

Cyclosporin-induced gingival overgrowth in a child treated with CO₂ laser surgery: a case report

Marcio Guelmann* / Leandro R. Britto** / Joseph Katz***

A case of a 10 year-old boy with gingival overgrowth due to cyclosporin therapy after heart transplantation is described. Different treatment approaches are discussed and the surgical effect of CO₂ laser is illustrated. The critical role of routine professional cleaning and good oral health maintenance for the healthy status of the gingival tissue is also emphasized in this paper. Replacement of cyclosporin by tacrolimus, another immunosuppressive agent associated with minimal to none gingival overgrowth, might be considered in cases with reported recurrences.

J Clin Pediatr Dent 27(2): 123-126, 2003

INTRODUCTION

Cyclosporin A (CyA), discovered in 1972 and in use since 1984, is an immunosuppressant medication primarily indicated for the prevention of graft rejection after major organ transplantation procedures such as heart, liver and kidney. In addition, CyA has been increasingly used for the treatment of a number of diseases with an autoimmune component, such as type 1 diabetes, lichen planus, Bechet's syndrome, pemphigus vulgaris, rheumatoid arthritis and multiple sclerosis. Side effects related to the chronic use of this drug included renal and liver toxicity, lymphomas, hypertension and hirsutism. Gingival overgrowth was the main oral discomfort reported with a prevalence varying between 8 and 85%.¹⁻⁵

The enlargement appeared to be half as frequent as that of phenytoin-induced gingival overgrowth and about the same as the occurrence, when elicited by calcium channel blockers (nifedipine).² Clinical studies suggest that children, especially adolescents and young females, seem to be more susceptible than adults,^{5,6} and a direct relationship was found between increased oral

debris and increased presence of gingival overgrowth.⁵ The growth is slow and usually develops within three months from therapy start.^{1,2,6} It begins as a papillary enlargement that is more pronounced on the labial aspects of the gingiva than on the palatal or lingual surfaces. The amount of overgrowth ranges from slight contour changes in the papillary tissues of the gingiva to complete coverage of the teeth. It is restricted to the width of attached gingiva but can extend coronally and interfere with occlusion, mastication and speech.^{1,2} The pathogenesis of cyclosporin-induced gingival overgrowth was not yet been fully established. A tentative multifactorial model emphasizing the influence of genetic factors, pharmacokinetics variables and plaque-induced inflammation has been suggested.⁷

During the last decade, an increase in the number of organ transplantations cases and an improvement in their survival rates was reported.⁸ Today it is expected that more and more immunosuppressant patients will seek dental care. Therefore, clinicians need to be aware of the drug manifestations and its side effects, as well as, be prepared to offer different treatment options.

The purpose of this report is to illustrate a case of gingival overgrowth in a 10-year-old child due to cyclosporin after heart transplantation and to discuss possible modes of treatment.

CASE REPORT

A 10 year-old boy was referred to the department of Oral Medicine in the Oral Maxillofacial Center Tel Hashomer, Israel, for the diagnosis and treatment of severe gingival overgrowth. The medical history was significant for heart transplantation one year ago. The patient's medication included cyclosporine 400 mg/day and prednisone 20mg/day.

On examination, the patient's face seemed edematous, with advanced hirsutism of the perioral region.

* Marcio Guelmann, DDS, Assistant Professor, Department of Pediatric Dentistry, University of Florida, Gainesville, FL.

** Leandro R. Britto, BDS, MS, Assistant Professor, Department of Endodontics, University of Florida, Gainesville, FL.

*** Joseph Katz, DMD, Associate Professor and Head, Division of Oral Medicine, University of Florida, Gainesville, FL.

Send all correspondence to Dr. Marcio Guelmann, University of Florida, Department of Pediatric Dentistry, Health Science Center, P.O.Box 100426, Gainesville, FL 32610-0426.

Voice: (352) 392-3195

Fax: (352) 392-8195

E-mail: mguelmann@dental.ufl.edu



Figure 1. Gingival overgrowth mainly affecting the maxillary left posterior area covering totally the primary molars and partially the permanent molar (compare to contralateral side). Also, note increased facial hair (hirsutism) as a side effect of the medication.



Figure 2. Mandibular view of the gingival overgrowth showing significant coverage of teeth.

Bilateral submandibular and cervical lymph nodes were palpated, and found to be asymptomatic. Angular cheilitis with mild scaling of the vermillion border was noted on the left corner of the mouth.

Intra-oral examination revealed a mixed dentition with generalized plaque deposits with no calculus and a hard-dense gingival tissue covering major proportion of the teeth. Traumatized keratinized tissue was evident on the left maxillary molar area (Figure 1) and massive gingival overgrowth covering almost the entire crowns of mandibular incisors was noted (Figure 2).

The parents mentioned that the gingival growth occurred two months following the transplantation and caused severe difficulties in chewing, making oral hygiene almost impossible with frequent episodes of oral bleeding. Based on the medical history and the clinical presentation of the gingival overgrowth, a tentative diagnosis of cyclosporin-induced gingival enlargement was suggested and the patient was scheduled for CO₂ laser gingivectomy following incisional biopsy.

The biopsy, taken from the mandibular molar area, showed widening of the epithelial layer with parakeratinized stratified squamous cell epithelium with elongated rete pegs. The connective tissue was moderately densified with chronic inflammatory cells.

Due to high risks involved in treating a severe medically compromised patient under general anesthesia and the very good patient cooperation, gingivectomy was performed in multiple appointments under local anesthesia. The child tolerated the procedures well and no post-operative complications were reported. The use of CO₂ laser allowed excellent bleeding control and good visualization of the operation field (Figure 3). After a week, a significant reduction of gingival tissue was obvious with satisfactory healing progress of the supportive tissues (Figure 4).

The patient was advised to have monthly oral prophylaxis sessions with a dental hygienist, however in spite of

good compliance, in a six month follow up appointment a considerable reoccurrence of the overgrowth was noted. Oral hygiene instructions were reinforced, mouthrinses with chlorhexidine for ten days prescribed and regular professional cleanings were recommended.

Close monitoring recalls appointments for gingival health condition and physician consultation for possible immunosuppressive medication replacement by tacrolimus has been suggested. However, due to medical considerations this was not adopted by the treating physician.

DISCUSSION

Drug-induced gingival overgrowth is frequently associated with anticonvulsants, cyclosporin and calcium channel blockers. Such lesions appear within the first months of treatment and are characterized clinically by inflammation.⁹

The overall histologic features of all drug-induced gingival overgrowths are comparable, consisting of connective tissue with an overlying irregular, multilayered, parakeratinized epithelium of variable thickness and pronounced inflammatory cell infiltrate.^{2,9,10}

Cyclosporin induced-gingival overgrowth is a rise clinical finding mainly because of the recently increasing rate of organ transplantations.^{5,6} A variety of clinical approaches have been suggested for treatment of the affected patients. The severity of the clinical scenario could be used as an indicator for the selection of treatment modalities. When the overgrowth tissue is at its preliminary stages, strict oral hygiene instructions and elimination of local factors, such as plaque and calculus, is of outmost importance.^{3,4,11,12} When the tissue happened to cover teeth causing difficulty in speech and function or in young children where behavior management is a factor, gingivectomy using a surgical scalpel and/or CO₂ laser is recommended.^{10,13}



Figure 3. Gingivectomy with CO₂ laser. Note the coagulation effect and minimal bleeding.



Figure 4. A week post-surgery. Note the improvement of the gingival tissue.

In the case reported, the use of CO₂ laser was selected by the oral surgeon as the preferred surgery technique. The advantages of using the CO₂ laser rather than the scalpel in the surgery for gingival lesions are the ability of the laser to coagulate and seal blood vessels, vaporize the tissue, accurate incision and improved healing effect due to its antimicrobial properties. Furthermore, surgery time is reduced with minimal postoperative pain and swelling.¹⁴ When treating children, these are considered key factors.

During the 90's, a new immunosuppressant drug, tacrolimus^{15,16,17}, has been reported to be a successful substitute for cyclosporine in kidney, liver and heart transplants. The great advantage of this new drug has been the marked reduction of the gingival enlargement reported by cyclosporine.¹⁸⁻²² In summary, whenever drug-induced overgrowths are in use, regardless the treatment mode, maintenance of strict oral hygiene habits is imperative for the health status of the gingival tissue. However, even after treatment, as in this case, some recurrence could be expected.²³ In cases where CyA is the prime medication, physician consultation is advised for possible drug replacement to prevent or diminish gingival enlargement.

REFERENCES

- Desai P, Silver JG. Drug-induced gingival enlargements. *J Can Dent Assoc* 64: 263-267, 1998.
- Boltchi FE, Rees TD, Lacopino AM. Cyclosporine A-induced gingival overgrowth: a comprehensive review. *Quintessence Int* 30: 775-783, 1999.
- Irshied J, Bimstein E. Oral diagnosis of Behcet disease in an eleven-year-old girl and the non-surgical treatment of her overgrowth caused by cyclosporine. *J Clin Pediatr Dent* 26: 93-98, 2001.
- Oettinger-Barak O, Machtei EE, Peled M, Barak S, L-Naaj IA, Laufer D. Cyclosporine A-induced gingival hyperplasia pemphigus vulgaris: Literature review and report of a case. *J Periodontol* 71: 650-656, 2000.
- Allman SD, McWhorter AG, Seale S N. Evaluation of cyclosporin-induced gingival overgrowth in the pediatric transplant patient. *Pediatr Dent* 16: 36-40, 1994.
- Karpinia KA, Matt M, Fennel RS 3rd, Hefti AF. Factors affecting cyclosporin-induced gingival overgrowth in pediatric renal transplant recipients. *Pediatr Dent* 18: 450-455, 1996.
- Seymour RA, Thomason JM, Ellis JS. The pathogenesis of drug-induced gingival overgrowth. *J Clin Periodontol* 23: 165-175, 1996.
- Parsons DA, Tracy SE, Handa KA, Greig PD. An update of the Canadian organ replacement register (1998). *Clin Transpl* 97-106, 1998.
- Katz J, Givol N, Chaushu G, Taicher S, Shemer J. Vigabatrin-induced-gingival overgrowth. *J Clin Periodontol* 24: 180-182, 1997.
- Santi E, Bral M. Effect of treatment on cyclosporine-and nifedipine-induced gingival enlargement: clinical and histological results. *Int J Period Res Dent* 18: 81-85, 1998.
- Hall EE. Prevention and treatment considerations in patients with drug-induced gingival enlargement. *Curr Opin Periodontol* 4:59-63, 1997.
- Somacarrera ML, Lucas M, Scully C, Barrios C. Effectiveness of periodontal treatments on cyclosporine-induced gingival overgrowth in transplant patients. *Br Dent J* 183: 89-94, 1997.
- Darbar UR, Hopper C, Speight PM, Newman HN. Combined treatment approach to gingival overgrowth due to drug therapy. *J Clin Periodontol* 23: 941-944, 1996.
- Barak S, Katz J, Kaplan I. The CO₂ laser in surgery of vascular tumors of the oral cavity in children. *J Dent Child* 58: 293-296, 1991.
- Shapiro R. Tacrolimus in solid organ transplantation: an update. *Transplant Proc* 31: 2203-2205, 1999.
- Plosker GL, Foster RH. Tacrolimus: a further update of its pharmacology and therapeutic use in the management of organ transplantation. *Drugs* 59: 323-389, 2000.
- Chand DH, Southerland SM, Cunningham RJ III. Tacrolimus: the good, the bad, and the ugly. *Pediatr Transplantation* 5: 32-36, 2001.
- Bader G, Lejeune S, Messner M. Reduction of cyclosporine-induced gingival overgrowth following a change to tacrolimus. A case history involving a liver transplant patient. *J Periodontol* 69: 729-732, 1998.
- Kennedy DS, Linden GJ. Resolution of gingival overgrowth following change from cyclosporin to tacrolimus therapy in a renal transplant patient. *J Ir Dent Assoc* 46: 3-4, 2000.

20. Hernandez G, Arriba L, Lucas M, de Andres A. Reduction of severe gingival overgrowth in a kidney transplant patient by replacing cyclosporin A with tacrolimus. *J Periodontol* 71: 1630-1636, 2000.
21. Asante-Korang A, Boyle GJ, Webber SA, Miller SA, Fricker FJ. Experience of FK506 immune suppression in pediatric heart transplantation: a study of long-term adverse effects. *J Heart Lung Transplant* 15: 415-422, 1996.
22. Oettinger-Barak, Barak S, Machtei EE, Ardekian L, Baruch Y, Peled M. Periodontal changes in liver cirrhosis and post-transplantation patients. I: clinical findings. *J Periodontol* 72: 1236-1240, 2001.
23. Pernu HE, Hannele Pernu LM, Knuutila MLE. Effect of periodontal treatment on gingival overgrowth among cyclosporine A-treated renal transplant recipients. *J Periodontol* 64: 1098-1100, 1993.