Case report. The management of cyclosporin A-induced gingival overgrowth

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Abstract

At the Iasi Transplant Centre, a significant number of patients have received cyclosporin A after transplants have been performed. An analysis of the medical records of all patients who had received cyclosporin A revealed a side-effect of the treatment, namely gingival overgrowth, present in the mouths of 16% of these patients. This paper reports the periodontal treatment of one of these patients, an 18-year-old female. After receiving a transplant, the patient took cyclosporin A for six months. This medication was then replaced with tacrolimus, resulting in a decrease in the size of her gingival overgrowth. The change in her gingival aesthetics, discomfort when chewing, and difficulties in performing adequate oral hygiene indicated the use of laser surgery (erbium, chromium: yttrium-scandium-gallium-garnet—Er,Cr:YSGG—hydrokinetic laser), which facilitated the removal of the overgrown gingival tissue in this immunosuppressed patient. This technique has the advantages that it reduces intra-operative haemorrhage, diminishes pain and post-operative oedema, and leads to a shorter healing process than would be the case with other surgical techniques.

Key Words: Gingival Overgrowth, Cyclosporin A, Er,Cr:YSGG Hydrokinetic Laser, Tacrolimus

Introduction

Gingival overgrowth, the term currently accepted to describe the increase in size of the gum, is a common feature of gingivitis. It is a strictly clinical description of the condition, avoiding the erroneous pathological connotations of the previously used terms 'gingival hypertrophy' and 'gingival hyperplasia'. Gingival overgrowth is caused by a multitude of factors, and its treatment relies on understanding its causes and the resulting pathology [1]. The most frequent cause is chronic gingival inflammation [2,3]. The factors inducing the occurrence and progression of gingival overgrowth include certain drugs. Drug-induced gingival overgrowth has been included in the generally accepted international classification of periodontal diseases and conditions, undertaken in the USA in 1999 [4]. Three classes of drugs have been clearly identified as factors in the development of gingival overgrowth as an adverse side-effect. They are certain calcium channel blockers (such as nifedipine), an immunosuppressant (cyclosporin A), and an anti-epileptic (phenytoin). Data in the literature demonstrate that cyclosporin A also has pro-angiogenic properties [4,5].

Cyclosporin A is a drug widely used as an immunosuppressant. It inhibits the immune response of T-lymphocytes. This property might result in the exacerbation of gingival microbial flora that would maintain the nonspecifically mediated inflammation, the activation of the fibroblasts and gingival fibrosis [4-6]. These effects may also be mediated as a result of the property of cyclosporin A to accumulate in the saliva. The results of studies carried out by various researchers on the influence of cyclosporin on gingival tissue have demonstrated that cyclosporin A is directly involved in the balance between collagen synthesis by the gingival fibroblasts and collagen phagocytosis. Cyclosporin A does not stimulate collagen synthesis but favours its accumulation and deposition in tissues by the inhibition of phagocytosis [7-11].

Preliminary Investigation

In Iasi town, at the C. I. Parhon Hospital, there is an authorised centre for kidney transplantation.

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Patients who have received a kidney transplant are medicated with immunosuppressants, one of which is cyclosporin A. An audit of the medical records of all 63 patients who had received kidney transplants (between January 2001 and November 2008) revealed that, post-operatively, they had all been medicated with either cyclosporin A, tacrolimus, or sirolimus. Thirty-eight (60%) of these patients received cyclosporin A, 24 (38%) tacrolimus, and only one (2%) sirolimus. Of the 38 patients followed-up by the Iasi Centre for Kidney Transplant and medicated with cyclosporin A, six (17%) developed gingival overgrowth at various intervals after starting medication.

Case Report

One of the six kidney transplant patients who had developed gingival overgrowth was an 18-year-old female whose transplant had been performed at the Iasi Centre for Kidney Transplant on 31st October, 2007. She requested treatment for the problem and gave her permission for her treatment to be written-up and published as a case report. Following the transplant, the patient was medicated with cyclosporin A, initially administered at a dose of 150-175 mg for the first three months and then for the next seven months at a reduced dose of 125-150 mg. After eight months of medication with cyclosporin A, at a review in June 2008, the patient complained of gingival overgrowth occurring one month earlier *(Figure 1).* Based on her complaint and routine tests (the concentration of cyclosporin A in blood and urine), her physician decided to switch her from cyclosporin A to tacrolimus, an immunosuppressive agent known not to cause gingival overgrowth. One month after switching to tacrolimus, a regression in gingival overgrowth started to occur and dental calculus deposits became more visible in both the upper and lower jaws *(Figure 2).*

Because the patient was unhappy with the appearance of her gingivae and the overgrowths made chewing uncomfortable, it was decided to treat the problem surgically using an Er,Cr:YSGG (erbium, chromium: yttrium-scandium-gallium-garnet) hydrokinetic laser to remove the gingival overgrowth and remodel the gingivae. The use of a traditional surgical approach was discounted because it was considered that bleeding would have been more severe and healing slow in an immunosuppressed patient.

Prior to performing surgery, the patient was given intensive oral hygiene instruction and a thorough scaling using an ultrasonic scaler. One week later, the overgrowth was excised and the gingivae remodelled using an Er,Cr:YSGG hydrokinetic laser. *Figure 3* shows the patient after Er,Cr:YSGG hydrokinetic laser surgery. The very good immediate post-operative result was obvious. *Figure 4* shows the patient one day after the Er,Cr:YSGG hydrokinetic laser surgery.

The patient maintained excellent oral hygiene and one month later, with the exception of mesio-buccally to her upper right lateral incisor, was free of plaque and gingivitis in the area of her surgery *(Figure 5).* She was given further instruction in oral hygiene to improve her brushing mesially to her upper right lateral incisor and asked to return every three months for review and further oral hygiene instruction and prophylaxis as required.

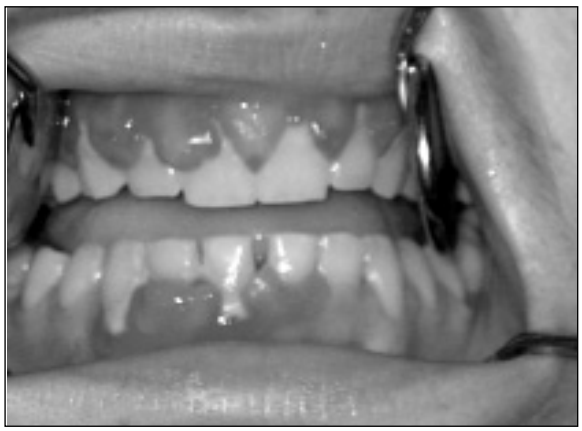

Figure 1. *Patient O.A., 18 years old, nine months following the transplant, and approximately one month following the occurrence of gingival overgrowth.*

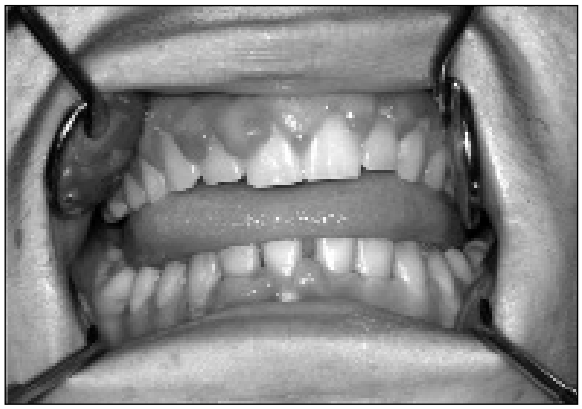

Figure 2. *Patient O.A., 18 years old, one month following the conversion from cyclosporin A to tacrolimus.*

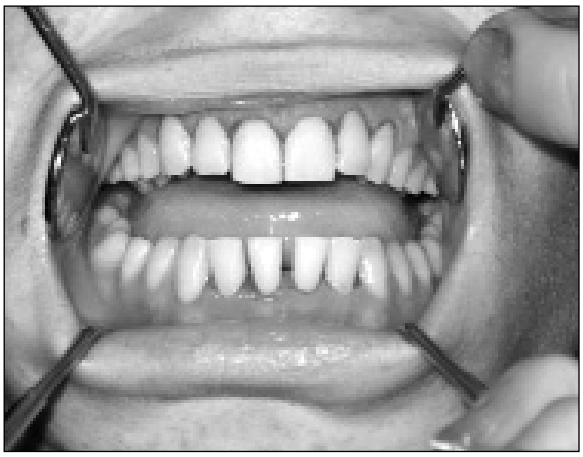

Figure 3. *Patient O.A., 18 years old, following hydrokinetic Er,Cr:YSGG laser surgery, 30th October 2008.*

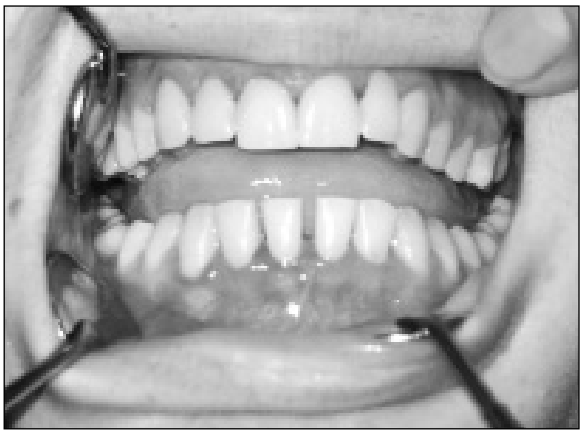

Figure 4. *Patient O.A., 18 years old, one day following hydrokinetic Er,Cr:YSGG laser surgery.*

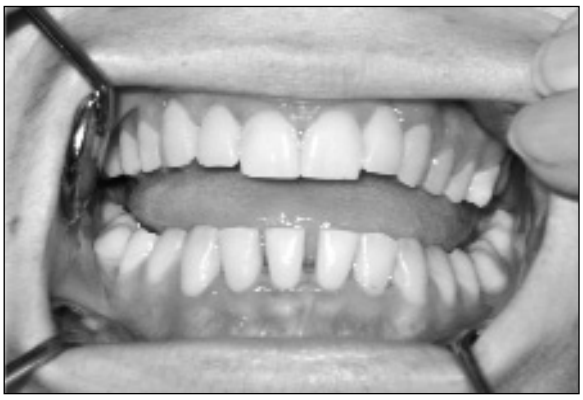

Figure 5. *Patient O.A., 18 years old, one month following hydrokinetic Er,Cr:YSGG laser surgery.*

Discussion

A number of features of this case merit discussion. First, prevention of dental plaque accumulation by toothbrushing three times a day, oral rinsing with antiseptic solutions and ultrasound scaling whenever necessary make the occurrence of inflammation and gingival overgrowth less likely. Bacterial plaque and consequent gingival inflammation seem to exacerbate drug-induced gingival overgrowth. Some authors suggest that poor oral hygiene is an important risk factor for the expression of drug-induced gingival overgrowth [6,7,11,12]. Most reports on the relationship between bacterial plaque and gingival overgrowth have been derived from cross-sectional studies, but there is no clear evidence that bacterial plaque is a contributory factor or a consequence of the gingival changes [13]. However, it can be assumed that adequate oral hygiene could delay the development of cyclosporin A-induced gingival overgrowth, possibly by eliminating the lesion-specific inflammatory component. Nevertheless, it may well be that improved oral hygiene alone cannot prevent gingival overgrowth [1,12,13].

Second, it should be noted that post-operative bleeding was insignificant. It is important to mention that this type of surgery does not require anaesthesia, thus no additional stress was given to an already immunosuppressed patient. By using Er,Cr:YSGG hydrokinetic laser surgery, both homeostasis and sterilisation of gingival tissues were ensured. This therapy is only slightly invasive, the aesthetic improvement is immediate, and sutures and dressings are unnecessary [14]. During the procedure, the patient reported that pain from the gingival overgrowth disappeared, bleeding was almost absent, and consequently the patient's discomfort was eliminated. The fact that laser surgery ensures disinfection, sterilisation of dental tissues with reduction of bacterial viability, and rapid haemostasis is an important consideration with regard to the prevention of post-operative infection and the enhancement of healing, especially in immunosuppressed patients.

Third, Suzuki and Charon (1989) included drug-induced gingival overgrowth among the forms of gingivitis, defining it as 'a drug-related gingival enlargement'. These authors believed that bacterial plaque is an essential causal factor of drug-related gingival hyperplasia [15]. Thus, the pathogenesis of this form of gingivitis is altered by the administration of some drugs determining hyperplastic growth of marginal gingiva. This entity is frequently described as the presence of some false periodontal pockets (the epithelium at the cemento-enamel junction preserves its attachment). 'Gingival overgrowth' is the preferred term to describe this form of drug-related gingival hyperplasia [16]. Other authors suggest that the presence

of inflammation is not essential for the occurrence of drug-induced gingival overgrowth, but that it could modulate its degree of development by exacerbating it [17].

The patient in this case report practised good oral hygiene after ultrasonic scaling and professional brushing, and this clearly demonstrated a beneficial effect. Excision of the remaining overgrown tissue in the frontal mandibular and maxillary regions resulted in the total removal of the gingival overgrowth.

Conclusions

- Gingival overgrowth is a side-effect of the long-term administration of cyclosporin A. A decreased dosage of cyclosporin A may lead to a reduction in gingival overgrowth, but not to its disappearance.
- Gingival enlargement may also be influenced by other predisposing factors, such as bacterial plaque.
- There is considerable variation in the response of the gingival tissues of individual patients taking cyclosporin A.
- In this case study, the use of Er,Cr:YSGG hydrokinetic laser surgery facilitated optimal removal of overgrown gingival tissue, with very good results.
- Such treatment to excise and remodel the gingival contour should be considered whenever gingival overgrowth causes aesthetic and functional problems.
- The use of an Er,Cr:YSGG hydrokinetic laser to removal gingival overgrowth surgically reduces a patient's stress by eliminating the need for local anaesthesia, decreasing intra-operative haemorrhage, and diminishing post-operative pain and oedema, thus shortening healing time.
- Because no suture is needed, the aesthetic result is immediate.

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