TITLE: CASES OF FUNGEMIA CAUSED BY *Candida haemulonii* var. *vulnera* RESISTANT TO AMPHOTERICIN B AMONG CHILDREN AT PHILANTHROPIC HOSPITAL BOLDRINI CHILD CENTER

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ABSTRACT:

The *Candida haemulonii* complex (*C. duobushaemulonii*, *C. haemulonii*, and *C. haemulonii* var *vulnera*) has been rarely described in candidemia cases, being considered an emergent pathogen, multi-resistant opportunistic yeast, closely related to *Candida auris*, that can be misidentified when using conventional diagnostic methods. This study reports a possible outbreak of *Candida haemulonii* complex fungemia in May and June 2020 at philanthropic hospital Boldrini Child Center through the identification and antifungal susceptibility profiles of four clinical isolates obtained from blood culture of four children. Identification at species level was not possible by conventional methods, and these samples were identified by DNA sequencing of the ITS4/ITS5 and D1/D2 regions of ribosomal DNA. Sequences were aligned and searched in GenBank using the BLAST tool for species identification. Phylogenetic analyses using ITS gene sequences and other references as *C. auris*, *C. haemulonii* var *vulnera*, and *C. duobushaemulonii* also was performed for identification. Antifungal susceptibility testing was carried out according to the Clinical Laboratories and Standards Institute (CLSI) guidelines using Dry Plate (Eiken Chemical, Japan). The four isolates were resistant to amphotericin B with minimal inhibitory concentration (MIC) ≥ 16 µg/mL and susceptible to fluconazole with MIC 1-2 µg/mL. Other antifungals and their concentration intervals were resulted as follows: itraconazole (MIC: 0.125 - 0.25 µg/mL), voriconazole (MIC: 0.03 – 0.06 µg/mL), miconazole (0.25 - 1 µg/mL), 5-flucytosine (MIC: ≤ 0.125 µg/mL), micafungin (MIC: 0.06 mg/L) and caspofungin (0.25 mg/L). The four isolates were identified as *C. haemulonii* var *vulnera* by molecular identification and confirmed by phylogenetic analyses using other reference sequences. The four children had leukemia, and one of them died in November 2020. This report reinforces the importance of molecular identification in differentiating species of the *C. haemulonii* complex. Moreover, this study highlights the emergence of *C. haemulonii* var *vulnera* as an opportunistic pathogen in immunocompromised patients and the requirement of susceptibility testing for an effective treatment.

Keywords: *Candida haemulonii*, *Candida auris*, bloodstream infection, multidrug-resistance, molecular identification

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