# Gingival Overgrowth in a Renal Transplant Recipient Using Cyclosporine A

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## ABSTRACT

Unsightly gingival enlargement is a frequent side effect in organ transplant recipients under immunosuppressive therapy with cyclosporin A (CsA). The purpose of this article was to report the treatment management of cyclosporin A-induced gingival overgrowth in a 9-year-old renal transplant recipient. Surgical reduction of the overgrown gingival tissue associated with an intensive biofilm control program and conversion from CsA to tacrolimus provided good clinical outcome with improvement of mastication, feeding, and phonetics. Gingival overgrowth stabilized with the change of medication. After approximately 3 months of follow-up, a regression of gingival enlargement was observed. (**J Dent Child 2008;75:313-7**)

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KEYWORDS: CYCLOSPORIN A, GINGIVAL OVERGROWTH, COMBINED MODALITY THERAPY, RENAL TRANSPLANT

Cyclosporin A (**CsA**) is a potent immunosuppressant drug widely used for prevention of solid organ transplant rejection and treatment of autoimmune diseases.[1-3] While it contributes to an increase in the survival rate of organ transplant patients, CsA therapy is associated with a number of side effects, including the development of gingival overgrowth. This condition may cause occlusal, phonetic, masticatory, eruption, and esthetic problems and affect the patient's self-esteem. It also might make oral hygiene difficult, which may facilitate the onset and progression of dental caries, periodontitis, and infections.[1,4,5]

Histologically, gingival overgrowth is characterized by a connective tissue with an irregular lining of multiple layers of parakeratinized epithelium of variable thickness. Epithelial grooves penetrate the subepithelial connective tissue, forming irregular connective fiber bundles. This tissue is highly vascularized and characterized by the accumulation of inflammatory cells.[6,7] The mechanism of action of CsA in the periodontal tissues remains unclear.[2,3,8,9]

The purpose of this paper is to report the treatment management of gingival overgrowth in a young renal transplant recipient who continuously used cyclosporine A. The proposed gingival intervention and drug therapy as well as the treatment outcomes are described.

## CASE REPORT

A 9-year-old male patient was brought to the clinic of the Center of Formation of Human Resources Specialized in Dental Care for Special Needs Patients, School of Dentistry of Ribeirão Preto, University of São Paulo, São Paulo, Brazil.

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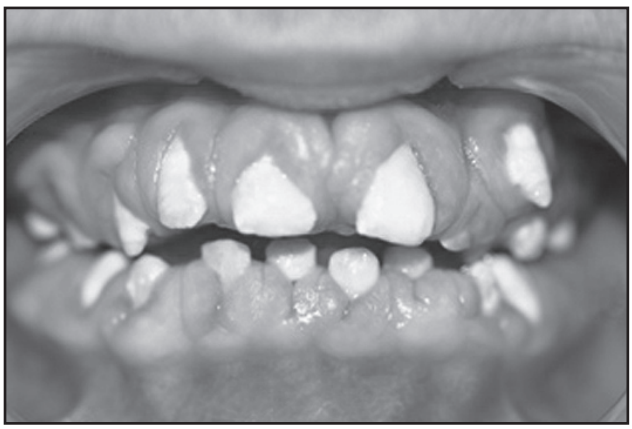

*Figure 1. Generalized gingival overgrowth and areas of hypoplastic enamel on the incisal third of incisors and canines.*

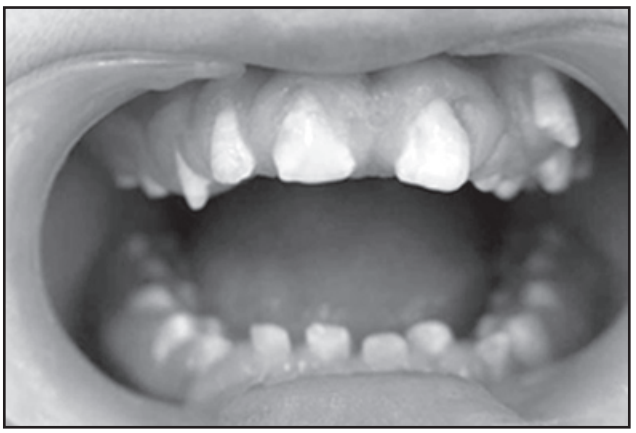

*Figure 2. Panoramic radiograph showing the presence of all germs of the unerupted permanent teeth and radiolucent areas in the anterior teeth compatible with enamel hypoplasia. Note advanced dental age, but absence of third molars.*

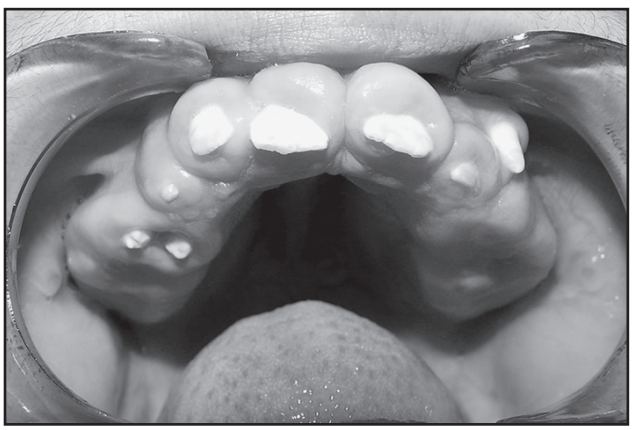

*Figure 3. Postsurgical view showing the interrupted vertical mattress sutures.*

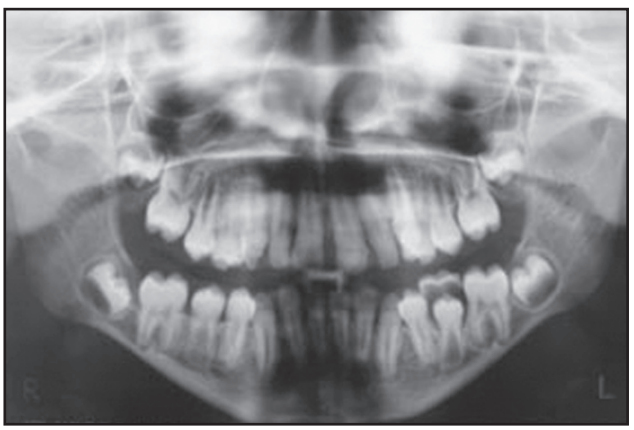

*Figure 4. Intraoral clinical view 1 month postoperatively, showing gingival tissue healing and the presence of several enamel hypoplastic areas.*

His chief complaints were difficulty and pain associated with mastication and oral hygiene and unpleasant esthetics due to gingival overgrowth. The child was a renal transplant recipient and was under immunosuppressive therapy with CsA (Sandimun, Sandoz, East Hanover, NJ).

The physical examination showed hypertrichosis, polydactyly on the feet and right hand, and hypertelorism. The intraoral examination revealed severe gingival enlargement on the maxillary and mandibular arches involving the anterior and posterior teeth and entirely covering the molar cups. Enamel hypoplasia was observed on the incisal thirds of incisors and canines (Figure 1). Heavy biofilm deposits were observed throughout the mouth, associated with gingival inflammation and bleeding. A panoramic radiograph (Figure 2) showed the presence of all germs of the unerupted permanent teeth, except for the third molars, and absence of dental anomalies of form and number. The portions of the crowns of the anterior teeth that were covered by the enlarged gingiva and could not be clinically examined presented radiolucencies compatible with enamel hypoplasia.

Because of the patient's high risk for caries and periodontal disease, the initial dental treatment consisted of 4 sessions scheduled on a quarterly basis. These sessions involved professional prophylaxis, 0.12% chlorhexidine gluconate mouthwashes (Periogard; Colgate-Palmolive, New York, NY), and topical applications of 1.23% acidulated phosphate-fluoride gel (Sultan Topex, DFL Ind e Com Ltda, Petrópolis, Rio de Janeiro, Brazil). The patient and his parents were given instructions on oral health care, information on caries and periodontal diseases, and counseling on a low-sucrose diet.

The surgical reduction of the enlarged gingival tissue included a classical gingivectomy on both anterior sextants (superior, inferior, buccal, lingual, and palatal) and wedges reaching the entire extension of the posterior alveolar ridges. Parallel 8- to 10-mm-wide incisions were made divergent towards the ridge and decreasing the flap thickness in order to expose the erupting teeth. In the interproximal sextants, interrupted vertical mattress sutures were placed to allow the formation of the interdental papillae (Figure 3). The surgical procedures were performed in a hospital setting under general anesthesia concomitantly with an orchiopexy (surgery to repair undescended testicles). After surgery, the medical team was asked about the possibility of withdrawing

CsA and placing the patient under therapy with tacrolimus to prevent the recurrence of gingival growth. The physicians, however, were concerned with tacrolimus' possible side effects in pediatric transplant patients who previously received CsA and did not recommend drug conversion at that time.

One month postoperatively, gingival healing was completed (Figure 4) and the restorative phase was started. The areas of hypoplastic enamel were restored with composite resin (Z-250, shade P, 3M/ESPE, St. Paul, Minn) and were carefully polished to improve esthetics and provide smooth surfaces to decrease dental biofilm accumulation. Professional prophylaxis and ultrasonic scaling (Profi-II, Dabi-Atlante, Ribeirão Preto, São Paulo, Brazil) were scheduled monthly to improve dental biofilm control. At every session, the importance of oral home care supportive to the professional care was reinforced and the maintenance of good oral hygiene habits was encouraged since it has been established that dental biofilm is an aggravating factor in cases of drug-induced gingival enlargement.[10]

The patient and his family were very committed to the treatment and collaborative. Despite family/patient cooperation and intensive professional hygienist professional support, however, significant gingival enlargement recurred. This is most likely because its primary etiologic factor in this case, the continuous use of CsA, had not been withdrawn (Figure 5). The possibility of conversion from CsA to tacrolimus was discussed again with the patient's medical team, and his immunosuppressant medication was changed. There were no side effects caused by changing the medications related to the physicians' original concerns.

Gingival overgrowth stabilized with the change of medication. After approximately 3 months of follow-up, a regression of gingival enlargement was evident with no need of surgical intervention (Figure 6). The progression of the case is under continuing evaluation.

## DISCUSSION

Continuous therapy with CsA to suppress graft rejection in organ transplant patients causes the overgrowth of gingival tissues, leading to occlusal, phonetic, masticatory, esthetic, and social problems.[1-3] The patient described in this case report presented lack of intercuspation due to the excessively enlarged gingival tissue covering the cups of all his posterior teeth. The overgrown gingiva covering the palatal surfaces of the anterior teeth compromised the pronunciation of certain phonemes, which interfered with the speech therapy. The liquid or soft-consistence diet imposed by the patient's gingival condition affected his socialization and led to psychosocial problems because he was not able to share either his family's or his classmates' feeding habits.

The pathogenesis of CsA-induced gingival overgrowth remains unclear.[1-3,8,9] The possible etiological factors suggested for its occurrence include abnormal balance of cytokines and growth factors,[2] collagenolytic activity of fibroblasts,[3] and high drug concentrations in saliva, gingival fluid, and dental biofilm.[5]

There has been evidence that the presence of dental biofilm induces inflammation and exacerbates CsA-induced overgrowth of gingival tissues.[5,6,10-12] It has been demonstrated that CsA concentration in the dental biofilm is higher than that found in the blood and body tissues.[10,11] Therefore, the chemomechanical control of dental biofilm is an essential part of the treatment of patients with gingival overgrowth. In addition, areas that are not properly cleaned are more prone to caries disease, periodontitis, and infections that may lead to septicemia in immunosuppressed patients.[1,7,10-12] In the present case, the patient followed a strict chemomechanical dental biofilm control regimen—consisting of professional prophylaxis, chlorhexidine mouthwashes, and topical fluoride application associated with a high standard of home care. These measures were important to minimize gingival inflammation, reduce caries risk, and improve the patient's oral status. The surgical reduction of gingival hyperplasia attenuated the masticatory, occlusal,

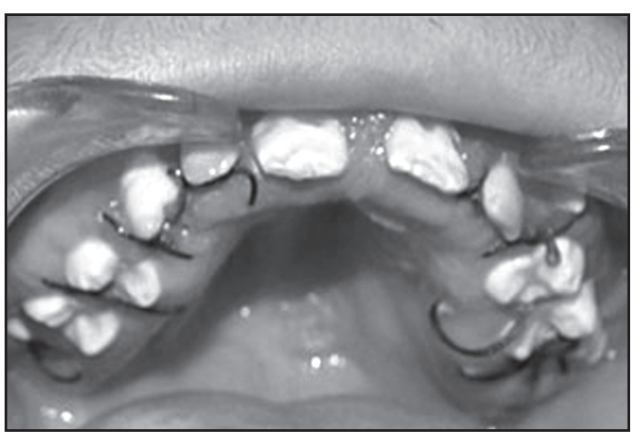

*Figure 5. Clinical aspect 3 months after surgery and restorations.*

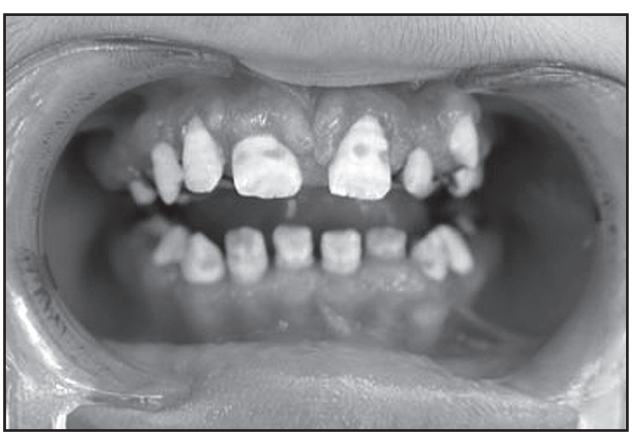

*Figure 6. Clinical aspect approximately 3 months after conversion from cyclosporin A to tacrolimus.*

and esthetic problems; the patient started to eat better and his general health status improved. The maintenance of CsA therapy, however, induced the recurrence of gingival overgrowth.

There is a minimal chance of discontinuing or reducing the immunosuppressive drug therapy in transplanted patients.[1] Recent studies have suggested that CsA withdrawal and its conversion to tacrolimus in organ transplant recipients who develop severe gingival enlargement may provide an effective means to control/reduce gingival hyperplasia, thus allowing a nonsurgical management of this condition with minimal risk of graft dysfunction.[13-16] Our patient showed a decrease in his gingival symptoms and in the size of the enlarged tissue after change of the immunosuppressant drug. His gingival conditions have progressively improved, with no need of an additional surgical intervention. Follow-up will be maintained to monitor case evolution.

Another oral finding reported in CsA therapy patients is the formation of eruption cysts.[17] In our patient, however, this was not observed. Other side effects associated with CsA therapy include nephrotoxicity, hepatotoxicity, cardiovascular and hematopoietic disorders, hypertension, and gastric, neurological, ophthalmologic, dermatologic, respiratory and metabolic alterations.[1,5,16] In the present case, hypertension, hypertrichosis, abdominal distension, irritability, and tiredness were reported, in addition to undescended testicles. It seemed suspicious that there could be some developmental defect relating all these conditions and the patient was referred to genetic investigation. It could not be determined, however, whether any kind of genetic disorder was actually present. The child's parents denied ophthalmologic, respiratory, neurological, or cardiovascular problems. The child's physicians did not indicate antibiotic prophylaxis for gingival treatment procedures. Because of the numerous surgical interventions the patient experienced, he was anxious, frightened, and noncooperative during the initial phase of the dental treatment. In addition, his blood pressure was high and increased even more under stress. For these reasons, the surgical reduction of the overgrown gingival tissue was performed in a hospital setting under general anesthesia, at the same time that he was submitted to an orchiopexy procedure.

The patient was satisfied with the result of the surgical treatment and became more cooperative in the subsequent clinical sessions for preventive and restorative procedures.

## CONCLUSIONS

Transplantion patients frequently develop gingival enlargement as a result of CsA immunosuppression. Surgical reduction of gingival overgrowth is required in many cases to improve mastication, feeding, phonetics, and esthetics, decrease the risk of caries, periodontal disease, and systemic infections, and increase patients' self-esteem and socialization. The settlement of a strict presurgical and postsurgical preventive program is of major importance for treatment success. After risk-benefit analysis, the replacement of CsA by another immunosuppressant drug that does not cause gingival overgrowth may be indicated.

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