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Case Report

Oral Manifestations in a Patient with Graft Versus Host Disease: A Case Report with a 12-month Follow-Up

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Abstract

Graft Versus Host Disease (GVHD) is a common but serious complication of allogeneic haematopoietic stem cell transplantation. Oral alterations of GVHD occur most of the patient with GVHD and may be early manifestation of this disease. The purpose of this case report was to present the unusual lesions of gingival tissues during, to understand and increase our knowledge about the oral alterations and the treatment required for GVHD. A 30-year-old woman was diagnosed with chronic myelocytic leukemia and underwent the bone marrow transplantation. Appropriate therapy was initiated, and it received a good clinical response at all sites affected by GVHD, except in the oral cavity. She was referred to the periodontology clinic of the Faculty of Dentistry, persisting oral ulceration (mucositis), pain and xerostomia associated with GVHD. According to the clinical and radiographic findings, periodontal treatment was started with an initial phase of mechanical therapy; including systematic scaling and planning of all accessible root surfaces, improved oral hygiene, use of topical medications and monitored diet. The oral evolution of the disease was excellent and all oral manifestations were eliminated. The management of GVDH can reduce oral alterations that can interfere with oral function and quality of life, and can reduce the need for more intensive immunosuppressive systemic therapies.

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Submitted: 06 June 2014

Accepted: 08 June 2014

Published: 04 July 2014

ISSN: 2333-7133

Keywords

- Immune system diseases
- Bone marrow transplantation
- Graft vs host disease
- Stomatitis
- Periodontal debridement

INTRODUCTION

Graft Versus Host Disease (GVHD) is a common complication after bone marrow transplantation and a leading cause of morbidity and mortality in recipients [1,2]. GVHD is a multi-systemic disorder with various clinical, pathological and immunological features that occur as a result of complex immunological interactions between the host and transplanted donor cells [3-8]. GVHD is characterized by primary immunodeficiency, diarrhea, weight loss, dermatological alterations and hepatic abnormalities [2-6].

The acute and chronic forms of GVHD have been described in the medico-dental literature and differ in both onset time and clinical features. Acute GVHD usually appears within the first 100 days following bone marrow transplantation and is diagnosed in 30-50% of recipients [1-6]. Chronic GVHD is developed 100 or more days after bone marrow transplantation, affecting 60–80% of the long-term survivors [2-5]. Chronic GVHD is classified as limited and extensive, depending on the degree of organ involvement [2-5]. Limited chronic GVHD manifests as localized skin involvement, liver dysfunction or both, whereas extensive chronic GVHD affects multiple organs, such as the liver, eyes, skin, oral mucosa, salivary glands and other target organs [8-11].

Selective epithelial damage of target organs is the main pathology of chronic GVHD. The squamous epithelium of the oral mucosa and the epithelium of the salivary glands have been shown to be affected early in the course of chronic GVHD, with an incidence of 80-100% [2,6,8]. Immunological mechanisms of chronic GVHD include donor-derived alloreactive T-lymphocytes, autoreactive T-lymphocytes and regulatory T-lymphocytes as well as the dysregulation of cytokine expression [2,4,8]. The pathophysiology of the disease still is unknown and may be related to the increased production of interferon-γ and cytokines such as interleukin-4 and 6 [1,8].

The earlier and more precisely the chronic GVHD diagnosis can be made, the greater the success will be in predicting the outcome of its and in defining an optimum treatment at an early stage [8]. The purpose of this case report was to present the unusual lesions of gingival tissues during, to understand and increase our knowledge about the oral alterations and the treatment required for GVHD.

CASE REPORT

In June 2012, a 30-year-old female was referred by her dentist

to the Department of Periodontology of the Faculty of Dentistry, Atatürk University, for evaluation and treatment of the persisting oral ulceration and intense pain.

The patient's medical history revealed that she was diagnosed with chronic myeloid leukemia in January 2001. She was first treated with chemotherapeutic agents, afterwards, in December 2002, she underwent bone marrow transplantation with bone marrow from her sister. Transplant prognosis was uneventful until the patient developed features associated with GVHD around the 120th day after transplantation. As it was considered possible that she could be suffering from chronic GVHD, the biopsy was performed and therapy with immunosuppressive (cyclosporin) and corticosteroid (prednisone) prescribed. After having undergone clinical and histopathological examinations she was diagnosed as having extensive chronic GVHD.

The extra-oral examination revealed diffuse scleritis in the right and left eyes (Figure 1) and hyperpigmentation skin lesions (Figure 2a and 2b). Her skin was pale. The intra-oral examination revealed that she was suffering from severe gingival bleeding and oral hygiene regiments could not be performed because of sensitivity, which resulted in heavy plaque formation. Gingival inflammation was also associated with bleeding on probing. Probing revealed a high frequency of periodontal pockets (>30% of sites were to 5-7mm) and accompaniment gingival recession defects. Localized tooth mobility was found. Lichenoid hyperkeratotic white lesions and ulcerations were seen on the buccal mucosa (Figure 3). In addition, erythema (red lesions) on the hard palate, were observed (Figure 4). The angular cheilitis, xerostomia, reduced mouth opening, a tongue with no papillae and painful ulcers were also noted.

A panoramic radiograph showed generalized alveolar bone resorption with localized angular defects on the molar teeth sites, indicating the presence of chronic periodontitis. The location and degree of resorption was correlated with inflammatory sites and was more pronounced on the upper jaw than on the mandible. Bone loss extended to the apical third of the roots around the upper and lower molars and the occlusal third of the roots around the other teeth (Figure 5).

According to the clinical and radiographic findings, after the antibiotic prophylaxis, periodontal treatment was started with an initial phase of mechanical therapy; including systematic scaling and planning of all accessible root surfaces, improved oral hygiene, use of topical medications and monitored diet. The patient's oral hygiene regimen included using a new soft toothbrush and toothpaste and 0.12% chlorhexidine mouth rinse (Kloroben®, Drogsan Drug Ltd., Istanbul, Turkey). Nystatin solution (Mikostatin®, Deva Drug Ltd., Istanbul, Turkey) for the angular cheilitis and a topical corticosteroid (triamcinolone acetonide 0.1%, Kenacort-A Orabase®, Deva Drug Ltd., Istanbul, Turkey) for lichenoid lesions and ulcerations were prescribed. Two weeks later, the gingival margin appeared less inflamed. The ulcerations had resolved. The lichenoid lesions and angular cheilitis had remained asymptomatic. Thereafter, a thorough scaling-root planning and curettage of periodontal pockets with 0.12% chlorhexidine digluconate was performed under local anesthesia (Ultracaine DS Forte®, Hoechst Roussel, Frankfurt, Germany). The patient was prescribed antibiotics (amoxicillin and clavulanate potassium 1g, and metronidazole 500mg, every 12 hours, 7 days). The periodontal status was reevaluated 6 weeks after and it is observed that the plaque control and bleeding indices were lower, and periodontal probing measurements had improved. The number of mobile teeth decreased as did the severity of the mobility. No extractions were performed for periodontal reasons. The carious lesions were treated and filled with composite resin, or the affected tooth, such as upper

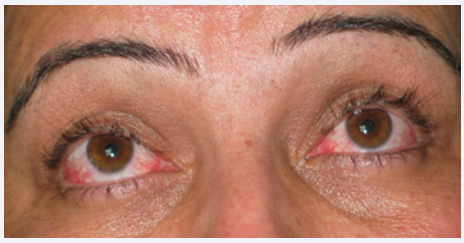

Figure 1 Clinical appearance of diffuse scleritis in the right and left eyes.

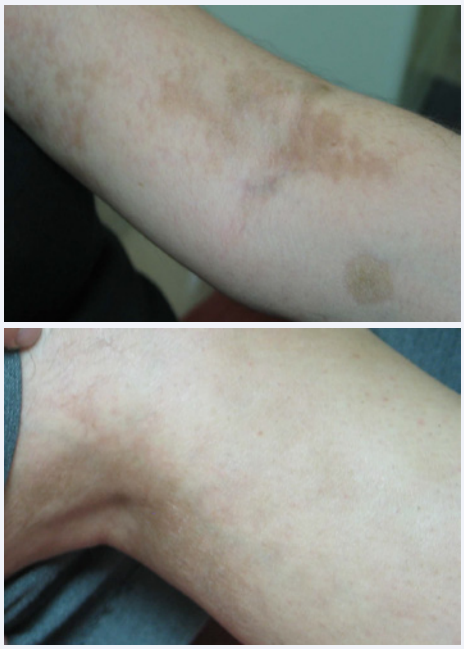

Figure 2 (a): Clinical view of skin changes on the arm. (b): Clinical view of skin changes on the leg.

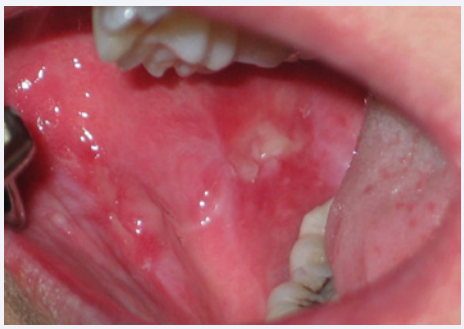

Figure 3 Lichenoid lesions consisted of white plaque in buccal mucosa.

left 3rd molar, was extracted. Supportive periodontal therapy was performed every 8 weeks for 12-month. Professional tooth cleaning was reinstituted, but no surgical therapy was performed after the initial periodontal treatment. Periodontal probing and clinical periodontal indices confirmed that the condition of periodontal tissue had stabilized (Figure 6). At a follow-up appointment 12-month later, the patient had no relapse of intraoral lesions.

DISCUSSION

To the best of our knowledge, this is one of the very few reports in the dental literature of a case of oral chronic GVHD that includes the manifestations of skin, eyes, and oral lesions. In addition, the case described here demonstrates that oro-dental treatments can be highly effective for medically compromised patients such as GVHD. The periodontal condition had stabilized, and no teeth were extracted for periodontal reasons.

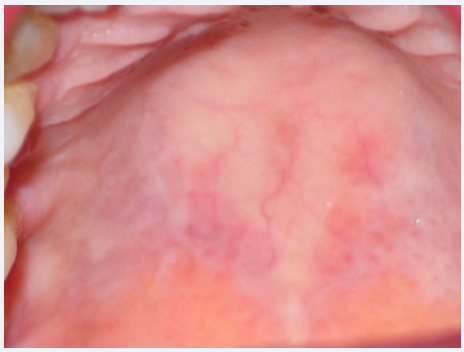

Figure 4 Clinical view of erythema on the hard palate.

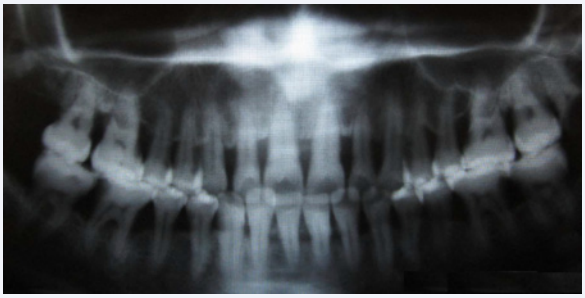

Figure 5 Panoramic radiograpy view of serious alveolar bone loss.

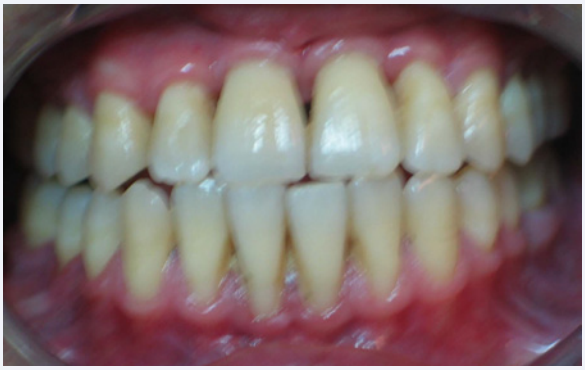

Figure 6 Periodontal status at the 12-month follow-up. Clinical view of the patient after periodontal therapy.

Chronic GVHD is a complex entity and major complication following allogeneic haematopoietic stem cell transplantation [1]. The most common sites of chronic GVHD involvement are the skin, oral cavity, eyes, gastrointestinal tract and lungs; however, the spectrum of clinical involvement is variable [1-6]. While skin and liver manifestations may be confused with signs of other disorders, the presence of oral chronic GVHD is a frequent, prominent and useful component of chronic GVHD diagnosis and staging [1,4,5]. Oral involvement has been described as a diagnostic sign of chronic GVHD and one of the first signs or symptoms of the disease [10]. Oral manifestations occur in about 80% of patients with extensive chronic GVHD. Generally, the first symptom is a series of whitish stria in the oral mucosa. The most common findings are erythema, mucosal atropy, lichenoid changes, stomatitis, infections, and reduced mouth opening [1,2,10-12]. There is usually accompanying oral pain and xerostomia that can interfere with eating, speaking and oral hygiene. This leads to a predisposition for caries, mucosal infections, and ulcers, as was observed in the present case.

Recently, only lichenoid changes are diagnostic for chronic GVHD, while other signs like erythema are considered insufficient alone to diagnose it [11]. The differential diagnosis of oral chronic GVHD includes reticular and ulcerative lichen planus, systemic sclerosis, lupus erythematosus and Sjögren's syndrome [1,2]. The lichenoid lesions commonly affect all mucosal surfaces with predominant reticular and papular forms; tongue lesions usually are plaque like [8,9]. Ulcerative lesions are not common, but when they appear, they usually are covered by a gray or yellow pseudomembrane surrounded by erythema and is localized mainly in the buccal mucosa, palate and dorsal part of the tongue. Atrophy of the oral mucosa also may be present, interspersed with areas of hyperkeratosis [2,4]. Salivary gland involvement in chronic GVHD manifests as increased xerostomia, accompanied by decreased levels of salivary immunoglobulins and an increased incidence of oral infections [1,2,12]. Moreover, oral mucosa and salivary gland alterations are reported to reflect the status of chronic GVHD better than other affected organs [10]. A biopsy of the salivary glands and an analysis of saliva can be carried out as, in GVHD patients, there is an increase in sodium albumin and IgG, and at the same time a decrease in the secretion of IgA and inorganic phosphate [1,12].

While patient's history and clinical assessments are necessary, the diagnosis of GVHD is ultimately dependent on histopathologic features [1,2,12]. A lip biopsy specimen frequently is used to diagnose and determine the stage of the GVHD, and the specimens need to include both mucosal and salivary gland tissue (10). As the biopsy was previously performed and diagnosed GVHD, the biopsy was not repeated in the present case. Both the presence of oral symptoms and histopathologic features has good properties regarding the diagnosis of chronic GVHD.

The primary treatment of GVHD usually consists of therapy with systemic corticosteroids and cyclosporine. If patients fail to respond to initial immunosuppressive therapy, various recovery protocols are available such as thalidomide, low-dose radiation and azathioprine [8,9]. In the case presented here, cyclosporin

and corticosteroid were prescribed by her physicians for treatment of disease.

The dentist should play a role in the improvement of the quality of life with pertinent local therapy in the cases with oral manifestation of chronic GVHD. To alleviate oral manifestations' symptoms, prophylactic regimens should be used that includes instructions for meticulous oral hygiene, the removal of sources of opportunistic infection, topical medications (i.e. corticosteroid and nystatin), effective analgesia [1-5]. In the case described here, instructions for oral hygiene, thorough periodontal therapy with clorhexidine and systemic combined antibiotics, and topical corticosteroid and nystatin were used for treating specific oral infections and providing pain control and oral health maintenance.

CONCLUSION

The management of GVDH can reduce oral alterations that can interfere with oral function and quality of life, and can reduce the need for more intensive immunosuppressive systemic therapies. In addition, periodontal status may also be stabilized by long-term supportive therapy.

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Cite this article

Dilsiz A, Sevinc S (2014) Oral Manifestations in a Patient with Graft Versus Host Disease: A Case Report with a 12-month Follow-Up. JSM Dent 2(4): 1041.