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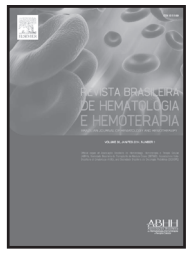

Scientific comment

Oral features of graft-versus-host disease☆

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Chronic graft-versus-host disease (cGVHD) is a late complication of allogeneic hematopoietic stem cell transplant (HSCT), occurring in 18% to 70% of recipients.[1-3] The oral tissues may be involved in up to 90% of the patients that present cGVHD in other organs.[4-10] Oral mucosa lesions and salivary gland dysfunction are the main manifestations of oral cGVHD, but a reduction of the mouth opening due to the perioral deposition of collagen may also occur.[10]

Patients with oral involvement of cGVHD may present sensitivity, pain, xerostomia, and dysgeusia,[10-12] and the severity of the oral manifestations may be associated to the severity of the disease.[5] The sites of the oral mucosa most commonly involved by the lesions are the buccal mucosa and the tongue.[10,13-15] The diagnosis of the oral lesions is based on clinical aspects. However, a biopsy of the oral mucosa and/or minor salivary glands may be requested when oral and systemic signs and symptoms are not sufficient for the diagnosis of cGVHD.[5]

According to the National Institutes of Health (NIH), the oral features of cGVHD may be classified as diagnostic (lichen planus-like changes, hyperkeratotic plaques, and reduction in mouth opening), distinctive (xerostomia, mucoceles, mucosal atrophy, pseudomembranes, and ulcers), and common to both acute graft-versus-host disease and cGVHD (gingivitis, mucositis, erythema, and pain).[16-18] The NIH criteria consider certain subjective data, such as xerostomia and reduction of mouth opening. However, some patients with reduced salivary flow rates and reduced range of mouth opening do not present these symptoms.[10] Thus, a definition of hyposalivation and the expected loss in the range of mouth opening would be more valuable for the clinician.

Oral lesions may persist even after the resolution of cGVHD in other organs.[2] Topical treatment is required in most cases, since oral cGVHD lesions do not completely respond to systemic therapies.[19] Some publications on case series reported good responses of oral lesions to topical treatment with cyclosporin,[20-21] azathioprine,[22-23] budesonide,[19] tacrolimus,[9] and psoralen/ultraviolet light (PUVA).[4,24] Few clinical trials have studied the topical treatment of oral cGVHD lesions with dexamethasone, budesonide, and PUVA.[24-26] Therefore, evidence-based studies on the topical treatment of oral cGVHD lesions with other drugs are needed.

Patients with oral cGVHD lesions frequently have secondary infections, mainly candidiasis. The higher susceptibility to fungal infections is due to factors such as the presence of oral mucosa lesions,[27] the immunosuppressive therapy,[2,4,28] and the reduced salivary flow rates.[1,8,29-35]

The salivary glands represent an important cGVHD target,[1,6,8,29-36] and the antimicrobial and buffer properties of the saliva are important for oral homeostasis.[37] However, individuals are able to distinguish xerostomia only when the salivary flow rates are very low.[38] Salivary gland dysfunction may be detected by scintigraphy and histopathology, but non-invasive exams such as sialometry and sialochemistry may detect quantitative and qualitative alterations, respectively.[37,39,40]

Reduced salivary flow rates may lead to discomfort, dysphagia, dysphasia, dysgeusia, halitosis, and consequent

☆See paper by Gomes AO et al. on pages 43-9.

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infections, including dental decay and candidiasis.[41,42] The early diagnosis of salivary gland dysfunction related to cGVHD is important for the management of dry mouth complications. Moreover, it will help the clinician with the investigation of the cGVHD in other organs. The management of hyposalivation has been extensively addressed, but only few clinical studies verified the improvement of salivary flow rates in a population of cGVHD patients.[1,29,39,43]

Scleroderma may be observed in cGVHD patients, and is characterized by cutaneous sclerosis, but may also involve oral tissues. An increased deposition of collagen may occur in cGVHD patients and lead to a reduction in the mouth opening, limited tongue movement, and dysphagia.[44,45] This will make oral hygiene procedures difficult and may be another factor contributing to infections.

In conclusion, oral features are frequently present in cGVHD patients. Health care professionals should be aware of early oral manifestations of cGVHD in order to manage the complications of these conditions.

In this issue of the Revista Brasileira de Hematologia e Hemoterapia Gomes et al. evaluate oral cGVHD manifestations in less than one year compared to over one year after hematopoietic cell transplantation.[46]

Conflicts of interest

The author declares no conflicts of interest.

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