ORIGINAL ARTICLE

Herpetic Oral Manifestation In Acute Myeloid Leukemia: case report

Thiago Pires Brito[1]
Alexandre Caixeta Guimarães[1]
Guilherme Machado de Carvalho[2]
Tammy Fumiko Messias Takara[3]
Felipe Henrique Yazawa Santos[3]
Icléia Siqueira Barreto[4]
Ana Cristina Dal Rio[5]
Maria Elvira Pizzigatti Corrêa[5]
Ester Maria Danielli Nicola[6]

Abstract:

Viral infections in the oral cavity are frequent complications in patients with immunosuppression. The herpes simplex virus is among the most frequent causes of these infections. In immunocompromised patients the presentation may be atypical, with more extensive lesions, painful and with slower recovery. The goal of this article is to present a illustrative case of herpes oral infection in an immunosuppressed patient. **Case report:** Female patient, 43 years old, 32 days after the start of chemotherapy for acute myeloid leukemia, began complaining of odynophagia and painful emergence of lesions in the oral cavity. She presented multiple whitish ulcerated lesions with an erythematous halo, measuring around 0.5 cm in diameter across the mouth and the posterior wall of oropharynx. Treated with acyclovir with rapid improvement of symptoms and lesions. Cytological changes were found compatible with herpes simplex. **Discussion:** In most cases of infection with herpes simplex the presentations are self-limited but severe infections may occur and atypical in immunosuppressed individuals. Additional exams help in diagnosis as diagnostic cytology, ELISA and direct immunofluorescence. Acyclovir is the drug of choice for the treatment recommended dose of 1 g/day for a minimum period of 10 days. **Conclusion:** The oral lesions of herpes virus in immunosuppressed patients may have varied presentations and can often go unnoticed, as in mild or asymptomatic cases. However, due to the possibility of systemic spread of infection and the occurrence of severe manifestations, one should be highly suspected before the appearance of any oral lesion in the immunosupressed patients.

Keywords: herpes simplex; immunosuppression; leukemia, myeloid, acute; oral medicine.

[1] UNICAMP (ENT Resident Doctor)
[2] UNICAMP (Campinas University) (M.D., ENT Doctor)
[3] Faculdade de Ciências Médicas da Santa Casa de São Paulo (Acadêmica de Medicina)
[4] UNICAMP (Médica Patologista, Departamento de Anatomia Patológica da FCM-UNICAMP)
[5] UNICAMP (Cirurgiã Dentista, Assistente do Ambulatório de Faringoestomatologia, Disciplina de Otorrinolaringologia da FCM-UNICAMP)
[6] UNICAMP (Médica Otorrinolaringologista, Chefe de Serviço de Faringoestomatologia, Disciplina de Otorrinolaringologia da FCM-UNICAMP)

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Corresponding Author:
Guilherme Machado de Carvalho.
E-mail: guimachadocarvalho@gmail.com

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INTRODUCTION

The viral infections of the oral cavity or perioral region are common infections in patient with cancer or those treating it. The early diagnosis and treatment are important, because they avoid the disease dissemination in patients with low immunity and relief the symptoms[1].

Most of the oral diseases secondary to the chemotherapy or inherent to the cancer are ulcerative lesions[2]. These injuries represent an important gateway to the air and digestive systems for various microorganisms when associated to mucositis caused by chemotherapy drugs[2].

In patients with different types of cancer (carcinoma, sarcoma and lymphomas) it has been found rates of 9.7% of oral infections, 10.7% of those caused by viruses. Several types of viruses are described as having the ability to cause infections in the oral cavity, among which the main ones are the herpes simplex virus (HSV), varicella zoster virus (VZV), Epstein-Bar virus (EBV) and cytomegalovirus (CMV)[3].

It is known that in patients undergoing bone marrow transplantation (BMT) opportunistic infections are very common, and each post-BMT they change, with an increase incidence of HSV, CMV, and VZV.

Infection with HSV is also a major cause of morbidity and mortality in haematological patients undergoing BMT and receiving myelosuppressive therapy[4]. During the immunosuppression induced by conditioning, there is a high incidence of the primary or late manifestation HSV[5].

In immunocompetent individuals, infection with herpes simplex virus is presented as erythematous plaque that progresses to a blistering coalescent crusted surface and may occur in both the skin and mucous[5]. However, in immunosuppressed patients there is an aberrant immune response due to a defect in cellular immunity, and it may result in an atypical clinical presentation[5]. In such patients, these lesions are usually extensive, painful and recovery takes longer compared to healthy subjects[6].

In this sense, the herpes simplex infection should be part of differential diagnosis in immunosuppressed patients with oral lesions, because the evaluation of these lesions involves a high possibility of infection by several other agents. In this way it reinforces the correct approach to the case and the need of multidisciplinary approach in diagnosis, avoiding the spread of these infections and their morbidity and mortality[7].

The goal of this article is to present a illustrative case of herpes oral infection in an immunosuppressed patient.

CASE REPORT

Female patient, 43 years old, housekeeper. After two months of nonspecific complaints such as myalgia, weakness and fever, it was initiated an investigation that resulted in the clinical diagnosis of acute myeloid leukemia. After the diagnosis, the patient was submitted to chemotherapy with cytarabine and daunorubicin and on the 32th day after starting treatment, she reported odynophagia and the emergence of painful lesions in the oral cavity. It was observed multiple ulcerated lesions, whitish, with an erythematous halo, measuring about 0.5 cm in diameter on the dorsum of the tongue, buccal mucosa, soft palate, tonsils and posterior oropharyngeal wall, painful at the touch and not bleeding (Figure 1).

Figure 1. The images show oral lesions observed on physical examination. Pay attention to the erythematous halo, with ulcerative aspect and whitish. The lesions were painful and bleeding.

Using a wooden spatula, samples were collected for cytologic diagnosis, with a diagnostic hypothesis of viral or fungal infection. Since the patient was already in use of antifungal medication without any change in the appearance of lesions, it was indicated the use of antiviral empirically. It was then started treatment with acyclovir at the dosage of 200 mg five times a day, orally, for ten days.

On the 7th day of treatment the patient presented a clear improvement of symptoms and complete resolution of lesions. The cytological exam of the lesions showed focal epithelial changes suggesting herpes simplex infection (Figure 2) and a secondary colonization and infection by *Candida sp* (Figure 3).

DISCUSSION

The *Herpes Simplex Virus* (type 1 and 2) commonly causes mucocutaneous lesions in patients with hematologic malignancies[8]. It is a DNA virus belonging to the subfamily *Alphaherpesvirinae*[8,9], In most cases, its infection generates self-limiting episodes but it may occur serious and atypical infections (meningitis, hepatitis, encephalitis) in immunosuppressed individuals[8,9]. It is transmitted by mucosal surfaces or breaks in the skin and the period of incubation is approximately seven days[9].

The first herpetic infection usually occurs in children and adolescents and is usually asymptomatic or causes nonspecific

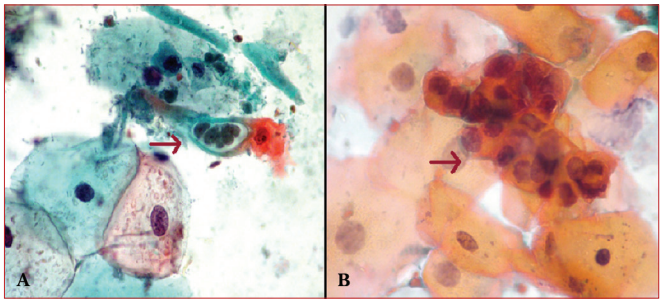

Figure 2. A: Note the presence of multinucleated squamous epithelial single cell (arrow) with nuclear moulding, sometimes evident nucleoli and perinuclear halo (Papanicolaou-immersion-objective 40x); B: Presence of squamous epithelial cells grouped together (arrow), noting enlarged nuclei with hyperchromasia and nuclear chromatin homogeneous, with the nuclear-cytoplasmic preserved (Papanicolaou-immersion-objective 40x).

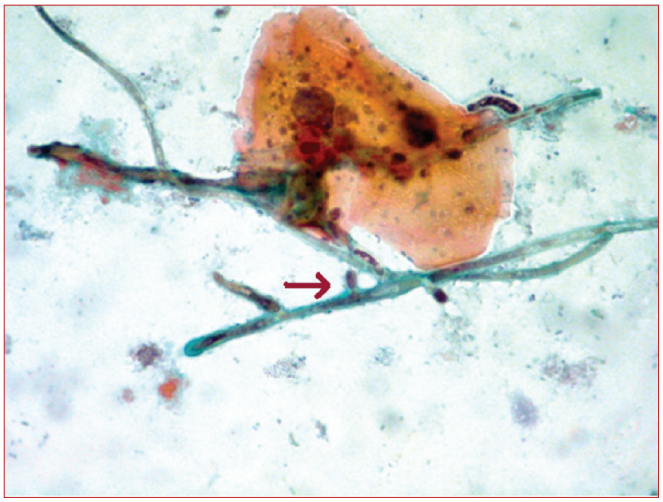

Figure 3. Note the presence of pseudo-hyphae and spores of Candida sp (arrow) next to a squamous epithelial cell (Papanicolaou-immersion-objective 40x).

systemic symptoms such as fever, myalgia and lymphadenopathy[9]. Up to 95% of patients exposed primarily to the HSV symptoms do not show sufficient for the fully characterization of the clinical picture[9]. After the emergence of the systemic symptoms, the localization of the infection occurs in the oral region, with the rise of erythematous, vesicular lesions that can coalesce, often accompanied by local burning[9].

The virus remains latent in ganglia of sensory neurons, and at any structural changes in this infected cell, HSV reactivation occurs. The factors capable of stimulating the reactivation are diverse, with emphasis on immunosuppression, hormonal changes and traumatic injury of the nerve[8]. Relapse usually happens in adults and can occur anywhere on the body, however, it seems to be more frequently on the lips or oral cavity. Over 80% of leukemia patients are seropositive for the virus, with the majority of these patients being affected by viral reactivation[10].

In immunosuppressed individuals, pictures of primary infection can occur, causing more severe clinical manifestations and long lasting. The atypical clinical profiles are also quite common and occur with the emergence of lesions of different morphologies, complicating the diagnosis and delaying the treatment. Some authors indicate the treatment of immunocompromised patients with antiviral only before suspected of being infected with herpes simplex, in this case, the emergence of an oral lesions[11].

The mouth is considered the first target for infection in patients with leukemia, especially in the initial period of chemotherapy treatment (4 weeks), in which granulocytopenia and lymphocytopenia are more pronounced[12].

It is important to mention that the fungus Candida is a commensal in most medical conditions, especially in oro-gastodigestivo and vaginal tract[13,14]. In situations of immunosuppression and/or changes in normal flora, this fungal colonization may be an aggravation of the infection caused by another agent (fungus or bacteria), similar to the clinical pictured above[15-18].

Additional studies support the diagnosis. The cytodiagnosis method of Tzanck is effective by showing multinucleated balloning cells with homogeneous cytoplasm[19]. The serologic evaluations, by ELISA, are the most useful method in clinical practice due to its low cost and high sensitivity and specificity, but the gold standard for diagnosis remains the isolation of virus from infected cells[20]. Direct immunofluorescence is also a good method of high sensitivity, but depends on the presence of active lesions for sampling. When the mucositis associated with chemotherapy is present, a clinical diagnosis of HSV becomes more difficult, requiring is thus these other diagnostic tools.

Acyclovir is the drug of choice in the treatment of herpes simplex, showing properties of shortening the course of the infection and prevent its severe forms. The drug has low interaction with other drugs and its dose is of 1g/day (5 doses of 200 mg) for a minimum of 10 days, and it can be used the duplicated dose for immunosuppressed or in extensive disease[21]. The treatment in immunosuppresesed patients is still controversial, especially due to the emergence of strains resistant to the antiviral.

CONCLUSION

The oral lesions of herpes virus in immunosuppressed patients can have varied presentations and can often go unnoticed, as in mild presentations or asymptomatic patients. However, due to the possibility of systemic spread of infection and the occurrence of severe complications, it should be highly suspicious when facing the emergence of any type of oral lesions in this patient. Therefore, the diagnosis of herpes in orofacial

lesions must always be considered. Also noteworthy is the importance of a multidisciplinary team in management of these infections (ENT, infectious disease specialists, dentists).

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