This case report illustrates the diagnosis, treatment and long-term follow-up of a patient with ciclosporin- and nifedipine-associated gingival enlargement. The patient was treated successfully without changing his medications. The main aim of the treatment was to reduce the extent of the gingival enlargement, thus restoring dental health, function and aesthetics. Following initial periodontal therapy, a surgical phase was performed. The patient was followed for two years with no recurrence of his gingival enlargement.

Introduction

A 33-year-old male patient was referred by his nephrologist to the National Dental Centre in Singapore, for the management of his gingival enlargement. His chief complaint was the enlargement of his gums that had resulted in difficulty in eating (Fig 1).

Medical history

The patient suffered from renal failure and had received a living (unrelated) renal transplant one year prior to the dental visit. He also presented with hypertension. His medications for his medical conditions following the renal transplant included: ciclosporin, prednisolone, mycophenolate mofetil, enalapril, nifedipine, calcium carbonate and dipyridamole (Persantin®). Furthermore, there were a number of medications the patient had to avoid due to drug interactions with immunosuppressive medications (allopurinol, carbamazepine, cimetidine, ...
danazol, diltiazem, erythromycin, clarithromycin, fluconazole, ketoconazole, non-steroidal anti-inflammatory agents, phenytoin, phenobarbital, rifampicin, verapramil, extra vitamin A/ retin A, vitamin E). He was a never-smoker.

### Examination

- **Extraoral examination**
The patient had an erythematous left eye due to his hypertension. No other abnormalities or signs of pathology were detected extraorally.

- **Intraoral examination**
No abnormalities, such as indurations and ulcerations, were noted on the oral mucosa, tongue and sublingual area.

- **Dental examination**
The dentition comprised 32 teeth, including a supernumerary incisor ($) between tooth 22 and tooth 23 (Figs 2a and 2b). Tooth 46 was missing. Tooth 36 had been restored with a porcelain-fused-to-metal crown (Fig 2d).

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Figs 1a to d Intraoral views at examination.
**Periodontal examination**

The patient presented with severe gingival enlargement affecting all four quadrants (Figs 2a to 2d). The gingival enlargement was most prominent interdentally and on the maxilla (Figs 3a to 3d). The periodontal chart showed probing pocket depths of up to 15 mm. Most of the probing depths corresponded to pseudo-pockets (Fig 4). Teeth 28 and 38 had Grade 2 mobility. The bleeding on probing (BOP) score was 70%.

**Radiological examination**

The radiological examination showed minimal generalised horizontal bone loss, with angular bone defects on teeth 27 (mesial) and 28 (mesial). Tooth 36 was endodontically treated. There was no sign of periapical pathology. Pneumatisation of the right and left maxillary sinuses was noted (Fig 5).

**Diagnosis**

Based on the findings of the examination, the patient had generalised drug-associated gingival enlargement with localised chronic periodontitis. He also had a class I occlusion with the presence of a supernumerary incisor. Caries was under control, and the patient presented with mandibular Kennedy class III partial edentulism.

**Aetiology**

The primary aetiological factors included supra- and sub-gingival plaque and calculus deposits. Ciclosporin and nifedipine medications contributed to the induction of the gingival enlargement, as modifying factors.
Prognosis

A pre-therapeutic single tooth prognosis, based on a modification from Lindhe et al was established. Teeth 18, 28, and 38 were considered 'irrational to treat', due to non-function. Teeth 26 and 27 were given a 'doubtful' prognosis, due to the large extent of attachment loss. The remaining teeth were considered to have a 'secure' prognosis.

Treatment planning and treatment sequence

The treatment planning consisted of four phases:
1. Systemic phase
2. Hygienic phase
3. Corrective phase
4. Maintenance phase

Systemic phase

In the systemic phase, clearance was obtained from the nephrologist regarding precautions before and during dental therapy. The patient was required to discon- tinue Persantin® two weeks before surgery and scaling/root planing therapy.
**Hygienic phase**

The patient was educated regarding the aetiology of periodontitis and the importance of good oral hygiene in the long-term success of his treatment. Oral hygiene instructions included the Bass technique and the use of the dental floss and interdental brushes. Debridement of all teeth (scaling and root planning) was performed under local anaesthesia. During this period, a 0.2% chlorhexidine mouthrinse was used for 1 minute twice a day. Teeth 18, 28 and 38 were extracted. Re-evaluation was scheduled at 6 weeks following completion of the hygienic phase. This was mainly to assess the oral hygiene and the periodontal status prior to the corrective phase. Also, the need and extent of additional treatment on the basis of the patient data was determined.

**Corrective phase**

For the corrective phase, gingivectomies were performed in all four quadrants to reduce the gingival enlargement. The surgeries were performed in four sessions. The sequencing of the surgeries was based on the severity of the gingival enlargement, beginning at the quadrant with the least amount of gingival enlargement (the fourth quadrant), followed by the first, the third, and finally the second quadrants. Gingival recontouring with electrosurgery was performed in the fourth, first and second quadrants. Electrosurgery was used because the electrodes could be shaped to access areas unreachable by normal scalpels. Haemostasis is achieved by sealing blood vessels before cutting, thus enabling a dry operative field with minimal bleeding, unlike conventional gingivectomies performed by scalpel.

Gingival recontouring with laser surgery was performed in the third quadrant. This technique was used as an alternative to the conventional scalpel and the electrosurgery. It enabled precise removal of small amounts of tissue, with haemostasis achieved at the same time. Other benefits included sterilisation of the wound area, minimal swelling, and reduced post-surgical pain. The use of local anaesthesia was required, however.

No restorative phase was planned, as the patient did not wish to restore the small edentulous space in region 46 (Fig 6).

**Surgical intervention**

In the fourth quadrant, electrosurgery (Whaledent, PerFect TCS Tissue Contouring System) was performed to remove and recontour the enlarged gingiva, thus achieving a ‘normal positive’ gingival architecture. Pre-operatively, a periodontal chart with probing depths was recorded for the teeth at the surgical site. As the patient had minimal or no bone loss around these teeth, final probing depths within 3 mm were achieved.

A long loop electrode was used for the procedure, with a ‘cutting’ mode at 5 units for gross removal of gingival tissue. This was followed by the ‘coagulation’ mode at 5 units for fine recontouring and haemostasis. The electrode was used with light brush strokes and cooling intervals between applications. Prolonged contact time with the tissues and deep electrode penetration were avoided. This was to reduce the amount of lateral heat produced, which may be detrimental to the adjacent tissues. At all times, care was also taken to avoid contact of the electrode with the teeth, the alveolar bone and the surrounding soft tissues. The operating field was kept dry, and damp gauze was used to retract the lip away from the surgical site. Throughout the procedure, high velocity evacuation equipment was used to minimise the offensive odour. The probing depths of the teeth at the surgical sites were within 3 mm after healing. A periodontal dressing was placed over the operation site for the comfort of the patient post-operatively. The patient was instructed to rinse with 0.2% chlorhexidine twice a day post-operatively for 2 weeks. If indicated, analgesics were prescribed for post-operative pain. The periodontal dressing was
removed 7 days post-operatively. At this time, the open wound from the surgery had epithelialised. It has been shown that epithelial closure is usually achieved by 72 hours\(^5\), followed by further maturation of the connective tissue\(^6\).

For the first quadrant, gingivectomy was performed using a scalpel, combined with electrosurgery. The scalpel blade was used in combination with electrosurgery to reduce the procedural time as the speed of excision was found to be the fastest with a scalpel blade\(^7\). It also reduced tissue damage. A blade (No.15) was used to excise enlarged gingiva in the interdental areas and distal to tooth 17. The electrosurgical unit was subsequently applied for fine recontouring. The post-surgical management was as described above.

Carbon dioxide laser (LUXAR Corporation, LX-20 Series) was used to recontour the gingival enlargement in the third quadrant. The CO\(_2\) laser was applied in continuous beam mode at a 6 W setting for gross gingiva recontouring. Both focused and defocused modes were used. A back-and-forth motion in brush-like strokes was employed to ablate the tissues. Charring of tissue was performed using a 3 W setting. No periodontal dressing was placed.

During the procedure, the patient, the assistant, and the operator wore clear protective goggles. Highly reflective instruments were avoided as the laser beam bounces off reflective surfaces. The CO\(_2\) laser is primarily absorbed by water molecules. In oral soft tissues that are high in water content, the energy is readily absorbed. This limits the penetration capacity.

Finally, the surgery for the second quadrant was only performed 1 year after hygienic phase due to the patient’s job schedule. During this period, the patient was able to keep high standards in oral hygiene. The gingival enlargement over the second quadrant was less severe than prior to the hygienic phase. Electrosurgery was performed for the second quadrant as well, without the planned open flap debridement. Immediately post-operatively, the probing depths of the teeth at the surgical sites were within 3 mm, except for teeth 26 and 27, which had an interdental probing depth of 4–5 mm.

For all the surgical procedures, the post-operative healing was uneventful. The patient experienced minimal pain and no bleeding and had no complaints throughout the healing phase.

Three months after the last surgery, the periodontal status was reassessed (Fig 7). There were five residual pockets of 4 mm. The patient’s BOP score at that time was 14%.

### Maintenance phase

The patient was placed on a maintenance care programme with a recall frequency of 3 months. Each recall visit included assessment of the oral hygiene status and the soft tissue architecture for any recurrence of gingival enlargement. Oral hygiene instructions were reinforced if necessary. Also, removal of supra- and sub-gingival plaque and calculus were performed if needed. This was to prevent the recurrence of the gingival enlargement.
Evaluation two years after the surgical phase

Two years after the final surgery was performed, a periodontal evaluation was obtained (Figs 8a and 8b). There were four residual probing pocket depths of 4 mm on teeth 17, 26 and 27. The BOP score was 2%. The patient was able to keep very good oral hygiene standards, with no recurrence of gingival enlargement (Figs 9a and 9b, 10a to 10c, 11a to 11c). During this period, there was no change in his medication.
Gingival enlargement is one of the known side effects of ciclosporin therapy. Between 25% and 70% of patients on ciclosporin therapy experience some form of gingival enlargement8-13. It has also been reported that the severity of gingival enlargement is greatly increased with combined therapy of both ciclosporin and nifedipine, as compared to ciclosporin medication alone10. Nifedipine represents a major risk factor for gingival enlargement, with an odds ratio of about 25 in comparison to ciclosporin medication alone, thus requiring surgery13. The pathogenesis of ciclosporin- and nifedipine-induced gingival enlargement, however, still remains unclear. Both medications affect calcium homoeostasis, with ciclosporin lowering free calcium, and nifedipine being a calcium channel blocker. The synthesis and release of collagenases are impaired, as they are calcium-dependent processes. This disrupts the balance between collagen production and breakdown, thus leading to the gingival enlargement. The combined inhibitory effects of both drugs on collagenase production may explain the synergistic effect of the combined medication on gingival enlargement.

Besides combined ciclosporin and nifedipine treatment increasing the risk of developing gingival enlargement, other risk factors were also identified in the patient of the present report. Age appeared to be a significant risk factor to recurrence of severe gingival enlargement14. The recurrence of the condition is inversely correlated to age in several studies12,15. Males appear to have more severe gingival enlargement compared with females13, with the males being three times more likely to develop gingival overgrowth16.

The patient was treated dentally without any substitution of his existing medications to reduce the gingival enlargement. The surgical phase was performed three months after the hygienic phase completion to allow for optimum reduction in soft tissue enlargement due to improvement in oral hygiene standards and root instrumentation17,18. Following hygienic phase completion, it was noted that the gingiva became less inflamed, and there was reduction in the enlarged tissues at some sites. Surgical therapy had to be performed in order to facilitate oral hygiene procedures, since non-surgical therapy was not adequate in eliminating the enlargements induced by ciclosporin and nifedipine.

From the clinical result attained with treatment, a combination of scaling and root planing, oral hygiene instructions and surgical therapy (electrosurgery and
laser surgery) was effective in reducing drug-induced gingival enlargement and maintaining the treatment outcomes for 2 years. The patient was able to maintain high standards of oral hygiene, thus preventing the recurrence of the gingival enlargement17.

Two different surgical techniques, electrosurgery and laser surgery, were used at different sites, to compare the different treatment modalities. It was found that both surgical methods achieved haemostasis, and were effective in reducing the gingival enlargement, with minimal difference in healing responses and long-term stability of the treated sites in this patient. With reference to electrosurgery, studies have shown that although tissue changes following incision differ from those of the surgical scalpel, the healing time5,6, and healing response19 were very similar. Similarly, for the CO2 laser, after 2 weeks of healing, there was minimal difference between the scalpel and laser wounds20.

In terms of manipulation, the CO2 laser required more time compared with electrosurgery7. It also lacked the tactile sensation when compared with electrosurgery and the surgical scalpel.

It was noted that for the second quadrant, the treatment performed was electrosurgical gingivectomy without a need for any open flap procedures. At the time of re-evaluation, the amount of gingival enlargement had reduced greatly due to the successfully completed hygienic phase.

At the completion of active periodontal therapy, the patient had a BOP score of 14%, with absence of probing pocket depths of 5 mm and above. This, in turn, may be considered as an excellent treatment outcome. The patient was satisfied with the results achieved in terms of aesthetics and function. He was happy that the treatment had enabled him to perform oral hygiene procedures with greater ease and to eat in comfort.

Considering his long-term medication of ciclosporin and nifedipine, together with other risk factors mentioned, the patient had been warned of the possible recurrence of the drug-induced gingival enlargement. Thus, the maintenance care was of utmost importance to this patient, as good oral hygiene has to be assured and any recurrence of gingival enlargement may be detected early. Ilgenli et al14 reported a lower rate of recurrence with regular recall visits, while others21 recommended strict plaque control in preventing recurrence of ciclosporin-associated gingival enlargement.

Although it had been reported that the recurrence rate of ciclosporin or nifedipine associated gingival enlargement was approximately 40% with-
in 18 months after surgical therapy\textsuperscript{14}, the patient of the present report was able to maintain his periodontal status and prevent the recurrence of his gingival enlargement for 2 years. The success of this patient’s treatment lies in his optimal oral hygiene performance, and his regular 3-monthly maintenance visits. Routine periodontal therapy and surgical intervention may play a role in the management of drug-associated gingival enlargement, with long-term stability being achieved, as documented by the present case report.

In summary, with adequate training in the use of the equipment, both techniques are safe and effective for the removal of gingival enlargement. The various precautions should be observed to avoid damage to the adjacent tissues and the teeth\textsuperscript{22}. There were no major post-operative complications related to both modes of treatment. However, the patient did mention that he preferred the use of electrosurgery to the CO\textsubscript{2} laser, in terms of comfort during the procedure and the post-surgical phase.

\section*{References}