Seropositive HIV diagnosis after oral histoplasmosis: the importance of multiprofessional care in health

Diagnóstico de soropositividade HIV após Histoplasmose oral: a importância do cuidado multiprofissional em saúde

Diagnóstico de seropositividad al VIH tras histoplasmosis oral: la importancia de la asistencia sanitaria multiprofesional

Received: 24/08/2020 | Reviewed: 29/08/2020 | Accept: 03/09/2020 | Published: 03/09/2020

Gabriela Fleury Seixas ORCID: https://orcid.org/0000-0002-2739-0307 Universidade Norte do Paraná, Brasil E-mail: fleuryseixas@gmail.com Aline Fernanda Spadrizani ORCID: https://orcid.org/0000-0001-7308-0118 Universidade Norte do Paraná, Brasil E-mail: afspadrizani@gmail.com **Danielle Gregorio** ORCID: https://orcid.org/0000-0002-0098-624X Universidade Norte do Paraná, Brasil E-mail: daanigregorio@gmail.com **Marcelo Lupion Poleti** ORCID: https://orcid.org/0000-0003-1904-5762 Instituto Federal de Educação, Ciência e Tecnologia do Paraná, Brasil E-mail: marcelo.poleti@ifpr.edu.br **Thais Maria Freire Fernandes** ORCID: https://orcid.org/0000-0002-4368-8568 Universidade Norte do Paraná, Brasil E-mail: thaismaria@hotmail.com

Abstract

Histoplasmosis is a systemic fungal disease, which can manifest with extrapulmonary lesions. Oral lesions are rarely the first manifestation of late histoplasmosis and can represent an important process of immune imbalance. The objective of this work is to present a clinical case of Histoplasmosis with an oral manifestation of a patient who was unaware of her condition with the Human Immunodeficiency Virus (HIV). The patient's main complaint was a painful ulcer in the central region of the tongue present for two months, whose incisional biopsy resulted in the diagnosis of Histoplasmosis. Although referred for medical treatment with an infectologist, the patient had complications resulting from the disease and died after one month. This situation demonstrates the importance of multidisciplinary care in the prevention, diagnosis and treatment of diseases. The correct diagnosis and treatment can be decisive in the prognosis of patients and demonstrates the relevance of the dentist's knowledge about the various systemic diseases that present oral manifestations.

Keywords: HIV Seropositivy; Histoplasmosis; Oral manifestations; Diagnosis, oral.

Resumo

A histoplasmose é uma doença fúngica sistêmica, que pode manifestar-se com lesões extrapulmonares. As lesões orais raramente são a primeira manifestação da histoplasmose tardia, e pode representar um importante processo de desequilíbrio imunológico. O objetivo desse trabalho é apresentar um caso clínico de Histoplasmose com manifestação oral de uma paciente que desconhecia sua condição portadora do Vírus da Imunodeficiência Humana (HIV). A queixa principal da paciente era uma úlcera dolorosa em região central da língua presente há dois meses, cuja biópsia incisional resultou no diagnóstico de Histoplasmose. Embora encaminhada para tratamento médico com infectologista, a paciente teve complicações decorrentes da doença e veio a óbito após um mês. Essa situação demonstra a importância do cuidado multidisciplinar na prevenção, diagnóstico e tratamento de doenças. O diagnóstico e tratamento acertados podem ser decisivos no prognóstico dos pacientes e demonstra a relevância do conhecimento do cirurgião-dentista acerca das diversas doenças sistêmicas que apresentam manifestação oral.

Palavras-chave: Soropositividade para HIV; Histoplasmose; Manifestações bucais; Diagnóstico Bucal.

Resumen

La histoplasmosis es una enfermedad fúngica sistémica que puede manifestarse con lesiones extrapulmonares. Las lesiones orales rara veces son la primera manifestación de histoplasmosis tardía y pueden representar un proceso importante de desequilibrio inmunológico. Este trabajo tiene como finalidad presentar un caso clínico de Histoplasmosis con manifestación oral de una paciente que desconocía su condición con el Virus de la Inmunodeficiencia Humana (VIH). Además, tuvo como principal síntoma una úlcera dolorosa en la región central de la lengua durante dos meses, cuya biopsia incisional resultó el diagnóstico de Histoplasmosis. Aunque hizo el tratamiento médico con un infectólogo, la paciente tuvo complicaciones debido a la enfermedad y falleció después de un mes. Por lo tanto, esta situación señala la importancia de la atención multidisciplinar en la prevención, diagnóstico y tratamiento de enfermedades. Al mismo tiempo, el diagnóstico correcto y tratamiento puede ser determinante en el pronóstico de los pacientes y demuestra la relevancia del conocimiento del odontólogo acerca de las diversas enfermedades sistémicas que presentan manifestaciones bucales.

Palabras clave: Seroposividad para VIH; Histoplasmosis; Manifestaciones bucales; Diagnóstico bucal.

1. Introduction

Histoplasmosis is a systemic mycosis that is caused by inhalation of the spores of *Histoplasma* Capsulatum (CDC, 2018) and can result a distinct clinic aspect depending on the host's immunological response, the size of the inhaled inoculum and the virulence of the pathogen (Almeida *et al.*, 2019; Oliveira *et al.*, 2020).

Disseminated form of the histoplasmosis can be observed months to years after contamination, and it is characterized by chronic progression of the primary infection and presents damage in several organs (Hendren *et al.*, 2017; Oliveira *et al.*, 2020). In the tardy manifestation, extrapulmonary lesions can be observed especially in the oral cavity and intestine (Azar & Hage, 2017; Evrard *et al.*, 2018). Lesions in the oral cavity rarely are the first finding and can represent a relevant progress of the disease or an immune deficiency (Telles, Karki & Marshall, 2016; Vidya *et al.*, 2016; Folk & Nelson, 2017), and the differential diagnosis must include tuberculosis and carcinoma (Valle *et al.*, 2016; Oliveira *et al.*, 2020). The correct diagnosis and treatment can be decisive in the prognosis of the patient and shows the importance of the dentist about it.

The purpose is to present a case of oral histoplasmosis in a patient who is unknown to Human Immunodeficiency Virus (HIV) positive. The case is discussed to call the attention of the importance of multi professional care in health.

2. Case Report

A female patient, 54 years-old, melanoderma, was referred to the clinic at Universidade Norte do Paraná - UNOPAR/PR for evaluation of complaints of pain in the tongue two months ago. The informed consent form was signed at the first appointment.

The medical history was not contributed to the diagnosis. The patient reported that has been attended at a hospital health unit in the municipality because of the facial lesion, but it was asymptomatic. Reported to the doctor that was been felt a lot of pain in your tongue. According to the patient, the doctor performed only a biopsy of the facial lesion 21 days ago but did not prescribe medication for tongue pain control nor requested serological tests. While waiting for the biopsy result, the patient returned to the doctor because she felt a lot of pain in your tongue. The doctor examined the patient again and asked her to wait for the biopsy result, as it was the same lesion on her face.

The patient reported not using continuous medications and not having chronic diseases. In the extraoral physical examination, an ulcerated lesion on the face was observed in the masseteric region (Figure 1a), which had already undergone a biopsy (later diagnosed as Kaposi's Sarcoma). On your face was possible observed several purplish papules (Figure 1b). The patient reported that the lesion of the figure 1a started like this lesion of the figure 1b.

Figure 1 - 1a - Extraoral view showing the ulcerated lesion in patient's right masseteric region; 1b - Extraoral view showing the purpish papule (arrow) in her face.



Source: Authors.

The intraoral physical examination showed an extensive ulcer (5cm) in the center of the back of the tongue (Figure 2). The lesion had a granulomatous background and high painful symptoms. It was possible to observe tissue destruction and exposure of muscle bundles, which justifies the patient-related pain.

Figure 2 - Extensive ulcer in the center of the back of the tongue.



Source: Authors.

Because of the distinct clinical condition, dental team choose to perform an incisional biopsy of the right side of the tongue lesion. The biopsy was performed anteriorly of the lesion to facilitate suturing. The presumptive diagnosis was made of histoplasmosis and squamous cell carcinoma.

The material was taken to anatomopathological examination, and microscopically a fragment of the mucosa with parakeratinized squamous epithelium and under connective tissue showing chronic inflammatory infiltrate was observed. It was also noted the presence of structures stained by periodic acid Schiff (PAS) and Gomori-Grocott (GMS) positive, compatible with *Histoplasma* (Figure 3).

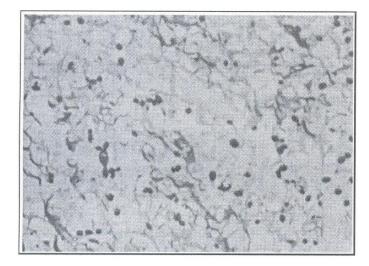


Figure 3 - Silver stain histoplasm (Gomori-Grocott)

Source: Authors.

The patient was referred to the doctor at hospital health unit, confirming the diagnosis of HIV seropositive and starting local treatment with nystatin prescribed by the medical team. She died 45 days after the diagnosis due to complications of Histoplasmosis, with pulmonary complications.

3. Discussion

The common clinical manifestations of progressive disseminated histoplasmosis are fever, fatigue, weight loss and hepatomegaly (Wheat *et al.*, 2016; Hendren *et al.*, 2017), and the most common areas of lesion manifestation are tongue, cheek mucosa and palate (Telles, Karki & Marshall, 2016; Folk & Nelson, 2017). The oral manifestation can often show

similarity with squamous cell carcinoma lesions, as was one of the diagnostic hypotheses raised: ulcers with inflamed base, irregular edges and high level of pain that last for several weeks. Tongue squamous cell carcinoma often occurs on the posterior lateral edge or the ventral surface. The clinical recognition about these pathologies is essential for the possibility of early diagnosis and adequate treatment.

Most individuals (immunocompetent) who contract histoplasmosis show no signs or symptoms of infection. In patients with Acquired Immune Deficiency Syndrome (AIDS), the clinical manifestations are similar, and changes occur, in the central nervous system, gastrointestinal and cutaneous, however in a small percentage of the population (Vidya *et al.*, 2016) and disproportionally the immunocompromised (Folk & Nelson, 2017). Approximately 10% of patients have shock and multiple organ failure (NIH, 2019). The approximate mortality of Disseminated Histoplasmosis is 30 to 50%, when treated and 100%, when not treated (Bongomin, Kwizera & Denning, 2019) and quite related to HIV infection (CDC, 2018).

Disseminated histoplasmosis is currently one of the factors that determine AIDS status (Vidya *et al.*, 2016; Hendren *et al.*, 2017). Histopathological examination shows a typical granuloma and with specific staining. That represents the gold standard for the diagnosis of histoplasmosis. The presence of hyphae is not pathognomonic of active disease and, when present, must be associated with clinical signs to conclude the diagnosis (Azar & Hage, 2017).

The Center for Disease Control and Prevention (CDC) indicates the training of laboratories in Latin America to perform Histoplasmosis, to carry out surveillance and reduce the burden of HIV-associated Histoplasmosis in these areas (CDC, 2018). Therefore, some facial and oral alterations can instigate the patient to seek a professional diagnosis of the alteration because they are visually accessible. Diagnosis time consuming and difficult to appropriate treatment can lead histoplasmosis may be killing numerous patients in Latin America (Nacher *et al.*, 2020). The treatment of disseminated histoplasmosis is usually carried out with amphotericin B and itraconazole.

4. Final Considerations

Although Histoplasmosis primary oral manifestations are rare, knowledge about the clinical characteristics (single ulcer with firm edges associated with high pain that last for several weeks) and need for appropriate diagnostic tests is of paramount importance for

dentists and doctors, who can assist in the diagnosis of systemic pathologies with immunological involvement. This case demonstrates the need for multidisciplinary care so that the correct diagnosis and treatment of oral lesions as manifestations of systemic diseases can occur to improve the prognosis.

Referências

Almeida, M. A., Almeida-Silva, F., Guimarães, A. J., Almeida-Paes, R. & Zancopé-Oliveira,
R. M. (2019). The occurrence of histoplasmosis in Brazil: A systematic review. *International Journal of Infectious Diseases*. 86:147-156.

Azar, M. M., & Hage, C. A. (2017). Clinical Perspectives in the Diagnosis and Management of Histoplasmosis. Clinics in Chest Medicine, 38(3), 403-415.

Bongomin, F., Kwizera, R. & Denning, D. (2019). Getting Histoplasmosis on the Map of International Recommendations for Patients with Advanced HIV Disease. *Journal of Fungi*. 5(3):1-7.

CDC. Center for Disease Control and Prevention. (2018). Available in < https://www.cdc.gov/fungal/diseases/histoplasmosis/index.html> Acess: 02/2020.

Evrard, S., Caprasse, P., Gavage, P., Vasbien, M., Radermacher, J., Hayette, M-P., Sacheli, R., Van Esbroeck, M., Cnops, L., Firre, E., Médart L., Moerman, F. & Minon, J-M. (2018). Disseminated histoplasmosis: case report and review of the literature. *Acta Clinica Belgica*. 73(5):356-363.

Folk, G. A. & Nelson, B. L. (2017). Oral Histoplasmosis. *Head and Neck Pathology*. 11:513-516.

Hendren, N., Yek, C., Mull, J. & Curtell, J. B. (2017). Disseminated histoplasmosis presenting as multiple oral ulcers. *BMJ Case Report*. 2017:bcr2017220364.

Klein, I. P., Martins, M. A. T., Martins, M. D. & Carrard, V. C. (2016). Diagnosis of HIV infection on the basis of histoplasmosis-related oral ulceration. *Special Care in Dentistry*. 36(2): 99-103.

Nacher, M., Coupplié, P., Epelboin, L., Djossou, F., Demar, M. & Adenis, A. (2020). Disseminated Histoplasmosis: Fighting a neglected killer of patients with advanced HIV disease in Latin America. *PLOS Pathogens*. 16(5):e1008449.

NIH. National Institutes of Health. (2019). Panel on Opportunistic Infections in Adults and Adolescents with HIV. Guidelines for the prevention and treatment of opportunistic infections in adults and adolescents with HIV: recommendations from the Centers for Disease Control and Prevention, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America. Available in http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf>. Acess: 08/02/2020.

Oliveira, D. G., Felix, K. C. S., Farias, J. V. C. & Farias, I. C. C. (2020). Clinical and laboratory aspects of histoplasmosis: a bibliographic review. *Research, Society and Development*. 9(7):1-26, e476974353.

Telles, D. R., Karki, N. & Marshall, M. W. (2017). Oral Fungal Infections. *Dental Clinics of North America*. 61(2):319-349.

Valle, A. C. F., Moreira, L. C., Almeida-Paes, R., Moreira, J. S., Pizzini, C. V., Muniz, M. M.
& Zancopé-Oliveira, R.M. (2006). Chronic Disseminated Histoplasmosis with lesions restricted to the mouth: case report. *Revista do Instituto de Medicina Tropical São Paulo*. 48(2):113-6.

Vidya, K. M., Rao, U. K., Nittayananta, W., Liu, H. & Owotade, F. J. (2016). Oral mycosis and other opportunistic infections in HIV: therapy and emerging problems – a workshop report. *Oral Diseases*. 22 (1):158-165.

Wheat, L. J., Azar, M. M., Bahr, N. C., Spec, A., Relich, R. F. & Hage, C. (2016). Histoplasmosis. *Infectious Disease Clinics of North America*. 30(1):207-227.

Percentage of contribution of each author in the manuscript

Gabriela Fleury Seixas – 20% Aline Fernanda Spadrizani – 20% Danielle Gregório – 20% Marcelo Lupion Poleti – 20% Thais Maria Freire Fernandes – 20%