Treatment Modalities for Drug–Induced Gingival Enlargement

Michelle Moffitt, RDH; Davide Bencivenni, DDS, MS; Robert Cohen, DDS, PhD

Abstract

Purpose: This paper identifies 3 specific classifications of commonly prescribed medications that are known to cause gingival enlargement and describes surgical and non–surgical treatment therapies. Primary risks associated with drug–induced gingival enlargement, including increased dental decay and periodontal disease are also discussed.

The precise bacterial etiology in gingival enlargement remains unclear, although sufficient evidence exists to support the role of good oral hygiene in decreasing the incidence and severity of gingival enlargement and improving overall gingival health. Etiology, treatment planning and coordination of care between physician, dentist or dental hygienist when indicated are important factors determining whether a surgical or non–surgical course of treatment should be considered.

Keywords: Gingiva, gingivectomy, calcium channel blockers, immunosuppressants

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Introduction

Gingival enlargement, regardless of its etiology, may be problematic and contribute to an increased risk for dental decay and periodontal disease.[1] Gingival overgrowth may decrease the efficacy of plaque control since enlarged gingival tissue often results in a periodontal pocket coronal to the cemento–enamel junction. The resulting pseudopocket represents overgrown gingival tissue rather than loss of periodontal attachment.[2–3]

The local conditions at the base of the pseudopocket, such as low oxygen tension, decreased access and inflammatory mediators, all may facilitate the growth of periodontopathic bacteria. Consequently, patients with gingival overgrowth are at a higher risk for harboring periodontal pathogens (Figure 1).[4–5]

While increased dental decay and periodontal disease are the primary risks associated with gingival enlargement, speech, mastication and alteration of tooth eruption patterns in children also can be affected. Extreme, although rare, consequences of drug–induced gingival enlargement have been documented. Bolger et al described a case of pronounced phenytoin–induced gingival overgrowth causing glossoptosis and subsequent airway obstruction in a child.[6] Gingival enlargement more frequently represents an esthetic concern for patients, especially if located in an anterior sextant or if the enlarged tissue extends to the occlusal margin. In cases where gingival enlargement is a long–standing condition, the tissue may become fibrotic, which has the potential to cause tooth migration. Secondary malocclusion is also possible with masticatory function alterations.[7]

Medications associated with gingival enlargement typically belong to 3 different therapeutic classes: calcium channel blockers, immunosuppressants and anticonvulsants. Although those classes are unrelated to one another, it remains unclear whether the inflammatory component is the cause or the effect of the enlargement.[7,8] Treatment planning is based on the patient's medical history and expectations, with the main focus being prevention and plaque control.[9] Some patients with drug–induced gingival enlargement may have serious systemic conditions, such as cardiovascular disease, and in those cases consultation with the patient's physician may be indicated to determine if an alternate drug might be considered. Treatment of drug–induced gingival enlargement may include non–surgical periodontal treatment, surgical therapy and, if necessary, drug modification. Consequently, in order to minimize the incidence of gingival alterations and to diminish possible side effects, prophylactic treatment can be considered whenever a patient is taking an at–risk medication.[10]

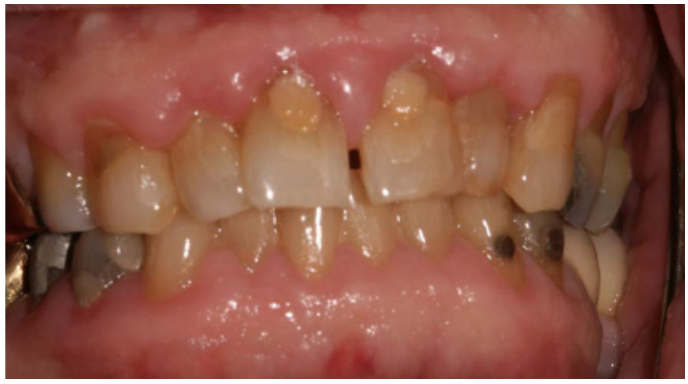
Non–Surgical Treatment of Drug–Induced Gingival Enlargement

Adequate plaque control is a primary factor in the prevention and control of drug–induced gingival enlargement.[11] Non–surgical treatment may include oral hygiene instructions, scaling and root planing,[12] drug substitution[4] and the use of antibiotics.[10] The exact role played by bacteria in the mechanism of such gingival changes is still unclear, although sufficient evidence exists to support the role of good oral hygiene and frequent professional maintenance in decreasing the incidence and severity of gingival enlargement and improving overall gingival health.[9,11,13] Appropriate post–surgical plaque control may aid in the prevention of gingival enlargement by reducing the presence and growth of pathogenic bacteria. A three month maintenance interval is often warranted to avoid plaque–related loss of attachment that can form as a result of enlarged gingiva.[14–15]

As an adjunct to mechanical plaque removal, studies have shown chlorhexidine rinses to be an effective aid in the non–surgical management of drug–induced gingival enlargement.[15–17] Chlorhexidine 0.12% bid (2 times a day) can substitute for daily mechanical cleansing in patients with impaired manual dexterity, while other mouth rinses, such as those containing phenolic compounds, essential oils and sanguinaria, can be used as an alternative to chlorhexidine, although their ability to inhibit plaque accumulation is generally inferior.[7]

In the last few years, systemic antibiotics have been gaining popularity in the management of drug–induced gingival enlargement. Case reports have indicated that short time courses of antibiotics, such as metronidazole or azithromycin,[16–18] may reduce the bacterial load in the gingival sulcus and consequently diminish the inflammatory component in individuals with gingival enlargement.[19,20] Wong et al evaluated a small group of women undergoing cyclosporin–A (CsA) therapy and reported complete resolution of drug–induced gingival alterations after only 1 week of metronidazole (1.2 g/day).[21] Gomez et al reported improvement of CsA–associated gingival enlargement in 27 patients treated for 1 week with azithromycin.[22] Nowicki et al documented partial resolution of severe CsA–induced gingival enlargement after 3 days of azithromycin administration, although recurrent gingival enlargement was evident 6 months post–treatment.[23] Wahlstrom et al also confirmed the efficacy of azithromycin in the management of drug–associated gingival conditions.[16] However, the outcome of antibiotic therapy has not always been consistent with such positive results. In a double–blind, controlled, randomized study, Mesa et al studied the effect of systemic metronidazole and azithromycin on patients with CsA–induced gingival enlargement. At 30 days, none of the patients showed complete remission and no clinical differences were observed when patients were compared to untreated control subjects.[24] Aufircht et al also reported no improvement in patients treated with metronidazole.[25] Such varying results may be attributable to the multifactorial etiology of drug–induced gingival enlargement. Local or systemic antibiotics may be effective in reducing or eliminating drug–associated gingival alterations when plaque–associated inflammation is present, but other therapeutic strategies, such as drug substitution or surgery, may be indicated in the absence of contributing plaque.[26] As there may be a recurrence of gingival manifestations after only a few months, potential side effects associated with long–term or extended use of antibiotics should be considered.

Figure 1: Example of gingival overgrowth as a result of periodontal pathogens



When attempting to control gingival enlargement, drug substitution in consultation with the patient's physician also can be considered when no significant improvement occurs after implementation of proper plaque control. Carbamazepine and valproic acid may be acceptable substitutes for phenytoin as both are associated with minimal gingival alteration.[27,28] Tacrolimus is a valid alternative to CsA and its use has been associated with an absence of gingival alteration. Resolution could take up to 1 year and during this time the patient's oral hygiene should be closely monitored.[29]

Nifedipine–induced gingival enlargement can often be controlled by substituting another calcium channel blocker, or a different anti–hypertensive drug. Figure 2 shows localized gingival

enlargement due to nifedipine. Calcium channel blocker alternatives to nifedipine include diltiazem and verapamil. The incidence of drug–induced gingival enlargement associated with those drugs is considerably below the 44% observed with nifedipine (20% and 4% for diltiazem and verapamil, respectively).[30] Alternative anti–hypertensive drugs might include diuretics, non–selective and selective β–antagonists, and angiotensin converting enzyme inhibitors. Those are all considered efficient medications in the treatment of high blood pressure and constitute possible alternatives to calcium channel blocking agents since they are normally not associated with alterations of the gingival tissue.[31]

Surgical Treatment of Drug–Induced Gingival Enlargement

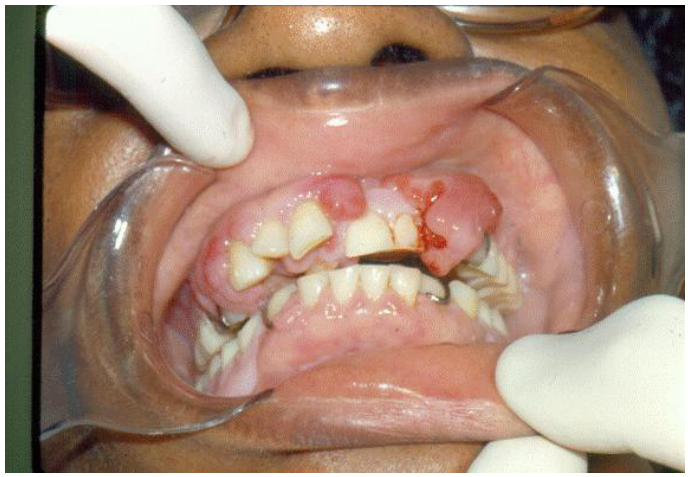
Indications for surgical treatment of drug–induced gingival enlargement include failure of non–surgical treatment, aesthetic considerations and soft tissue impaction of erupting teeth.

Failure of non–surgical therapy may be apparent by lack of resolution or continuous gingival enlargement, despite drug substitution or adequate plaque control. Refractory cases may be managed by periodontal surgical procedures to achieve more definitive results.[32]

Aesthetic concerns, such as enlarged gingival tissue that masks the natural shape and contour of the clinical crown, may be an indication for surgical treatment. Removal of enlarged tissue allows for more precise gingival recontouring, and can establish an ideal architecture for both better plaque control and improved esthetics. While non–surgical therapy typically requires between 2 and 3 months for the effects to be clinically apparent, a surgical approach allows for more rapid results, with immediate patient satisfaction.[9,12]

Selection of the surgical technique, typically gingivectomy/gingivoplasty, or a periodontal flap procedure, is based upon the extent of gingival enlargement, the presence of osseous defects and the relationship between the base of the pseudopocket and mucogingival junction. Gingivectomy is ideal where gingival enlargement is confined to a limited area, usually fewer than 6 teeth.[8] This technique is typically quicker and easier than a flap procedure, but does not allow for contouring of intra–bony osseous defects. In order to avoid mucogingival defects, gingivectomy is contraindicated if the initial incision falls in close proximity to, or at, the mucogingival junction. A gingivectomy procedure classically is initiated by marking

Figure 2: Example of severe nifedipine gingival overgrowth



the deepest point of each pseudopocket on the external gingival wall with a pocket marker or periodontal probe. A series of bleeding points is produced to function as a guide for the initial external beveled incision. An intra–sulcular incision then follows to free the band of enlarged tissue. Once the redundant tissue is removed, a gingivoplasty can be performed to remove tissue tags and recreate the physiologic gingival contour.[8]

An alternative to blade gingivectomy is the use of argon, carbon dioxide or diode lasers. Advantages associated with the use of lasers include the of coagulation and sealing of blood vessels resulting in a significant reduction of post–operative bleeding, which can be particularly beneficial with less cooperative patients such as children.[33–36] Compared to patients treated with conventional gingivectomy, laser patients reportedly display less intra– or post–operative bleeding, have a reduced need for periodontal dressing and require less post–operative analgesics.[35] Similarly, lasers have also found applications in cases of gingival enlargement associated with orthodontic treatment.[36,37] However, a limiting factor in laser treatment may be equipment cost.

The periodontal flap technique is frequently considered when large areas (more than 6 teeth) require treatment, osseous defects are present or in cases where gingivectomy would remove excessive amounts of keratinized tissue resulting in the development of a mucogingival defect.[9] A periodontal flap technique used to eliminate enlarged gingival tissue is similar to the procedure employed for periodontal pocket reduction.

Pilloni et al compared the long–term efficacy of periodontal flap surgery to gingivectomy in 10 patients. Clinical measurements were taken at

baseline, 6 weeks, 6 months and 1 year post–surgically. Results showed that probing depths were similar for both procedures at 6 weeks, but at 6 months and 1 year there were significantly greater numbers of teeth with probing depths within 1 to 3 mm in the flap surgery group compared to the gingivectomy group.[38]

To assist tooth eruption, when tooth impaction is a consequence of gingival enlargement, flap surgery allows for complete exposure of the impacted tooth by apically repositioning a thinned gingival flap. In such cases, gingivectomy could result in complete elimination of the keratinized tissue with possible creation of a mucogingival defect.[39]

Drug–induced gingival enlargement has potential to recur if proper oral hygiene is not performed. Meticulous oral hygiene, chlorhexidine rinses and regular maintenance can diminish the rate of recurrence. Although recurrence may be evi¬dent as early as 3 months post–surgery, surgical results have, in general, been maintained for at least 12 months.[8] Ilgenli et al followed a group of 38 CsA and nifedipine–treated patients displaying drug–induced gingival enlargement. Gingivectomy was performed at baseline and during the post–operative period. During that time patients were scheduled for periodontal maintenance at 3 month intervals. An average recurrence rate of 34% was observed 18 months following gingivectomy. Multiple regression analysis indicated that patients' age, oral hygiene status and attendance at recall appointments were important determinants in the recurrence of drug–induced gingival enlargement.[31] Similarly, Nishikawa et al observed no recurrence at 12 months in nifedipine–treated patients who underwent surgical therapy and were maintained at 4 month intervals.[36]

Conclusion

The management of drug–induced gingival enlargement is often multidisciplinary in nature. Modification of drug or dosage, in consultation with the patient's physician, should be considered as a first option. Removal of local predisposing factors, such as plaque, also can be attempted prior to considering a surgical approach. Aesthetic concerns and unsatisfactory outcomes of non–surgical therapy are indications for surgical treatment, via gingivectomy or periodontal flap procedures.

Michelle L. Moffitt, RDH, is a research assistant at the Department of Periodontics and Endodontics at the University at Buffalo, the State University of New York, School of Dental Medicine. Davide Bencivenni, DDS, MS, is a professor at the School of Dental Medicine, University of Modena and Reggio Emilia, Modena, Italy. Robert E. Cohen, DDS, PhD, is a professor at the Department of Periodontics and Endodontics at the University at Buffalo, the State University of New York, School of Dental Medicine.

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