frequently found in the neonatology ward/ICU.
- We were able to demonstrate a geographical relationship between the patients in only 50% of the clusters.
- In most patients with 2 episodes, the genotype causing both episodes was the same.

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