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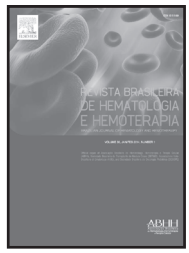

Original article

Early and late oral features of chronic graft-versus-host disease

Alessandra Oliveira Ferrari Gomes[a], *Sandra Regina Torres*[a], *Angelo Maiolino*[a], *Cesar Werneck Noce dos Santos*[a], *Arley Silva Junior*[a,b], *Maria Elvira Pizzigatti Correa*[c], *Maria Cláudia Rodrigues Moreira*[d], *Lucio de Souza Gonçalves*[a]

[a] *Universidade Federal do Rio de Janeiro (UFRJ), Rio de Janeiro, RJ, Brazil*
[b] *Universidade Federal Fluminense (UFF), Niterói, RJ, Brazil*
[c] *Universidade Estadual de Campinas (UNICAMP), Campinas, SP, Brazil*
[d] *Instituto Nacional de Câncer (INCA), Rio de Janeiro, RJ, Brazil*

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ABSTRACT

Background: Chronic graft-versus-host disease is a serious complication of allogeneic hematopoietic cell transplantation, and the mouth is one of the affected sites.
Objective: The aim of this study was to evaluate the oral features of this disease after hematopoietic cell transplantation.
Methods: This was a cross-sectional multicenter study that enrolled patients submitted to transplantation. Oral evaluations used the National Institutes of Health criteria, salivary flow rates, and the range of mouth opening. Pain and xerostomia were evaluated through a visual analogue scale. Patients were divided into two groups based on the transplantation time (up to one year and more than one year).
Results: Of the 57 evaluated recipients, 44 had chronic graft-versus-host disease: ten (22.72%) in the group with less than one year after transplantation, and 34 (77.27%) in the group with more than one year after transplantation. Lichenoid/hyperkeratotic plaques, erythematous lesions, xerostomia, and hyposalivation were the most commonly reported oral features. Lichenoid/hyperkeratotic plaques were significantly more common in patients within the first year after the transplant. The labial mucosa was affected more in the first year. No significant changes occurred in the frequency of xerostomia, hyposalivation, and reduced mouth opening regarding time after transplantation.
Conclusion: Oral chronic graft-versus-host disease lesions were identified early in the course of the disease. The changes observed in salivary gland function and in the range of mouth opening were not correlated with the time after transplantation.

Corresponding author at: Universidade Federal do Rio de Janeiro, Departamento de Patologia e Diagnóstico Oral, Avenida Brigadeiro Trompowski, s/n, Ilha do Governador 21941-590, Rio de Janeiro, RJ, Brazil.
E-mail address: alessofg@gmail.com (A.O.F. Gomes).
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Introduction

Allogeneic hematopoietic cell transplantation (HCT) is associated with early and late oral complications. Most of these complications are related to graft-versus-host disease (GVHD) and may cause transitory and/or permanent sequelae. Many studies have reported oral manifestations of chronic GVHD (cGVHD),[1-3] but to the authors' knowledge, only one study has addressed the temporal outcomes of some of these features.[4] Most studies focus on specific oral alterations of cGVHD, and have not used the National Institutes of Health (NIH) criteria to evaluate the oral features.

cGVHD affects from 50% to 80% of the adult patients who undergo HCT, regardless of prophylaxis and donor-patient matching techniques.[2]

Oral manifestations can be the first signs of cGVHD, and might be considered a disease marker.[3,5] These oral manifestations are observed in the majority of cases of cGVHD,[2,5-7] and are considered an important cause of morbidity and loss of quality of life in long-term survivors.[5]

According to the NIH Consensus Criteria for GVHD, the disease is currently diagnosed by its clinical manifestations and no longer according to time post-transplantation.[8] The clinical manifestations of cGVHD are classified as diagnostic, distinctive, or common clinical features. The finding of a 'diagnostic' feature of cGVHD establishes the condition without further testing. In the oral cavity, these features include lichen planus-like lesions, hyperkeratotic plaques, and restriction of mouth opening due to skin sclerosis. 'Distinctive' features are likely to support the diagnosis of cGVHD; however, they are not enough to establish the diagnosis. The oral 'distinctive' features include xerostomia, mucoceles, mucosal atrophy, pseudomembranes, and ulcers. 'Common' features of cGVHD refer to the manifestations found in both acute GVHD and cGVHD, which include gingivitis, mucositis, erythema, and pain.[8]

Some clinical changes of oral cGVHD such as vasculitis-like features or a telangiectatic appearance of the mucosa, inflammation, and loss of the stippling of the attached gingiva may represent early alterations of oral cGVHD, even though they are not considered in the NIH criteria.[2] Erosive lesions are observed in the most severe forms of cGVHD, and are followed by pain, which may interfere in oral hygiene and food ingestion.[9] Xerostomia generally causes discomfort, but hyposalivation, that is, reduced salivary flow rates (SFR), which have more serious consequences, have not been included in the NIH criteria.[10-12]

Temporal features of systemic cGVHD have previously been addressed. However, although oral cGVHD has been analyzed in many publications,[1-3] data regarding the temporal relationship of oral features is lacking. The present study aimed to perform a cross-sectional evaluation of the oral features of cGVHD according to the time after HCT.

Methods

This was a cross-sectional multicenter study conducted in two hospitals in Brazil: Hospital Universitário Clementino Fraga Filho (HUCFF) of the Universidade Federal do Rio de Janeiro (UFRJ) and the Center for Hematology and Hemotherapy of the Universidade Estadual de Campinas, from January of 2008 to January of 2011. Adult patients who underwent HCT for hematological conditions were included. All patients signed an informed consent. This study was approved by the institution's review board and conducted in accordance with the Helsinki Declaration as revised in 2008.

Demographic and clinical characteristics were assessed from medical records. After the transplantation, oral evaluations were performed by a trained dentist. The oral exam was performed using frontal light-emitting diode illumination, with the patient sitting on a chair.

Oral features were classified according to NIH criteria as diagnostic, distinctive, and common features.[8] These features referred to any changes related to oral signs and symptoms (mucosal lesions, perception of changes in salivary flow rate and moisture, changes in sensitivity, and reduction of mouth opening). Oral lesions were defined as morphological changes of the oral mucosa.

The severity of oral symptoms was scored according to the NIH criteria:[8] no symptoms (0); mild symptoms with disease signs not limiting the oral intake (1); moderate symptoms with disease signs, with partial limitation of oral intake (2); and severe symptoms with disease signs and major limitation of oral intake (3). Moreover, the patients graded oral sensitivity through a visual analogue scale (VAS) graduated from 0 (no sensitivity) to 10 (worst possible pain).[13,14] Positive sensitivity was recorded when patients reported symptoms greater than 0 on the VAS.

Resting SFR were used to assess salivary function under standard conditions.[15] Saliva samples were collected between 9:00 a.m and 11:30 a.m.[16] Participants were asked not to eat until the exam was performed. Patients were instructed to spit the accumulated saliva periodically into a disposable cup for five minutes. They were instructed not to eat nor swallow during the exam.[16] The liquid part of the SFR was then measured with a disposable syringe. The SFR results were determined as milliliters per minute, and reduced SFR was defined as < 0.3 mL/min.[11]

Oral dryness was also evaluated using a VAS graduated from 0 (no dryness) to 10 (the worst possible oral dryness). To eliminate common causes of dry mouth feeling, xerostomia was considered when the patient recorded a score > 2.[13]

The oral involvement of scleroderma was evaluated using a Willis compass to measure the maximum range of mouth opening (RMO). The device measured the midline distance from the border of the central upper incisors to the border of the central lower incisors. Reduced RMO was defined as < 35 mm.[17]

In order to analyze the temporal manifestations of cGVHD, the patients were separated in two groups: within one year post-HCT and over one year post-HCT. In general, cGVHD develops from three to 15 months after HCT,[1] and the period of one year post-HCT has been used in some studies to evaluate cGVHD.[18,19] The date of the transplant was an accurate datum and was available for all patients.

The SPSS© version 13.0 (IBM - Chicago, USA) was used to store and analyze data. The differences between groups were analyzed with Fisher's exact test and the Mann-Whitney test for the comparison of categorical and continuous variables, respectively. The level of significance was set as a p-value < 0.05.