

Case Report

# Oral Manifestations of Graft Versus Host Disease – Clinical Presentations After Allogeneic Hematopoietic Cell Transplantation

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## Abstract

Oral chronic graft versus host disease (OcGvHD) is characterized by a myriad of clinical signs and symptoms. The oral health status can be debilitating to the patient by exacerbated mucosal symptoms and decreasing quality of life. Oral manifestations may acutely present as mild to moderate erythematous lesions on mucosal surfaces, painful recurrent mucosal ulcers, and salivary gland hypofunction. At later stages, oral lesions presents with more severe signs and symptoms, including lichenoid lesions characterized by white striations, plaques, and erosions resembling oral lichen planus, mucosal atrophy characterized by thin, fragile mucosa prone to ulcerations and oral infections, trismus due to temporomandibular joint fibrosis, persistent salivary gland hypofunction leading to dysphagia and increased risk of caries and oral candidiasis, and heightened susceptibility to bacterial and viral infections due to impaired mucosal integrity. Amongst oral manifestations, other organs may be involved including the skin, eyes, liver and gastrointestinal tract. The oral manifestations of OcGvHD should be carefully monitored for its progression due to its malignant potential. This case report presents oral manifestations of OcGvHD appeared to develop 4 months after allogeneic hematopoietic cell transplantation in a 58-years old male patient who was referred to the Oral Medicine clinic from his hematologist for evaluation of widespread oral lesions.

## Keywords

Oral Chronic Graft-Versus-Host Disease, Allogeneic Hematopoietic Cell Transplantation, Lichenoid Mucositis, Xerostomia

## 1. Introduction

Graft-versus-host disease is the most frequent and potentially fatal complication of an allogeneic hematopoietic progenitor cell transplantation [1]. It appears when immunocompetent T cells from donor origin recognize antigens from

recipient origin as foreign [1]. The immune response activates donor T cells and destroys recipient tissues [1]. It can present as acute and chronic affecting multiple organs; skin, liver, gastrointestinal tract and the oral cavity [1].

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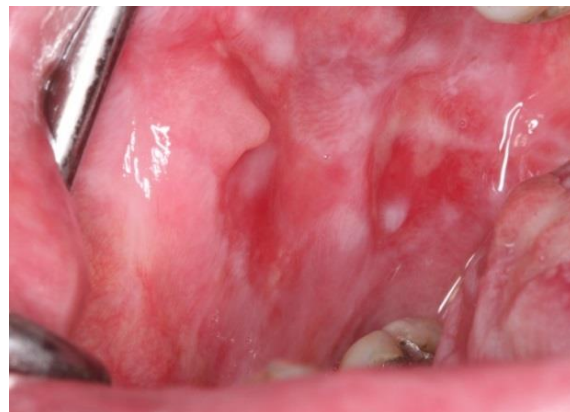
Oral chronic graft versus host disease (OcGvHD) is characterized by a range of signs and symptoms, including mucosal erythema, painful ulcerations, lichenoid lesions, and salivary gland hypofunction [2]. These manifestations are a result of the inflammatory process affecting the oral mucosa and salivary glands [2]. OcGvHD can lead to severe discomfort, difficulty eating, speaking, and swallowing, and increased susceptibility to dental caries and infections [3]. Other manifestations may result in tissue fibrosis and long-term damage to the oral tissues, complicating both oral health and overall patient well-being [4].

The management of OcGvHD requires a balanced immune suppression to control disease activity with efforts to preserve salivary function to avoid long term complications such as fibrosis and dental decay [5]. This includes topical therapy such as corticosteroids which is the first-line treatment for localized inflammation in the form of corticosteroid mouthwash [3]. As for systemic therapy it is indicated for severe OcGvHD or when other organs are involved, which comprise systemic corticosteroids; prednisone (0.5-1 mg/kg/day), immunosuppressive agents and biologic agents [3]. In addition, saliva substitutes, oral hygiene and dietary modifications are recommended to manage further complications of the disease [6].

## 2. Case Report

A 58-years old male patient was referred to the Oral Medicine clinic from his hematologist for evaluation of widespread oral lesions. The patient was presented with extensive oral ulcerations involving the buccal mucosa bilaterally consistent with lichenoid mucositis (Figures 1 and 2). The right buccal mucosa showed a relatively more extensive involvement than the left buccal mucosa. The tongue showed multiple large ulcerations surrounded by erythema and plaque-like background lesion affecting the full dorsum surface of the tongue. In the left aspect of the tongue, an indurated ulcer is noted. The extent of its involvement seems to involve the latero-ventral aspect of the tongue. Upon detailed history and examination, the lesions appeared to develop 4 months after allogeneic hematopoietic cell transplantation. Initially, there were no symptoms associated with the development of oral lesions; however, the present clinical status was accompanied by pain with spicy and acidic foods, altered saliva quantity and quality thereby compromising nutrition, speech and swallowing. The impact of salivary dysfunction has recently become debilitating to the patient by exacerbating mucosal symptoms and decreasing quality of life. Systemically, the eyes demonstrated dryness, and recent gastrointestinal symptoms are under further investigation by gastroenterology. The short and long-term management plan for the patient comprises of the prescription of topical corticosteroid mouthwash to reduce the lichenoid inflammatory process thereby facilitating healing of the presenting mucosal ulcerations. Close observation following the use of topical therapy is

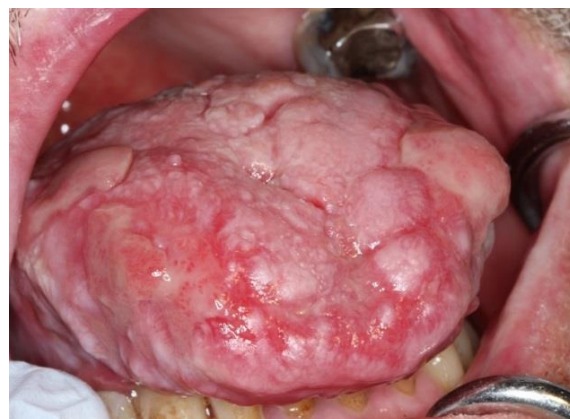
mandatory, followed by long-term clinical follow-up reviews to monitor clinical progression. The mainstay of the overall patient care is to prevent malignant transformation of mucosal lesions and improve quality of life by addressing the current signs and symptoms.



**Figure 1.** Right buccal mucosa extensive mucosal ulcerations surrounded by erythematous background consistent with lichenoid mucositis.



**Figure 2.** Left buccal mucosa lichenoid mucositis.



**Figure 3.** Extensive ulcerations involving the dorsum surface of the tongue with erythematous and plaque-type background extending to the latero-ventral surface (right).

### 3. Discussion

#### 3.1. Diagnosis of OcGvHD

In the presented case, the patient developed signs and symptoms of OcGvHD 4 months post-hematopoietic cell transplantation. OcGvHD can present with a variety of symptoms, often reflecting the severity and stage of the disease [7]. Recognizing these symptoms early is essential for diagnosis and management [7]. In the acute phase, typically occurring within 100 days post-transplant, oral acute graft versus host disease manifests as mild to moderate erythematous lesions on mucosal surfaces such as the buccal mucosa, soft palate, and tongue, painful recurrent mucosal ulcers, and salivary gland hypofunction due to salivary gland damage, which can increase the risk of oral infections [7]. OcGvHD, which often manifests after the first 100 days post-transplant but may also develop at later stages of the disease, presenting with more severe symptoms, including lichenoid lesions characterized by white striations, plaques, and erosions resembling oral lichen planus, mucosal atrophy characterized by thin, fragile mucosa prone to ulcerations and oral infections, trismus due to temporomandibular joint fibrosis, persistent salivary gland hypofunction leading to dysphagia and increased risk of caries and oral candidiasis, and heightened susceptibility to bacterial and viral infections due to impaired mucosal integrity [8]. The diagnosis of OcGvHD involves a comprehensive clinical assessment supported by a detailed patient history, especially regarding the type of transplant (autologous vs. allogeneic), the time since transplantation, and the use of immunosuppressive medications, along with documentation of oral signs and symptoms [8]. Early recognition of these symptoms is critical for timely diagnosis and management [8]. While clinical examination provides essential findings, a definitive diagnosis often requires histopathological assessment from lesional tissue to exclude malignancy [8]. Incisional biopsy of affected oral mucosa can reveal characteristic findings: in the acute phase, a band-like lymphocytic infiltrate at the basal epithelial layer, vacuolar degeneration of basal cells, and apoptotic keratinocytes may be seen [9]. In OcGvHD, denser lymphocytic infiltrates, epithelial atrophy, submucosal fibrosis, and thinning of the mucosa may be seen [5]. Histopathological findings should be interpreted in the context of the patient's clinical history, particularly regarding transplant type and timing, as well as differential diagnoses such as oral lichen planus, infections such as oral candidiasis and herpes simplex, and drug reactions due to immunosuppressive medications [9].

#### 3.2. Complications of OcGvHD

OcGvHD is a significant complication of hematopoietic stem cell transplantation, presenting a range of challenges in both diagnosis and management [8]. OcGvHD commonly manifests symptoms such as mucosal dryness, pain, extensive

ulcerations, erythema, and lichenoid-like changes, impairing mastication, speech, and oral hygiene maintenance [8]. The chronic nature further complicates its impact on the patient's quality of life, with potential psychological consequences such as anxiety, depression, and social withdrawal [10]. Impaired salivary gland function and mucosal integrity also increase the risk of oral infections, dental caries, and periodontal disease, making oral care even more challenging [11]. As the disease progresses, fibrosis and atrophy may permanently damage the oral tissues, contributing to long-term functional impairments [11].

Management typically involves immunosuppressive therapy, such as corticosteroids, and requires a multidisciplinary approach, including collaboration with dental professionals to address complications such as dry mouth, infections, and mucosal irritation [5]. Early recognition and intervention are crucial to mitigating long-term sequelae, such as tooth loss and diminished oral function [5].

#### 3.3. Management of OcGvHD

The management of this patient with oral chronic graft-versus-host disease (OcGvHD) is centered on immune suppression, symptom relief, oral health preservation, and infection prevention. Topical dexamethasone mouthwash (0.1 mg/mL, 5 mL, 2–6× daily) was prescribed as first-line therapy to control oral ulcerations, lichenoid mucositis, erythema, and pain, in accordance with current clinical guidelines [12]. The patient was instructed to swish the solution for 3–5 minutes before spitting it out and to wait 10–15 minutes before eating or drinking to enhance efficacy [12]. To manage salivary gland dysfunction and prevent complications such as fibrosis, dental caries, and mucosal infections, the patient was encouraged to use artificial saliva substitutes and was prescribed sialogogues, such as pilocarpine (5–10 mg, 3× daily), to stimulate saliva production [13].

Furthermore, oral hygiene optimization was prioritized by recommending fluoride toothpaste, and regular professional dental cleanings every 3–6 months. These measures aimed to minimize the risk of secondary infections, mucosal irritation, and dental decay [12]. Dietary modifications, including the avoidance of spicy, acidic, and hot foods, were suggested to reduce mucosal irritation and discomfort [13].

Given the increased risk of oral infections, particularly oral candidiasis due to topical steroid use, prophylactic fluconazole (100 mg/day for 1 week, if needed) was prescribed to prevent fungal overgrowth [12].

The risk of secondary malignancy necessitated routine oral cancer screenings every 6–12 months, with a plan for biopsy of any persistent or suspicious lesions [13]. To ensure a comprehensive treatment strategy, a multidisciplinary approach was implemented, involving hematologists, oral medicine specialists, ophthalmologists, and gastroenterologists to address both oral and systemic manifestations [13].



## 4. Conclusion

Oral chronic graft-versus-host disease (OcGvHD) remains a significant and challenging complication of allogeneic hematopoietic cell transplantation, impacting both oral health and overall patient well-being. The case presented highlights the diverse clinical manifestations of OcGvHD and underscores the importance of early diagnosis and multidisciplinary management. Effective treatment strategies, including topical and systemic immunosuppressive therapies, alongside supportive oral care, are crucial in minimizing disease progression and improving the patient's quality of life. Given the potential for malignant transformation, long-term monitoring and individualized treatment plans are essential. Patient education and regular follow-ups play a crucial role in preventing secondary complications such as xerostomia, infections, and fibrosis. Future research should focus on refining treatment modalities, optimizing immunosuppressive regimens, and exploring novel targeted therapies to enhance clinical outcomes. By integrating comprehensive oral healthcare strategies with advancements in transplantation medicine, the burden of OcGvHD can be mitigated, ultimately improving patients' survival and quality of life.

## Abbreviations

OcGvHD    Oral Chronic Graft-Versus-Host Disease

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## Author Contributions

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**Qutaibah Alfadallah:** Project administration, Writing – original draft, Writing – review & editing

## Conflicts of Interest

The authors declare no conflicts of interest.

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