


# Identification of *Candida colliculosa* in an oral ulcer of a pediatric hematological patient

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## Abstract:

**Introduction:** *Candida colliculosa* is a yeast of food origin classified as *Non-Albicans Candida* (NAC), with its pathogenic potential confirmed, but little known. Like other opportunistic infections, diseases caused by NAC species are most commonly found in immunosuppressed patients. **Objectives:** The objective of this work is to report the case of a pediatric patient who developed an atypical lesion associated with *Candida colliculosa* in the mouth. **Case report:** A 9-year-old boy under chemotherapeutic treatment for Acute Myeloid Leukemia developed edema in the lower lip, with a persistent crusted ulcer circumscribed by an erythematous, painless, and progressing negatively. He was using antibiotics, antifungals, antiemetics, and antihistamines. **Results:** It was decided to perform complementary exams for final diagnosis. Cell smears were collected for exfoliative cytology, direct mycological, bacterial and viral culture, and fungi investigation. No viruses and bacteria were identified. A direct mycological examination showed yeast cells without pseudohyphae and a MALDI-TOF technique confirmed the diagnosis of *Candida colliculosa*. **Final considerations:** The use of antifungal agents associated with the patient's immunological recovery led to the complete healing of the lesion and hospital discharge. Identification of the fungal species was important not only to establish the diagnosis and most appropriate treatment but also to avoid the fungus spreading in the hospital environment. **Keywords:** Hematology, Diagnosis Oral, *Candida*

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## INTRODUCTION

The most common cancer in children is acute leukemia, accounting for about 80% of the malignant neoplasms in pediatric patients<sup>1</sup>. Oral lesions can be both indicative of the disease, when it has not yet been diagnosed, or also manifest as a consequence of the immunosuppression caused by the evolution of cancer or its treatment cytotoxicity<sup>1</sup>.

A study by Aggarwal & Pai (2018) investigated oral manifestations in pediatric patients diagnosed with acute leukemia and found manifestations associated with *Candida* in about 14% of them<sup>1</sup>.

Yeasts of the genus *Candida* ssp. are associated with invasive fungal infections and can be considered one of the main causes of morbidity and mortality in patients with systemic involvement or in a hospital environment<sup>2</sup>. The most commonly found and known is *C. albicans*, however, other *Non-Albicans Candida* (NAC) species also have pathogenic potential and can colonize and cause disease in other tissues and organs such as the skin, mouth, vagina, liver, and heart<sup>2</sup>.

*Candida colliculosa* is a yeast that can survive in different environmental conditions and features pathogenic potential and virulence similar to *Candida albicans*<sup>3</sup>.

Since immunosuppressed patients are more predisposed to the development of opportunistic infections, it is a protocol to prescribe antifungals, antibiotics, and antivirals prophylaxis before the infusion of chemotherapy<sup>1</sup>.

The aim of this study is to report the case of a lesion with atypical clinical manifestation in the lower lip caused by *C. colliculosa* in a pediatric onco-hematological patient.

## CASE REPORT

A 9-year-old boy diagnosed with Acute Myeloid Leukemia was hospitalized due to immunosuppression after the chemotherapy cycle. He was being followed up by the Dental team due to oral mucositis. After a couple of days, the mucositis lesions presented an improvement

but the patient showed edema in the lower lip, with a crusted ulcer circumscribed by an erythematous and painless area (figure 1A). After one week, there was an increased ulcerated area and erythema (figure 1B). The patient was using cefepime, fluconazole, vancomycin, metronidazole, hydrocortisone, and tretinoin, as well as antiemetic and antihistamine drugs. The prescription of antihistamine was carried out due to a suspicion that it could be an allergic reaction, as one of the clinical characteristics of the lesion was the intense edema of the lower lip. The ulcer evolved with a painless hardened dark crust and pseudomembrane (figures 1C-1D). A biopsy for histopathological analysis was not performed due to pancytopenia. Cell smears were collected for cytology, direct mycological, bacterial, and fungal culture. No viruses and bacteria were identified. The direct mycological examination showed the presence of yeast cells without pseudohyphae and a Maldi-TOF for fungi strain was positive for *Candida colliculosa*. The antifungal dose was increased from a prophylactic to a therapeutic dose. The improvement of the lesion accompanied the patient's immune recovery, no prescription was needed for broad-spectrum antifungals. The patient was discharged after complete lip lesion resolution and continued the oncological treatment on an outpatient basis.

## DISCUSSION

Since immunosuppressed patients, due to both disease and treatment, are more likely to develop opportunistic infections, it is common to prescribe low-dose antibiotics, antifungals, and antivirals for prophylactic purposes<sup>1</sup>. The patient in this case report used cefepime, fluconazole, vancomycin, metronidazole, hydrocortisone, and tretinoin.

It is known that patients diagnosed with systemic diseases are more likely to develop fungal infections<sup>1</sup>. A study by Hu et al (2019) researched the *Candida* species most commonly associated with oral infections<sup>5</sup>, and *C. colliculosa* was not described in their results.

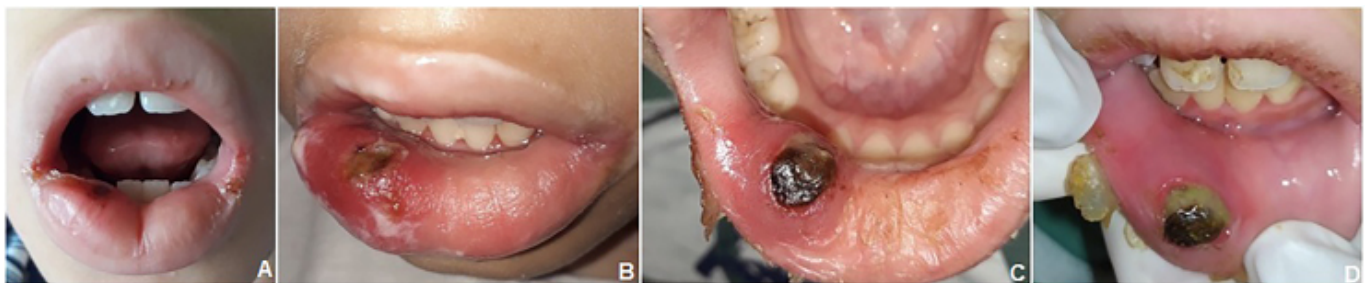


Figure 1. Evolution of the lesion on the lower lip. A - initial aspect. B - Increase in erythema. C, D - Presence of blackish crust and hard edges on palpation.

The incidence of infections caused by NAC species has increased significantly in the last decade<sup>2,5</sup>. For this reason, a study conducted by Rajkowska & Kunicka-Styczyńska (2018) investigated the virulence factors of food fungi. As a result, the authors found that 9 of the 18 *Candida* strains of food sources surveyed showed clinical similarities in relation to biotype and virulence factors when compared to *C. albicans*<sup>2</sup>. *C. colliculosa* was described as part of a group of potential pathogens<sup>2</sup>.

Infections NAC species can vary from 35 to 65% of all diagnosed candidemia, and occur most commonly in patients with onco-hematological diseases and patients undergoing hematopoietic stem cell transplant<sup>6,7,8</sup>. The mortality associated with NAC species can vary from 15% to 35%, with values similar to *C. albicans*<sup>6,7,8</sup>.

Since fungal infections can be caused by different species of *Candida ssp*, it is important to identify species since the sensitivity to antifungals can differ between the strains of *Candida ssp*<sup>2</sup>. Furthermore, one should consider mixed infections with 2 or more strains of *Candida ssp*. Unlike the behavior of *C. albicans*, the antifungal sensitivity of NAC species varies significantly. Some species such as *C. krusei* and *C. glabrata* commonly show resistance to fluconazole<sup>6</sup>. Other species such as *C. rugosa* and *C. lusitanae* may show resistance to amphotericin B<sup>6</sup>. This fact makes the specificity of the fungal strain even more important before prescription<sup>6</sup>. There is a lack of evidence on the most suitable drug and antimicrobial resistance when treating *C. colliculosa*. However, Kaygusuz et al. (2003) report a case in which a patient developed fungal endocarditis associated with *C. colliculosa* and was treated with fluconazole followed by amphotericin B, previously to the surgical approach of the infected tricuspid valve<sup>4</sup>. As far as we know, this study<sup>4</sup> was the only case identified in the literature of infection associated with the fungal species *C. colliculosa*, and our study is the first to report the identification of *C. colliculosa* in an oral ulcer. Furthermore, a study conducted by Shirkhani et al. (2016) observed isolates of *Candida ssp*. of 80 cases of vulvovaginitis in order to observe phospholipase and proteinase activities, and one of the identified species was *C. colliculosa*. They report that 100% of the isolates of this strain produced high proteinase activity, confirming its rarely discussed virulence and pathogenic potential<sup>9</sup>.

One of the techniques used to identify the strain is mass spectrometry (MALDI-TOF), which allows the characterization of isolated yeast in a quick way with diagnostic fidelity<sup>10</sup>. This technique is based on the detection of molecules of greater mass, identifying a wide spectrum of proteins, being able to better discriminate the species of microorganisms. MALDI-TOF stands out

for its ease of implementation, high-performance capacity, high speed, and low cost<sup>10</sup>. This was the technique used to diagnose *C. colliculosa* in the lip lesion reported.

## FINAL CONSIDERATIONS

*Candida colliculosa* should be considered as a potential infective agent in non-specific or refractory lesions in immunosuppressed individuals under oncologic treatment. Despite the several weeks of persistent injury, the recovery of the patient's immune status appeared to play an important role in the regression of the lesion. Fluconazole may have also played an important role for lip lesion complete healing although no broad-spectrum antifungals prescription was needed.

Identification of the fungal species was important not only to establish the diagnosis and most appropriate treatment but also to avoid the fungus spreading in the hospital environment.

## ETHICAL ASPECTS

This study was approved by the Research Ethics Committee of the institution where it was conducted under the number CAAE: 44582521.9.0000.0096

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