Oropharyngeal candidiasis in children with lymphohematopoietic malignancies in Mashhad, Iran

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(Received: 29 November 2015; Revised: 6 December 2015; Accepted: 27 December 2015)

Abstract

Background and Purpose: Over the past years, the role of fungi as a cause of nosocomial infections in hospitalized patients has been accentuated. Candida species constitute an important group of fungi causing diseases in immunocompromised patients. Oropharyngeal candidiasis continues to be a prevalent infection in immunodeficient patients. In this study, we aimed to determine the incidence of oropharyngeal candidiasis in children with lymphohematopoietic malignancies.

Materials and Methods: In total, 102 patients with lymphohematopoietic malignancies and 50 healthy controls were examined in terms of Candida infections via direct sampling of the oropharyngeal cavity. Fresh smears were prepared with 10% potassium hydroxide and Gram staining was carried out. Subsequently, the obtained specimens were cultured on Sabouraud dextrose agar for further analysis.

Results: The most common Candida species were Candida albicans (31%), other non-C. albicans species (14.7%), C. glabrata (6.8%), and C. krusei (0.98%) in the case group, while in the control group, other non-C. albicans species (10%) and C. albicans (8%) were the most common species.

Conclusion: In the present study, Candida species were the most common fungal pathogens in pediatric cancer patients; therefore, efforts should be made to prevent fungemia and fungal pneumonia. Also, non-C. albicans species must be considered as a new risk factor for pediatric cancer patients.

Keywords: Candida, Hematopoietic Malignancies, Oral candidiasis

How to cite this paper:
Berenji F, Zabolinejad N, Badiei Z, Kakhi S, Andalib Aliabadi Z, Ganjbakhsh M. Oropharyngeal candidiasis in children with lymphohematopoietic malignancies in Mashhad, Iran. Curr Med Mycol. 2015; 1(4): 33-36. DOI: 10.18869/acadpub.cmm.1.4.33

Introduction

Over the past years, the role of fungi as a cause of nosocomial infections in hospitalized patients has been accentuated [1]. These fungi are a major cause of morbidity and mortality, given the increased length of hospital stay [2, 3].

Oropharyngeal candidiasis, which is caused by Candida species through the involvement of hard and soft palates, tongue, buccal mucosa, and floor of the mouth, is a very common problem of the mucosal membranes of oropharynx. Although in the majority of patients, this infection is caused by Candida albicans as a commensal organism [1, 4-6], it may be also caused by other Candida species, such as C. glabrata, C. tropicalis, and C. krusei [1, 7].

The prevalence of oropharyngeal candidiasis continues to be high in immunocompromised patients [8-10]. In many cases, clinicians dealing with immunocompromised and critically ill patients have shown a link between Candida colonization and subsequent infections [11, 12]. Colonization of Candida species occurs in up to 80% of critically ill patients receiving intensive care.

Despite the recent advances in microbiological techniques, primary diagnosis of invasive candidiasis remains challenging, resulting in the delayed detection of candidiasis [12]. Accurate identification of Candida strains is highly important, considering the ability of these strains to cause infections and induce susceptibility to antifungal agents. Compared to C. albicans, the importance of non-C. albicans
species such as C. glabrata and C. krusei has been more recognized due to their improved resistance to certain antifungal agents [13].

Physiologic differences between pediatric and adult patients alter susceptibility to infections caused by different Candida species [3]. Therefore, the aim of the present study was to evaluate the incidence of oropharyngeal candidiasis and compare the causative agents among children with lymphohematopoietic malignancies and healthy controls.

Material and Methods

This cross-sectional study was conducted in the hematology-oncology ward of Dr Sheikh Children’s Hospital, affiliated to Mashhad University of Medical Sciences and Parasitology and Mycology Laboratory of Imam Reza Hospital in July 2009-2010. In this study, three methods including direct smear, staining, and culture were used for laboratory investigation of Candida infections.

In total, 102 patients with lymphohematopoietic malignancies and 50 healthy individuals (control group) at the nurseries of Qaem and Imam Reza hospitals were examined for Candida infections via direct sampling of the oropharyngeal cavity, fresh smear with 10% potassium hydroxide (KOH), and direct microscopic examination with Gram staining of each sample. Subsequently, the samples were inoculated into Sabouraud dextrose agar (SDA, Himedia Laboratories, Mumbai, India), and positive cultures were transferred to CHROMagar Candida medium (HiMedia Laboratories, Mumbai, India) for further analysis.

Results

This study was conducted among 102 patients with lymphohematopoietic malignancies (mean age: 7 years) and 50 healthy children (mean age: 4.5 years) as the control group. In the case and control groups, the most prevalent age range was 3-6 years, accounting for 30% and 50% of the subjects in the case and control groups, respectively. Overall, 66% and 33% of the subjects in the case group were male and female, while 56% and 44% were male and female in the control group, respectively.

Among 102 patients with lymphohematopoietic malignancies, acute lymphoblastic leukemia was the most common underlying hematological malignancy (83.3%), followed by lymphoma (6.8%), acute myeloblastic leukemia (3.9%), non-Hodgkin’s lymphoma (3.9%), and sarcoma (1.9%). It should be mentioned that all the patients had received chemotherapy.

In the case group, positive results were reported in 37% and 56% of the subjects in direct smear and culture, respectively, while in the control group, positive results were reported in 8% and 24% of the participants in direct smear and culture studies, respectively. Therefore, culture studies showed sensitivity and specificity of 51% and 92%, respectively.

Among patients with lymphohematopoietic malignancies, 54% had clinical signs including white spots on the mouth and tongue (30%), redness of the mouth (14%), lip fissures (12%), burning mouth (10%), sore throat (7%), and fissure of tongue (5%). On the other hand, 22% of the subjects showed no clinical signs or symptoms; however, in the control group, no signs or symptoms of candidiasis were reported in the oral cavity.

The most common Candida species on CHROMagar Candida were C. albicans (31%), other non-C. albicans species (14.7%), C. glabrata (6.8%), and C. krusei (0.98%) in the case group, while in the control group, the most common species was other non-C. albicans species (10%), followed by C. albicans (8%) (Table 1).

Discussion

Fungal organisms are a cause of nosocomial infections and a major source of morbidity and mortality. Modern medicine is faced with great challenges, considering the increased length of hospital stay and high healthcare costs in critically ill or immuno-compromised children and patients with nosocomial infections, hematological diseases, or other malignancies [3, 14-18].

In studies by Kumar et al. in Chennai, India and Walsh et al. in France, invasive fungal
Infections such as aspergillosis and candidiasis were introduced as important causes of morbidity and mortality in immunocompromised children, particularly those with hematologic malignancies, stem cell transplantation, and acquired immunodeficiency [14, 19].

The prevalence of fungal infections is increased by the rise in the number of immunocompromised patients, chemotherapy dose intensity, increased length of hospital stay, extensive ulceration of mucous membranes, prolonged treatment with multiple broad-spectrum antibiotics, and common use of indwelling intravascular devices [11, 15, 20].

Based on a study by Saha et al., the ascribable mortality of acute candidiasis is 10-15% in children suspected of septicemia [21]. The present study was performed to evaluate the incidence of oropharyngeal candidiasis and to compare the type of causative fungi in children with lymphohematopoietic malignancies and control subjects.

In this study, the most common Candida species were C. albicans (31%), other non-C. albicans species (14.7%), C. glabrata (6.8%), and C. krusei (0.98%) in the case group, respectively. In the control group, the most common species were other non-C. albicans species (10%) and C. albicans (8%), respectively. C. albicans has been long recognized as the most common cause of disseminated candidiasis, followed by C. glabrata and other non-C. albicans species in pediatric and adult patients [11, 14, 20, 22].

Another aspect of candidemia is the economic burden on the patient and hospital. This economic impact has been associated with the increased costs of care including the use of antifungal agents and prolonged length of hospital stay, especially in severely immunosuppressed patients with hematological malignancies [20, 23-26].

Conclusion

C. albicans, other non-C. albicans species, and C. glabrata were the most common Candida species among the evaluated patients. Candida species were the most common fungal pathogens in pediatric cancer patients. Therefore, efforts should be made to prevent fungemia and fungal pneumonia. Also, non-C. albicans species must be considered as a new risk factor for pediatric cancer patients.

Acknowledgments

The authors greatly acknowledge the Research Council of Mashhad University of Medical Sciences (MUMS) for the financial support. The results presented in this study were extracted from a thesis by Soraya Kakhi (No.: 6519).

Authors’ Contributions

F.B., N.Z., and Z.B. designed and supervised the research. F.B. and Z.AA. edited the final manuscript, and Soraya Kakhi and M.G. performed the tests.

Conflicts of interest

The authors declare no conflicts of interest regarding the publication of this paper.

Financial disclosure

The authors declare no financial interests related to the materials of the study.

References

1. Viscoli C, Girmenia C, Marinus A, Collette L, Martino P, Vandercam B, et al. Candidemia in cancer patients: a prospective, multicenter surveillance study by the [continues]
invasive fungal infection group (IFIG) of the European organization for research and treatment of cancer (EORTC), Clin Infect Dis. 1999; 28(5):1071-9.
2. Ahmad Sarji S, Wan Abdullah W, Wastie M. Imaging features of fungal infection in immunosuppressed patients in a local ward outbreak. Biomed imaging Interv J. 2006; 2(2):e21.
3. Zaoutis T. Candidemia in children. Curr Med Res Opin. 2010; 26(7):1761-8.
4. Chow BD, Linden JR, Bliss JM. Candida parapsilosis and the neonate: epidemiology, virulence and host defense in a unique patient setting. Expert Rev Anti Infect Ther. 2012; 10(8):935-46.
5. Vazquez JA. Optimal management of oropharyngeal and esophageal candidiasis in patients living with HIV infection. HIV AIDS (Auckl). 2010; 2(1):89-101.
6. Fidel PL Jr. Candida-host interactions in HIV disease implications for oropharyngeal candidiasis. Adv Den Res. 2011; 23(1):45-9.
7. Collins CD, Cookingham S, Smith J. Management of oropharyngeal candidiasis with localized oral miconazole therapy: efficacy, safety, and patient acceptability. Patient prefer and Adherence. 2011; 5:369-74.
8. Villar CC, Dongari-Bagtzoglou A. Immune defence mechanisms and immunoenhancement strategies in oropharyngeal candidiasis. Expert Rev Mol Med. 2008; 10:e29.
9. Azizi A, Rezaei M. Prevalence of Candida species in the oral cavity of patients undergoing head and neck radiotherapy. J Dent Res Dent Clin Dent Prospects. 2009; 3(3):78-81.
10. Petraitis V, Petraitiene R, Kelaher AM, Sarafandi AA, Sein T, Mickiene D, et al. Efficacy of PLD-118, a novel inhibitor of candida isoleucyl-tRNA synthetase, against experimental oropharyngeal and esophageal candidiasis caused by fluconazole-resistant C. Antimicrob Agents Chemother. 2004; 48(10):3959-67.
11. el-Mahallawy HA, Attia I, Ali-el-Din NH, Salem AE, Abo-el-Naga S. A prospective study on fungal infection in children with cancer. J Med Microbiol. 2002; 51(7):601-73.
12. Eggimann P, Pittet D. Candida colonization index and subsequent infection in critically ill surgical patients: 20 years later. Intensive Care Med. 2014; 40(10):1429-48.
13. Byadarahally Raju S, Rajappa S. Isolation and identification of Candida from the oral cavity. ISRN Dent. 2011; 2011:487921.
14. Kumar CP, Sundararajan T, Menon T, Venkatadesikalu M. Candidosis in children with onco-hematological diseases in Chennai, south India. Jpn J Infect Dis. 2005; 58(4):218-21.
15. Safdar A, Chaturvedi V, Cross EW, Park S, Bernard EM, Armstrong DS, et al. Prospective study of Candida species in patients at a comprehensive cancer center. Antimicrob Agents Chemother. 2001; 45(7):2129-33.
16. Marchetti O, Bille J, Fluckiger U, Eggimann P, Ruet C, Garbino J, et al. Epidemiology of candidemia in Swiss tertiary care hospitals: secular trends, 1991–2000. Clin Infect Dis. 2004; 38(3):311-20.
17. Al-Rawahi GN, Roscoe DL. Ten-year review of candidemia in a Canadian tertiary care centre: Predominance of non-albicans Candida species. Can J Infect Dis Med Microbiol. 2013; 24(3):e65-8.
18. Spampinato C, Leonardi D. Candida infections, causes, targets, and resistance mechanisms: traditional and alternative antifungal agents. Biomed Res Int. 2013; 2013:204237.
19. Walsh TJ, Lutsar I, Driscoll T, Dupont B, Roden M, Ghalramani P, et al. Voriconazole in the treatment of aspergillosis, scedosporiosis and other invasive fungal infections in children. Pediatr Infect Dis J. 2002; 21(3):240-8.
20. Chaskar P, Anuradha ND, Agarwal S, Hans C. Nosocomial Candidemia in intensive care units of a tertiary care hospital, New Delhi, India. Int J CurrMicrobiol App Sci. 2014; 3(6):513-7.
21. Saha R, Das Das S, Kumar A, Kaur IR. Pattern of Candida isolates in hospitalized children. Indian J Pediatr. 2008; 75(8):858-60.
22. Horn DL, Neoftyos D, Anaissie EJ, Fishman JA, Steinbach WJ, Olyaei AJ, et al. Epidemiology and outcomes of candidemia in 2019 patients: data from the prospective antifungal therapy alliance registry. Clin Infect Dis. 2009; 48(12):1695-703.
23. Olaechea PM, Palomar M, León-Gil C, Alvarez-Lerma F, Jorda R, Nolla-Salas J, et al. Economic impact of Candida colonization and Candida infection in the critically ill patient. Eur J Clin Microbiol Infect Dis. 2004; 23(4):323-30.
24. Sipsas NV, Lewis RE, Tarrand J, Hachem R, Rolston KV, Raad II, et al. Candidemia in patients with hematologic malignancies in the era of new antifungal agents (2001-2007): stable incidence but changing epidemiology of a still frequently lethal infection. Cancer. 2009; 115(20):4745-52.
25. Berenji F, Rajabi O, Azish M, Minoochehr N. Comparing the effect of ozonized olive oil with clotrimazole on three Candida species C. albicans, C. glabrata, C. krusei. E3 J Microbiol Res. 2014; 2(1):9-13.
26. Katiraei F, Teifoori F, Soltani M. Emergence ofazole-resistant Candida species in AIDS patients with oropharyngeal candidiasis. Curr Med Mycol. 2015; 1(3):11-16.