

*Case Report***Salivary Gland Involvement in Chronic Graft-Versus-Host Disease**Amani Aroua¹, Abdellatif Chokri¹, Faten Hammedi², Sameh Sioud¹, Hajer Hentati¹, Jamil Selmi¹¹Department of Medicine and Oral Surgery of the Dentistry Clinic of Monastir, Tunisia,²Department of Anatomy and Pathological Cytology, Fattouma Bourguiba University Hospital of Monastir, Tunisia.

Corresponding Author: Amani Aroua

*Received: 03/06/2015**Revised: 21/06/2015**Accepted: 29/07/2015***ABSTRACT**

Graft-Versus-Host-Disease (GVHD) is the major complication of allogeneic hematopoietic stem cell transplantation. It is available in two forms (acute and chronic) chronologically separated by the post-transplant hundredth day. Various target organs and tissues can be infiltrated, like the skin, liver, intestinal tract, conjunctivae and oral tissues including the oral mucosa and the salivary glands.

The purpose of this article is to precise the oral manifestations of chronic GVHD, particularly on the salivary glands and for which systemic immunosuppression as well as corticosteroid treatment may offer symptomatic relief.

Keywords: Graft-Versus-Host-Disease, salivary gland, xerostomia, corticosteroids.

INTRODUCTION

Chronic Graft-Versus-Host-Disease (CGVHD) is a common complication of patients undergoing allogeneic transplantation of hematopoietic cells. [1] The disease is mediated by auto reactive T lymphocytes, which infiltrate various target organs and tissues, like the skin, liver, intestinal tract, conjunctivae and oral tissues including the oral mucosa and the salivary glands. [2-4]

Oral manifestations can be the first signs of cGVHD, and might be considered as a disease marker. [1] They are observed in the majority of cases of cGVHD, and are considered an important cause of morbidity. [5]

Involvement of cGVHD on the salivary glands will cause a lack of saliva

production. [6] Hyposecretion or xerostomia will influence the oral mucosa by a reduced quantity and altered quality of the saliva. [7]

The immunosuppressive drugs including corticosteroids and cyclosporine are the most frequently used in the treatment of cGVHD. [1]

The aim of this article is to report clinical case of a patient with recurrent cGVHD suffering from xerostomia which treatment with corticosteroids showed a marked improvement.

CASE REPORT

The patient (O.A) a 36 -year-old man was referred to the department of Medicines and Surgery Oral of the Dentistry Clinic of Monastir, Tunisia for dental care.

The patient is followed in the national center for bone marrow transplant for very severe idiopathic aplastic anemia. He made an allograft in July 2009.



Figure 1: Dry and red conjunctiva, cornea irritated.

The patient has discontinued his immunosuppressive treatment for a year ago and is currently under a local antifungal treatment.

The extra oral examination revealed a painful and limited mouth opening and ocular conjunctivitis (figure 1), hypopigmented beaches at neck and hyperpigmented at trunk.



Figure 2: Tongue dried, smooth and depapillated.

The intraoral examination revealed a red and inflamed gum, pseudo lichenoides

lesions at inner sides of the cheeks, dried and depapillated tongue (figure 2). Also we note a remarkable dry mouth.



Figure 3: Sugar placed during 5 minutes under the tongue (a) and it was a little wet after 5 minutes (b).

A sugar cube test confirmed this xerostomia, which revealed that this one after 5 minutes was very little wet under tongue (Figure 3).



Figure 4: Biopsy of the salivary glands.

The laboratory tests reveal a normal hemostatic balance and viral serology AIDS, hepatitis B and C negative.

A salivary gland biopsy was realized for this patient in our department of the lower lip (figure 4). The result of the histological exam showed severe fibrosis of

the minor salivary glands and reduced number of acini (Figure 5).

From these oral manifestations, a cGVHD has been diagnosed and the patient has been remapped to the national bone marrow transplant center for care where he received treatment with systemic corticosteroids.

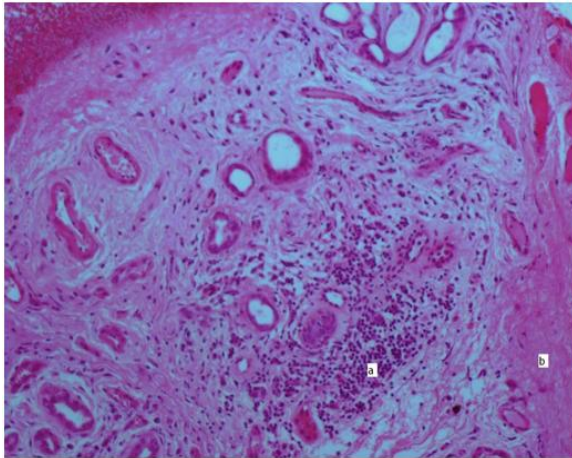


Figure 5: histological section of minor salivary glands showing abundant inflammatory infiltrate (a) and areas of fibrosis (b).



Figure 6: Wet tongue with saliva.

Currently the patient has a marked improvement in the general state. Oral signs regressed with more salivation after his treatment by corticosteroids (Figure 6).

A sugar cube test confirmed this improvement, which revealed that this one after 5 minutes was wet and partially melted (Figure 7).



Figure 7: Sugar placed during 5 minutes under the tongue (a) and it was wet and partially melted after 5 minutes (b).

DISCUSSION

CGVHD is the major complication of allogeneic hematopoietic stem cell transplantation [6] and is defined when the clinical manifestations comes after more than a hundred days. [8]

Frequent sites with cGVHD involvement were skin, conjunctiva, liver, gastrointestinal tract and oral tissues including the oral mucosa and the salivary glands. [2] The oral manifestations of cGVHD consist of xerostomia, erythema, leukoplakia, lichenoid lesions, ulcers, mucosal atrophy, sclerodermatous changes and pyogenic granuloma. [2]

The oral mucosa may be involved in up to 90% of the patients that present cGVHD. [1,9] Involvement of cGVHD on the salivary and lacrimal glands can cause many manifestations such as seen in Sjogren's syndrome-like manifestations including hyposalivation of saliva and tears. [6] Chronic GVHD of the salivary glands cause quantitative and qualitative alterations in saliva, including altered concentrations of electrolytes, epidermal growth factor, and salivary proteins [8] Xerostomia can cause difficulty with speaking, chewing and swallowing, as well as recurrent candidiasis.

In salivary gland hypofunction associated with cGVHD, a biopsy of the

minor salivary glands can provide valuable confirmatory information. [8] The reduced number of acini, inflammatory infiltration often with associated fibrosis characterizes salivary gland cGVHD.

The mechanisms underlying cGVHD are not well understood but the dental professionals should be aware about oral manifestations of GVHD and its treatments. [6,8]

The general therapeutic options in cGVHD have been rather limited until recently, consisting of immunosuppressive agents, mainly methylprednisolone and cyclosporine. [10]

Systemic immunosuppressive therapy is indicated for extensive cGVHD. [6] However, the disadvantage of systemic therapy can cause opportunistic infections and many complications.

Topical management of oral cGVHD may be indicated as complementary therapy to systemic treatment in locally refractory cases or as the sole therapy in cases whereby the oral cavity is the only site involved, this is may prevent the severe side effects associated with systemic treatments. [2] The primary objectives of oral cGVHD management are to reduce symptoms and maintain oral function. [8]

The first-line therapy for oral mucosal cGVHD is intensive topical corticosteroid therapy that can be delivered in various formulations like solutions (Dexamethasone, Budesonide, Prednisolone, Triamcinolone) and gels (creams and ointments). [8]

Other treatment are indicated like the application of tacrolimus ointment used in combination with a corticosteroid solution in patients that do not have an adequate response to topical steroid therapy alone, [1,8] and intralesional injections of triamcinolone acetonide particularly for resolution of refractory and symptomatic localized ulcerative lesions. [8]

The salivary gland damage can be reversible thanks to treatment with corticoid drugs or refractory for this treatment, then we need to use saliva substitutes who help to reduce this xerostomia. Salivation can be stimulated by gustatory and masticatory means through the use of sugar-free chewing gums and candies. [8]

CONCLUSION

In conclusion, diagnosis of cGVHD can be established by the presence of oral manifestations where the role of the dental professionals. The treatment can significantly improve the patient's clinical status.

REFERENCES

1. André Eckardt, Oliver Starke, Michael Stadler, Christoph Reuter, Bernd Hertenstein. Severe oral chronic graft-versus-host disease following allogeneic bone marrow transplantation: highly effective treatment with topical tacrolimus. *Oral Oncology*. 2004; 40: 811-814.
2. Sharon Elad, DMD, a Reuven Or, MD, b Adi A. Garfunkel, DMD, c and Michael Y. Shapira, MD, d Jerusalem, Israel. Budesonide: A novel treatment for oral chronic graft versus host disease. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod*. 2003; 95:308-11.
3. James W. Curtis, Jr, DMD, a and Gretchen B. Caughman, PhD, b Augusta, Ga. An apparent unusual relationship between rampant caries and the oral mucosal manifestations of chronic graft-versus-host disease, *Oral Surg Oral Med Oral Pathol*. 1994; 78:267-72.
4. Nathaniel S. Treister, 1 Earl Francis Cook, Jr., 1 Joseph Antin, 2 Stephanie J. Lee, 3 Robert Soiffer, 2 Sook-Bin Woo. Clinical Evaluation of Oral Chronic Graft-Versus-Host Disease, *Biology of Blood and Marrow Transplantation*. 2008; 14:110-115

5. Alessandra Oliveira Ferrari Gomesa, Sandra Regina Torresa, Angelo Maiolinoa, Cesar Werneck Noce dos Santosa, Arley Silva Juniora,b, Maria Elvira Pizzigatti Correac, Maria Cláudia Rodrigues Moreirad, Lucio de Souza Gonçalve. Early and late oral features of chronic graft-versus-host Disease. Rev Bras Hematol Hemoter. 2014; 36(1):43-49.
6. Martin M. Imaniguli,¹ Jane C. Atkinson,² Sandra A. Mitchell,³ Daniele N. Avila,¹ Rachel J. Bishop,⁴ Edward W. Cowen,⁵ Manuel B. Datiles,⁴ Frances T. Hakim,¹ David E. Kleiner,⁶ Michael C. Krumlauf,¹ Steven Z. Pavletic¹. Salivary Gland Involvement in Chronic Graft-Versus-Host Disease: Prevalence, Clinical Significance, and Recommendations for Evaluation. Biol Blood Marrow Transplant. 2010; 16: 1362-1369.
7. Nagler RM, Nagler A. Major salivary gland involvement in graft-versus-host disease: considerations related to pathogenesis, the role of cytokines and therapy. Cytokines, Cellular and Molecular Therapy. 1999; 5(4):227-32.
8. Michal Kuten-Shorrer, DMDa, Sook-Bin Woo, DMD, MMScb, Nathaniel S. Treister, DMD, DMScb. Oral Graft-Versus-Host Disease. Dent Clin N Am. 2014; 58:351-368.
9. Sandra Regina Torre. Oral features of graft-versus-host disease, Rev Bras Hematol Hemoter, 2014; 36(1):9-11.
10. Raphael M. Nagler MD DMD PhD¹ and Arnon Nagler MD MSc². Salivary Gland Involvement in Graft-Versus-Host Disease: the Underlying Mechanism and Implicated Treatment, Imaj. 2004; 6:167-172.

How to cite this article: Aroua A, Chokri A, Hammedi F et al. Salivary gland involvement in chronic graft-versus-host disease. Int J Health Sci Res. 2015; 5(9):552-556.

International Journal of Health Sciences & Research (IJHSR)

Publish your work in this journal

The International Journal of Health Sciences & Research is a multidisciplinary indexed open access double-blind peer-reviewed international journal that publishes original research articles from all areas of health sciences and allied branches. This monthly journal is characterised by rapid publication of reviews, original research and case reports across all the fields of health sciences. The details of journal are available on its official website (www.ijhsr.org).

Submit your manuscript by email: editor.ijhsr@gmail.com OR editor.ijhsr@yahoo.com