

# Case report: drug-induced gingival overgrowth associated with the use of a calcium channel blocker (amlodipine)

## Précis

A case of gingival overgrowth induced by: (i) poor plaque control; and, (ii) a calcium channel blocker (amlodipine), and its conservative and surgical management.

## Abstract

**INTRODUCTION:** Many factors can contribute to the development of gingival overgrowth (hyperplasia), including: plaque control; periodontal variables; medications and their relative dose; age; sex; and, genetic factors. Nifedipine is a calcium channel blocker commonly reported to result in drug-induced gingival overgrowth (DIGO). This report outlines a case of gingival overgrowth induced by amlodipine (a calcium channel blocker less frequently reported to cause gingival hyperplasia), exacerbated by the presence of plaque.

**CASE REPORT:** A 63-year-old male presented to the dental outpatient clinic at the Dublin Dental University Hospital with severe DIGO. He reported that his gums had started to enlarge two years previously, but that he was now concerned as they were increasing in size and had become firmer. Medically, the patient had hypertension, hyperlipidaemia, was taking amlodipine 10mg once daily, and was a former smoker. Following initial oral hygiene instruction and local debridement to reduce the gingival inflammation, some of the remaining excess gingival tissues were removed surgically and sent for histopathological analysis.

**DISCUSSION:** Two possible causative agents were identified as: (i) amlodipine medication; and, (ii) poor plaque control. The removal of the pedunculated lump mesial to tooth 1-3 and the hyperplastic mandibular gingiva allowed for definite histopathological analysis of "fibroepithelial overgrowth showing moderate chronic inflammation". Following the excisional biopsies there was improved access for professional and at home cleaning, in addition to an improved aesthetic outcome.

**CONCLUSION:** It is important that we are aware that individuals taking calcium channel blockers need to demonstrate excellent plaque control to reduce their risk of developing DIGO, and to reduce its severity should it arise.

## Key terms

**GINGIVAL HYPERPLASIA:** 'an abnormal increase in the number of normal cells in a normal arrangement in an organ or tissue, which increases in volume'.<sup>1</sup>

**GINGIVAL OVERGROWTH (GO):** Many terms have been used in the literature to describe clinically apparent enlargement of the papillary and marginal gingiva. It has been suggested that GO is a more general term that better describes the lack of understanding of the pathogenesis of the condition.<sup>2</sup>

Journal of the Irish Dental Association 2015; 61 (5): 248-251.



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## Introduction

Many factors can contribute to the development of gingival overgrowth (GO), including: plaque control; periodontal variables; medications and their relative dose; age; sex; and, genetic factors.<sup>3</sup> Medications associated with drug-induced gingival overgrowth (DIGO) are broadly categorised according to their therapeutic actions, namely anticonvulsants, immunosuppressants and calcium channel blockers.<sup>4</sup>

In 1994, Bokenkamp *et al.* graded gingival overgrowth:<sup>5</sup>

0: No sign of enlargement

Grade 1: Enlargement confined to dental papilla

Grade 2: Enlargement involving dental papilla and marginal gingiva

Grade 3: Enlargement covering three-quarters of crown of tooth or more

Calcium channel blockers are regularly prescribed in the treatment of conditions such as hypertension and angina. They may be classified chemically as dihydropyridines (nifedipine, isradipine and amlodipine), phenylalkylamine derivatives (verapamil) and benzothiazepine derivatives (diltiazem).<sup>1</sup> Nifedipine is the calcium channel blocker most commonly cited to induce GO,<sup>6,7</sup> with approximately 10% of medicated patients presenting with the condition.<sup>8</sup>

Other risk factors for calcium channel blocker DIGO include: gender; duration of therapy; concomitant medications; plaque; and, oral hygiene.<sup>3</sup> Males appear to be at greater risk and tend to present with more severe gingival hyperplasia.<sup>9</sup> Combination therapies, in particular in relation to nifedipine and ciclosporin, can produce more GO than if either drug was used independently.<sup>10,11,12</sup>

There is a lack of data reporting amlodipine specifically as a causative agent.<sup>13</sup> The mechanism by which amlodipine may induce these changes remains poorly understood and the literature is sparse, with few case reports outlining its association.<sup>9,10,12</sup> Regarding the clinical presentation of DIGO, the mandibular anterior gingiva is the most commonly affected site, but in severe cases the condition may affect multiple areas of the mouth. If oral hygiene is good, the swelling tends to be less apparent, with a reduction in inflammation seen. However, in the presence of plaque the inflammatory changes appear to enhance the activity of the fibroblasts, thus increasing their number and also increasing the production of collagen fibres and proteoglycans, worsening the severity of the hyperplasia. The hyperplasia tends to mainly be constructed of highly vascular fibrous tissue with acanthosis of the epithelial lining in a dense collagenous matrix.<sup>8</sup>

The care pathway for these patients generally involves an initial non-surgical approach alongside surgical management as required.

## Non-surgical management

Selection of a treatment modality depends on the severity of the DIGO. Elimination of local factors, plaque control and regular periodontal maintenance therapy may ameliorate but not prevent DIGO in a susceptible patient.<sup>9</sup> Plaque control should always be a first-line measure in an attempt to control the inflammatory oedematous gingivitis.<sup>14,15</sup> There is evidence that good oral hygiene and plaque removal decreases the degree of GO and improves periodontal health.<sup>16,17</sup> The use of chlorhexidine digluconate mouthwash (0.1% w/v) may reduce the incidence of DIGO recurrence following gingival surgery.<sup>18</sup>

## Surgical management

Surgical treatment is only advocated where GO is severe and should be combined with cause removal where possible and non-surgical management.<sup>16</sup> GO may be assessed using the method described by Seymour *et al.* (1985).<sup>19</sup> The

index measures the degree of GO in a labio-lingual and apico-coronal direction. Surgical interventions have been suggested with GO index scores in excess of 30%.<sup>20</sup> If drug therapy is likely to be continued for life, psychosocial considerations must be taken into account in an effort to reduce the frequency and extent of surgical intervention.<sup>20</sup> Factors to be considered when deciding on appropriate treatment include the extent of the surgical area, the presence of periodontitis, the presence of osseous defects combined with gingival enlargement, and the position of the base of the periodontal pocket in relation to the existing mucogingival junction.<sup>15</sup> If the mucogingival junction is too close to the base of the periodontal pocket, a surgical approach such as a gingivectomy would be inappropriate. This is because there would not be enough attached gingiva remaining after the procedure and rapid recession could occur as a result.

The conventional external bevel gingivectomy is a viable treatment option in small areas (up to six teeth), with no evidence of attachment loss.<sup>15</sup> The internal bevel periodontal flap is indicated in situations with larger areas of GO, or areas where attachment loss is combined with an osseous defect.<sup>15</sup> It was found that no difference exists between flap surgery and conventional gingivectomy with respect to recurrence of GO.<sup>21</sup> Provided clinical guidelines based on research are adhered to, evidence supports the biological compatibility of electrosurgery to excise papillary enlargement.<sup>22</sup> The carbon dioxide (CO<sub>2</sub>) laser has been advocated in surgical management of DIGO due to decreased surgical time and rapid postoperative haemostasis.<sup>20</sup> A comparison split-mouth crossover study conducted by Mavrogiannis *et al.* (2006) revealed less recurrence of DIGO within a six-month period with laser excision than with conventional gingivectomy.<sup>21</sup> The use of CO<sub>2</sub> lasers in combination with conventional gingivectomy has been advocated for dual DIGO.<sup>23</sup>

## Follow-up care

Meticulous oral hygiene is required in order to maintain a healthy periodontal condition. Poor plaque control is likely to result in recurrence of the GO and thus these patients should be provided with regular hygiene visits. With adequate plaque control, recurrence is less likely, although the patient remains at risk.<sup>24</sup> In a study of induced severe DIGO (nifedipine and ciclosporin), a recurrence rate of 34% was reported over an 18-month review period following periodontal surgery.<sup>25</sup> Using multiple regression analysis, it was also reported that age, gingival inflammation and attendance at recall appointments were significant factors in determining the likelihood of recurrence. For this reason, regular follow-up appointments are required to recognise any signs of deterioration early.<sup>25</sup>

## Case report

A 63-year-old male was referred to the accident and emergency department at the Dublin Dental University Hospital (DDUH) complaining of swollen gums. The patient reported that they had started to enlarge two years previously, but that he was now concerned as they were increasing in size and had become more firm. Medically, the patient had hypertension, hyperlipidaemia and was taking amlodipine 10mg OD (calcium channel blocker) and aspirin 75mg daily. He was a former smoker, having quit 12 years previously (**Figures 1-5**).

Extra-oral examination revealed no cervical lymphadenopathy, no swelling and cranial nerve responses were normal; however, there was marked halitosis. Intra-orally there was moderate gingival hyperplasia affecting the mandible extending from tooth 3-3 to 4-3, affecting buccal and lingual gingiva, and also hyperplasia



FIGURES 1-5: A 63-year-old male was referred to the accident and emergency department at the Dublin Dental University Hospital (DDUH) complaining of swollen gums. The patient reported that they had started to enlarge two years previously, but that he was now concerned as they were increasing in size and had become more firm.



FIGURE 6: The mucosa overlying the area was intact, mobile and firm to touch.



FIGURE 7: Special investigations included an OPG.



FIGURE 8: Appearance post biopsy and gingivectomy.



FIGURE 9: Image following initial root surface debridement.



FIGURE 10: Appearance post biopsy and gingivectomy.



FIGURES 11-13: Results post treatment. The clinical team and the patient remain happy with the results.



affecting the maxillary gingiva palatal to teeth 2-3 and 2-4. There was a pedunculated lump mesial to tooth 1-3 on the attached gingiva measuring 7x7mm in size. The mucosa overlying the area was intact, mobile and firm to touch (Figure 6). Special investigations included an OPG (Figure 7) and blood tests (full blood count and white cell differential). Diagnosis was grade 2 gingival hyperplasia due to a combination of poor oral hygiene and the use of

calcium channel blocking medication.

Initial management was provided in the form of intensive oral hygiene instruction and gross supra-gingival calculus removal. Figure 9 was taken following the initial root surface debridement.

The polyp-like growth mesial to 1-3 was removed with an external bevel gingivectomy. This was completed under local anaesthetic only with buccal and

palatal infiltrations using 2.2ml of Lignospan (2% lidocaine) 1:80,000 epinephrine. The biopsy site was sutured with black silk and a sample was sent for histopathological analysis. The diagnosis was “marked fibroepithelial overgrowth associated with patchy chronic inflammation”.

Following review, oral hygiene was greatly improved, plaque score reduced and gingival inflammation lessened. The hyperplasia remained prominent in areas buccal and lingual to 3-3 to 4-3. The decision was made to complete surgical periodontal treatment with a gingivectomy of the hyperplastic tissue buccal and lingual to the mandibular anterior gingiva. This was also completed under local anaesthetic using infiltrations (4.4ml of Lignospan (2% lidocaine) 1:80,000 epinephrine). A Coe-pac dressing was placed to protect the surgical site, postoperative instructions were explained and the patient was booked for review in one week. **Figures 8-10** demonstrate the appearance post biopsy and gingivectomy. Tissue removed was sent for histopathological analysis. The diagnosis was ‘gingival overgrowth’, which was further described as ‘fibroepithelial overgrowth showing moderate chronic inflammation’.

Currently, the gentleman is undergoing regular reviews within the periodontal department and feels a great improvement in his confidence since the gum condition was addressed. The clinical team and the patient remain happy with the results (**Figures 11-13**). If his plaque scores and bleeding scores remain stable and there is no recurrence noted, he should be able to be discharged back to his GDP for maintenance in the future.

### Discussion and conclusions

Two possible causative agents were identified as: (i) poor plaque control; and, (ii) amlodipine medication. Initial treatment commenced with identification of causative factors and conservative management, highlighting the essential role of excellent oral hygiene and providing professional cleaning and support for the patient. The removal of the excess hyperplastic gingival tissues anteriorly in both the maxilla and mandible allowed for definite histopathological analysis, improved access for professional and at home cleaning/maintenance, and facilitated the good aesthetic outcome.

If the condition recurs we may contact the patient’s general medical practitioner to discuss the possibility of an alternative antihypertensive to help to reduce the likelihood of such severe GO occurring. However, changing a patient’s medication should only be considered as a last resort, when local measures have had limited success. The dihydropyridine group of calcium channel blockers (amlodipine, nifedipine, felodipine) are more commonly involved with GO.<sup>26</sup> Non-dihydropyridine (phenylalkylamine) calcium channel blockers such as verapamil have a reduced rate of gingival overgrowth, but do not have the same systemic vasodilating effects.<sup>27</sup> Therefore, consultation with the patient’s GP is appropriate, and medication would only be changed once risks and benefits were assessed appropriately. The most important factor is of course recognising those who are at risk of developing the condition and advising the maintenance of a low plaque score, and thus a low bacterial load.

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