Management of Gingival Overgrowth in a Cardiac Transplant Patient Using Laser-Assisted Gingivectomy/Gingivoplasty

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Abstract

Drug-induced gingival overgrowth (DIGO) is an oral clinical manifestation associated with certain medications such as immunosuppressants that are administered to organ transplant patients to prevent graft rejection. In patients with cardiac transplants, management of DIGO is critical. In such patients, plaque biofilm accumulation at the gingival interface might be detrimental as it may lead to transient bacteremia as well as systemic inflammation resulting in thromboembolic events. This case report describes the management of DIGO in a cardiac transplant recipient by change of immunosuppressant medication, non-surgical periodontal therapy and laser-assisted gingivectomy.

Keywords: DIGO, cyclosporine A, cardiac transplantation

Introduction

Gingival overgrowth is characterized by an increase in the size of the gingival tissue that may result from a variety of medications, including anticonvulsants, calcium channel blockers and immunosuppressants (Dongari-Bagtzoglou *et al.*, 2004; Alandia-Roman *et al.*, 2011). The immunosuppressant cyclosporine A (CsA) is associated with drug-induced gingival overgrowth (DIGO) especially in organ transplant patients (Wysocki *et al.,* 1983; Rateitschak- Plüss *et al.,* 1983; Wright *et al.*, 2005; De Oliveira Costa *et al.*, 2006; Oliveira Costa *et al.*, 2007; Cota *et al.*, 2010). Cyclosporine A is designed to modulate the T lymphocyte activity and thus afford relief from symptoms of graft-versus-host disease. Past studies have shown that CsA decreased the production of matrix metalloproteinases (MMP-1 and 2), which are responsible for normal physiological degradation of collagen (Gagliano *et al.*, 2004). Furthermore, CsA induced elevated levels of transforming growth factor (TGF-β1) in fibroblasts, responsible for increase in extracellular matrix (ECM) production (Gagliano *et al.*, 2004). These changes in the connective tissue homeostasis ultimately lead to increased ECM production, resulting in gingival overgrowth (Gagliano *et al.*, 2004).

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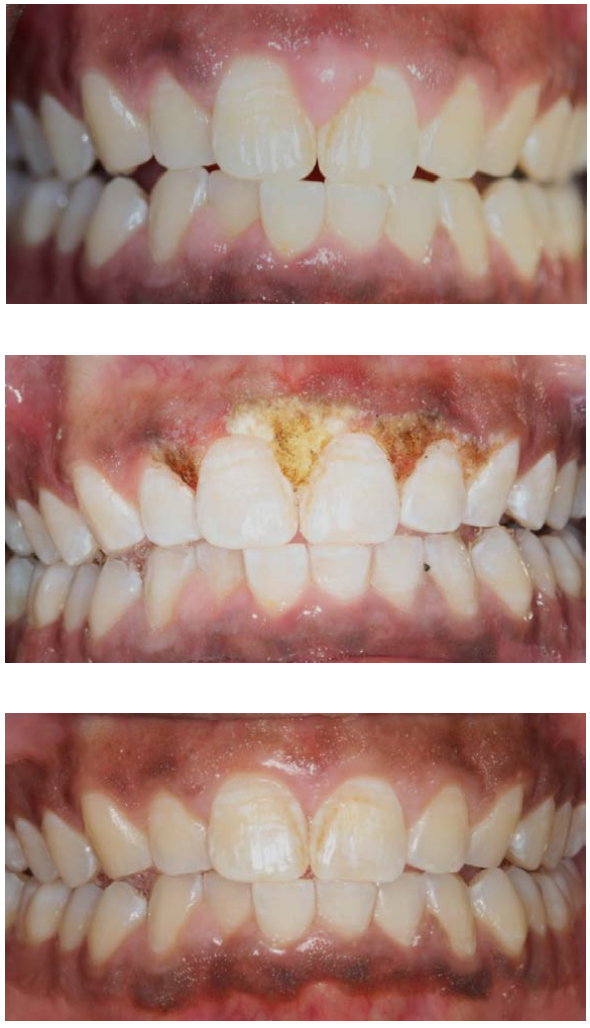
Severe gingival overgrowth may interfere with mastication, occlusion and speech, and create an unaesthetic appearance, thus affecting the patient's lifestyle. Moreover, it also makes plaque biofilm control difficult and may lead to periodontal disease. Accumulation of oral plaque biofilm may also lead to systemic inflammation and disease (Maddi and Scannapieco, 2013), which could be detrimental, especially in a patient with an organ transplant. The treatment for DIGO is considered challenging because of the high recurrence rate due to long-term need for immunosuppressant therapy, especially in organ transplant patients. The initial treatment approaches for managing DIGO include patient education, substitution of medication, and meticulous oral hygiene instructions (Ciancio *et al.*, 1990, Mavrogiannis *et al.*, 2006a). Initial treatment is complemented by non-surgical periodontal therapy, topical or systemic administration of antibiotics, and antimicrobial mouth rinses (Mavrogiannis *et al.*, 2006a). However, if the gingival overgrowth persists, then surgical treatment such as gingivectomy and/or gingivoplasty are performed (Camargo *et al.*, 2001, Mavrogiannis *et al.*, 2006b). This clinical case report describes the management of CsA-induced gingival overgrowth in a cardiac transplant patient using laser-assisted gingivectomy/gingivoplasty.

Case report

A 31-year-old male African-American presented to the Periodontics Clinic, School of Dental Medicine, State University of New York at Buffalo with the chief complaint of "my gums are getting bigger." The patient's medical history was significant for cardiac transplantation four years prior to his visit.

The patient's drug history included CsA for 4 years since cardiac transplantation. The other medications that the patient was placed on included ACE inhibitors for hypertension, levothyroxine for hypothyroidism, and provastatin for hypercholesterolemia. Furthermore, the patient has allergies to peanuts, soy, shellfish and iodine, and was on antihistamines for the past 8 years. Extra-oral physical examination of the head and neck revealed no abnormalities. Intra-oral examination revealed generalized pigmentation of the gingiva due to a racial predilection. Gingival overgrowth involving the interdental papillae between the maxillary central incisors and facial gingivae from the right maxillary canine to left maxillary canine was observed (*Figure 1A*). Additionally, the mandibular gingival tissues demonstrated relatively subtle but widespread involvement of gingival overgrowth from the left canine to the right canine region (*Figure 1A*). The dental surfaces in close approximation to the gingival overgrowth showed enhanced plaque biofilm deposits. Periodontal charting revealed 4-5 mm probing depths in areas associated with the gingival overgrowth, especially at the interproximal areas. Alveolar bone loss was not detectable in the radiographs (not shown). Thus, the deeper probing depths were only due to pseudopocketing resulting from gingival overgrowth. Based on the patient's medical history, drug history of CsA and periodontal findings, our final diagnosis was drug-induced gingival overgrowth (DIGO).

The periodontal management was planned in four phases that included medical consult, nonsurgical therapy, surgical therapy and maintenance with a 3-month recall. Initially the patient's cardiologist was consulted for a possible change of immunosuppressive medication to lessen the side effect of DIGO. The cardiologist changed the medication from CsA to sirolimus, which has a significantly lower incidence of DIGO (Cota *et al.*, 2010). The non-surgical treatment protocol involved instruction and demonstration of proper oral hygiene methods that included brushing and flossing techniques. Scaling and root planing was then performed in all the quadrants with antibiotic prophylaxis (2 g amoxicillin orally one hour before the procedure) as recommended by the American Heart Association. The non-surgical therapy was followed by a periodontal re-evaluation after 4 weeks. The non-surgical treatment in combination with change in medication was successful in the reducing gingival overgrowth, especially for the lower anterior teeth. Although the non-surgical approach was successful to some extent, surgical correction of the gingival overgrowth was still necessary for the maxillary anterior region. The surgical phase of the treatment involved use of lasers for gingival overgrowth reduction. Following the institution of antibiotic prophylaxis (2 g of amoxicillin orally one hour before the procedure), gingivectomy was performed under local anesthesia (2% xylocaine with 1:100,000 epinephrine) using a diode laser (Odyssey Diode Lasers, Ivoclarvivadent Inc., Amherst, NY; *Figure 1B*). Postoperative follow-ups were performed on a weekly basis for 2 weeks. After completion of surgical therapy, the patient was placed on a maintenance program and monitored every 3 months. At 1 year, the gingival overgrowth had completely subsided and did not show any signs of recurrence (*Figure 1C*).



1A.

1B.

1C.

Figure 1. Gingivectomy using lasers. 1A: Cyclosporine A-induced gingival overgrowth at baseline. 1B: Facial view immediately following laser treatment of gingival overgrowth. 1C: Post-operative followup after 1 year shows no recurrence.

Discussion

There has been a rise in the number of patients receiving organ transplants over the last few decades for treating end stage organ failure (Watson and Dark, 2012). This case report describes the management of DIGO in a patient who underwent heart transplantation and was placed on the immunosuppressant CsA to prevent graft rejection.

Cyclosporin A binds to cyclophilin in T lymphocytes, forming a cyclosporine-cyclophilin complex (Taylor *et al.*, 2005; Watson and Dark, 2012). This complex inhibits calcineurin and transcription of IL-2 by preventing dephosphorylation of the nuclear factor of activated T-cells (NFATc; Taylor *et al.*, 2005). Furthermore, CsA inhibits production of other lymphokines and interleukins, thus reducing the function of effector T cells to prevent graft rejection (Taylor *et al.*, 2005; Watson and Dark, 2012). In doing so CsA also affects gingival fibroblasts, resulting in excessive production of ECM leading to DIGO. Furthermore, CsA causes multiple systemic side effects such as hypertension, hypercholesterolemia, nephrotoxicity, neurotoxicity, hirsutism, and diabetes (Hefti *et al.*, 1994; Boratynska *et al.*, 2003; Taylor *et al.*, 2005; Watson and Dark, 2012). In a patient having several systemic disorders, the use of CsA may exacerbate the existing conditions. Hence, the patient's cardiologist was consulted and the medication was changed from CsA to sirolimus. Sirolimus, an immunosuppressive agent, has a lower incidence of nephrotoxicity (Gourishankar *et al.*, 2002; Ciancio *et al.*, 2004; Jorga and Johnston, 2005) and gingival overgrowth when compared to CsA (Cota *et al.*, 2010).

Drug-induced gingival overgrowth can be induced by medication; however, it is exaggerated by the presence of dental plaque biofilm and lack of proper oral hygiene (Seymour and Smith, 1991; Ilgenli *et al.*, 1999). Past studies have shown that the concentration of CsA in the dental plaque biofilm is higher than that found in the blood and tissues (Seymour and Smith, 1991; Ilgenli *et al.*, 1999). The periodontium responds to lipopolysaccharide (LPS) endotoxin present in dental plaque biofilm and secretes inflammatory mediators such as PGE_2, IL-1beta and TNF-alpha. These inflammatory mediators increase vasodilatation, vascular permeability and recruit inflammatory cells to initiate degradation of connective tissue and bone, resulting in periodontal disease. Furthermore, transient bacteremia from periodontal tissues may lead to atherosclerosis and thromboembolic events (Beck *et al.*, 1997). Hence, treatment of DIGO is critical for oral as well as systemic health, especially in a patient with a cardiac transplant for whom even a disproportionate transient bacteremia associated with brushing and flossing could be detrimental.

Drug-induced gingival overgrowth usually affects the entire mouth, while in this patient it was limited to the labial aspect of the upper and lower anterior region. Patient education, drug substitution to sirolimus, and non-surgical therapy reduced gingival overgrowth in the mandibular anterior region. However, gingival overgrowth still persisted in the maxillary anterior region and thus surgical correction was needed.

Laser therapy is one of the recent advances in dentistry. Lasers are classified, based on their wavelength, into soft tissue and hard tissue lasers (Coleton, 2008).

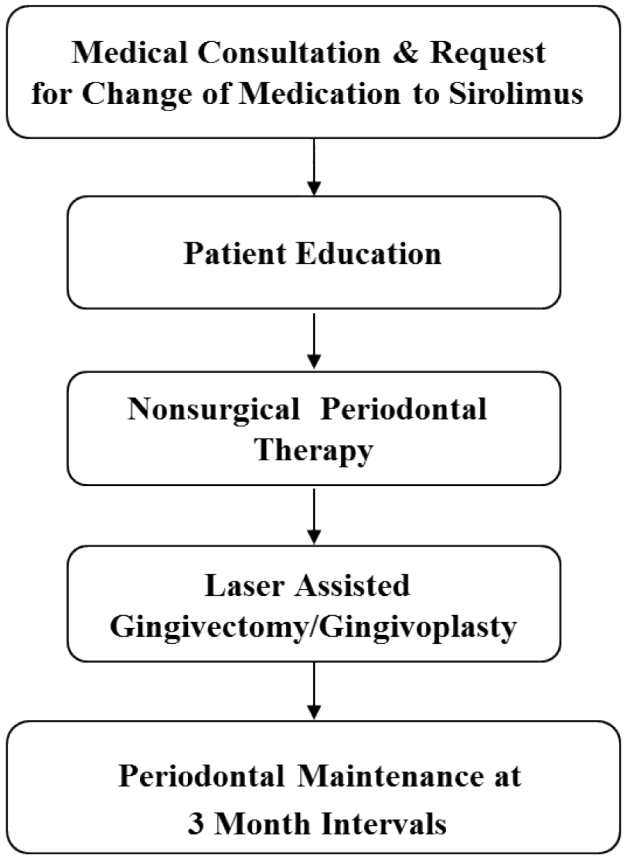


Figure 2. Treatment protocol for management of gingival enlargement in cardiac transplant patients.

CO_2, Nd:YAG and diode lasers wavelengths are used specifically for soft tissue surgeries. Erbium wavelength is used for both soft and hard tissues (Coleton, 2008). In the present case gingivectomy and gingivoplasty were done from the right canine to the left canine area in the anterior sextant using a diode laser (*Figure 2*). Lasers are more advantageous as compared to scalpel surgery and electrosurgery. They are effective in the removal of excessive gingival tissues (Roed-Petersen, 1993) and provide significant cutting, coagulability (Goharkhay *et al.*, 1999) and good visualization of the operative field during the procedures due to hemostasis, (Mavrogiannis *et al.*, 2004) and uncomplicated wound healing (Faria Amorim *et al.*, 2006). Lasers also minimize postoperative swelling, scarring and pain while stimulating wound healing (Mavrogiannis *et al.*, 2004). Furthermore, use of lasers reduces the need of periodontal dressing, use of analgesics and may reduce the reoccurrence of DIGO (Mavrogiannis *et al.*, 2006b).

Lasers should be a first choice of surgical therapy in patients with cardiac transplants as they avoid bleeding and transient bacteremia. Our cardiac transplant patient was successfully treated for gingival overgrowth using surgical laser therapy (*Figure 1*). Following surgical therapy the patient was placed on a 3-month recall maintenance to reinforce oral hygiene practices and to perform plaque control. At one year following the treatment the patient did not have any recurrence of gingival overgrowth (*Figure 1C*).

Summary and conclusions

Cardiac transplantation has been on the rise and patients are placed on immunosuppressive agents such as CsA to reduce graft rejection. Drug-induced gingival overgrowth is a common manifestation of long-term immunosuppressive therapy with CsA. Having gingival overgrowth in the cardiac transplant patient might be detrimental by leading to periodontal disease and may also have systemic implications due to plaque biofilm accumulation at the gingiva and tooth interface. In this report we describe the successful management of DIGO in a cardiac transplant patient and propose a clinical protocol (*Figure 2*). This case report demonstrates that laser surgery is highly effective for cardiac transplant patients as it avoids bleeding and minimizes the possibility of transient bacteremia.

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ERRATUM

The authors of the following paper, published in 2015 as *Journal of the International Academy of Periodontology* **17(2)**; 42-48 have requested that the authorship be modified from those shown in the published manuscript to the following:

Efficacy of Subgingivally Delivered Satranidazole in the Treatment of Type 2 Diabetes Subjects with Chronic Periodontitis: A Randomized Controlled Clinical Trial

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