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Case Report

Drug Induced Gingival Overgrowth: A Case Study and Clinical Analysis

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Abstract

Gingival enlargement is the most common side effect seen with the use of three major classes of drugs namely anticonvulsants, calcium channel blockers and immunosuppressants. We reported a case of 42-year-old female treated with Amlodipine for 3 years and developed gingival overgrowth in past 1 year. The GE had affected both mandibular and maxillary arches. Amlodipine was suspected for the GE in agreement with her physician. One month after the substitution of drug with the physician's consent and periodontal therapy, the GE was subsided completely. Later, the deep periodontal pocket measuring ≥5mm were treated with surgical periodontal therapy and patient was followed up regularly for 3 months.

No recurrence of gingival enlargement was experienced by the patient for next 1 year. This unique case should encourage every dental practitioner to be diligent while treating such cases and to consider the potential side effects of using these drugs.

Keywords: Gingival Enlargement (GE); Gingival Overgrowth; Calcium Channel Blockers; Drug Induced Gingival Enlargement (DIGO)

Introduction

Gingival enlargement or gingival overgrowth refers to the abnormal proliferation of the gingival soft tissues. Gingival enlargement has an impact on the individual's esthetics, speech and mastication. They are caused due to local and systemic factors, that needs to be identified thoroughly. Gingival enlargement is classified as inflammatory enlargement, drug induced enlargement, gingival overgrowth associated with systemic conditions. Gingival overgrowth associated with systemic diseases and gingival fibromatosis or idiopathic gingival enlargement [1].

Drug induced gingival enlargement are caused due to the side effect of certain drugs that are used for the treatment of systemic diseases. Drugs that cause gingival enlargement are broadly classified into three categories: anticonvulsants, calcium channel blockers and immunosuppressants. The first case of drug induced gingival enlargement was reported in 1939 by Kimball associated with long term usage of anti-epileptic drug phenytoin [2]. Later on, the other drugs were identified. The prevalence of drug induced gingival enlargement varies substantially for different drugs. 30% to 80% of patients consuming these above-mentioned drugs are at higher risk of developing gingival overgrowth over a period of time [1].

Calcium channel blockers are used to treat cardiovascular diseases such as peripheral vascular diseases, angina, cardiac arrhythmias and hypertension [3]. Some of the drugs that come under this category are nifedipine, amlodipine, diltiazem, verapamil, flunarizine. Prevalence rate of nifedipine induced gingival enlargement was 43.6% of cases and that of amlodipine was 3.3% which is comparatively lesser to the prior drug [4,5].

We present and discuss a case treated by Amlodipine for hypertension for past 3 years and has subsequently developed gingival enlargement in its due course.

Case Report

A 42 year old female was referred to the Department of Periodontology in The Oxford Dental College and Hospital, Bengaluru for severe gingival enlargement. Her past medical history included

hypertension in the last 3 years. She was treated with Amlong 5mg once a day. On further investigation patient gave a history of change of drug from past 8 months to Amlokind AT once a day prescribed by her family physician.

The intraoral examination revealed nodular gingival enlargement affecting the interdental papillae and marginal gingiva. The GE was present on facial/buccal and palatal/lingual surfaces of the teeth. The lower anterior teeth 41, 42, 31 and 32 were grade III mobile. Subgingival calculus deposits, bleeding on probing and generalized periodontal pockets were present. The orthopantomogram of the patient revealed generalized horizontal bone loss. The laboratory investigation advised for the patient was complete blood count.

On the basis of the blood report of the patient she was diagnosed with microcytic hypochromic anemia. (Table 1,2) (Figure 1-16)

Test	Result	Normal value
Haemoglobin	7.3gm/dl	14-16gm/dl
R.B.C count	4 millions/cu. mm	4.5-6.5 millions/cu. mm
P.C. V	24.9%	40-45%
M.C. V	62.0 fL	80-99fL
M.C.H	18.1pg	27-33pg
M.C.H.C	29.1g/dl	32-37 g/dl
Platelet count	4.43 lakhs/cu. mm	1.5-4.5 Lakhs/cu. Mm
Total W.B.C Count	9300/cumm	4000-11000/cumm

Table 1: Complete haemogram.

Test	Result	Normal value
Neutrophils	70.5%	40-75%
Lymphocytes	23.3%	20-45%
Monocytes	4.2%	2-10%
Eosinophils	1.9%	1-6%
Basophils	0.1%	1-2%

Table 2: Differential leukocyte count.

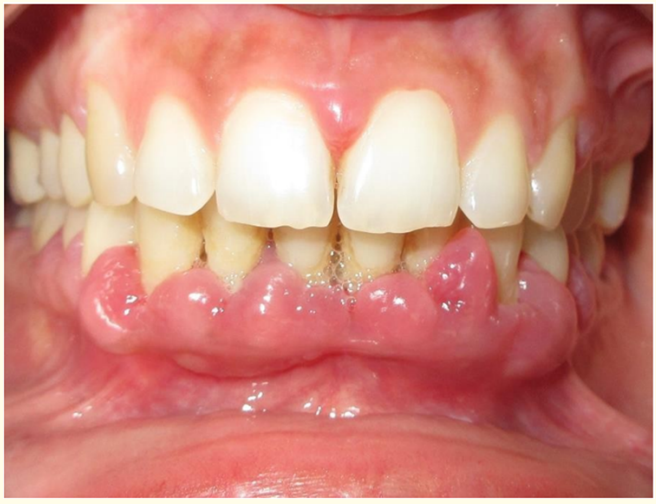

Figure 1: Pre-operative Frontal view.

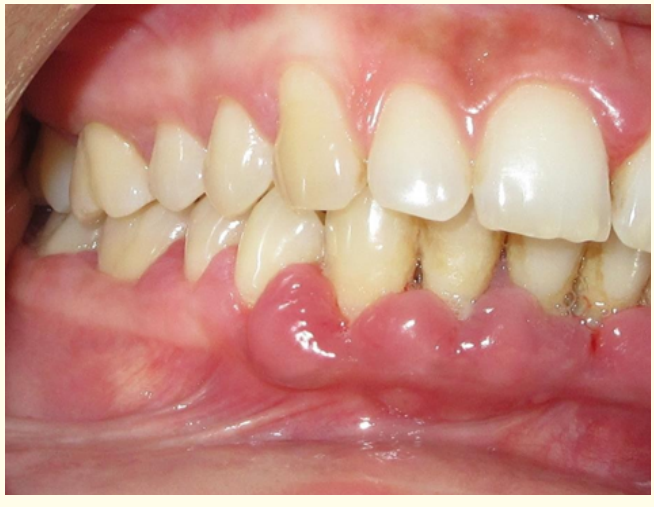

Figure 2: Pre-operative Right Lateral view.

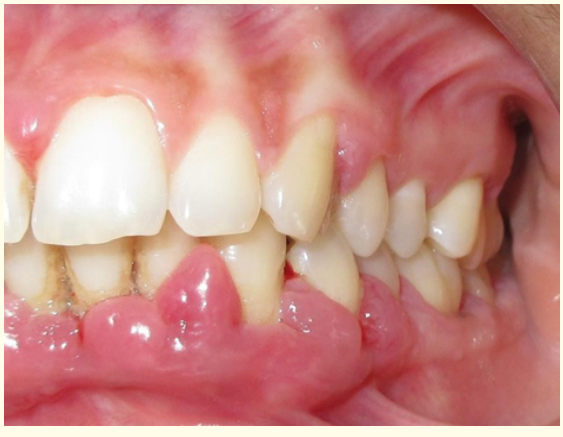

Figure 3: Pre-operative Left Lateral View.

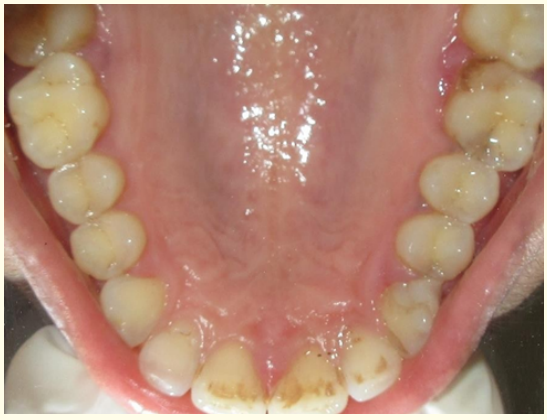

Figure 4: Pre-operative Palatal View.

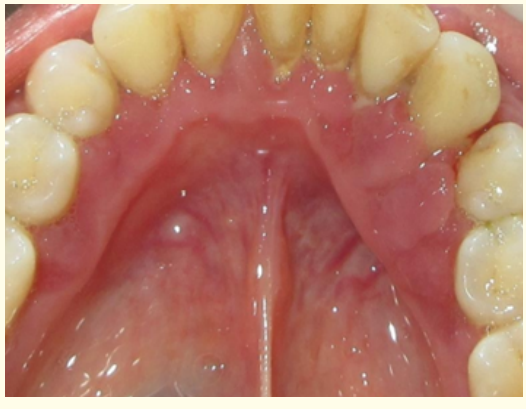

Figure 5: Pre-operative Lingual View.

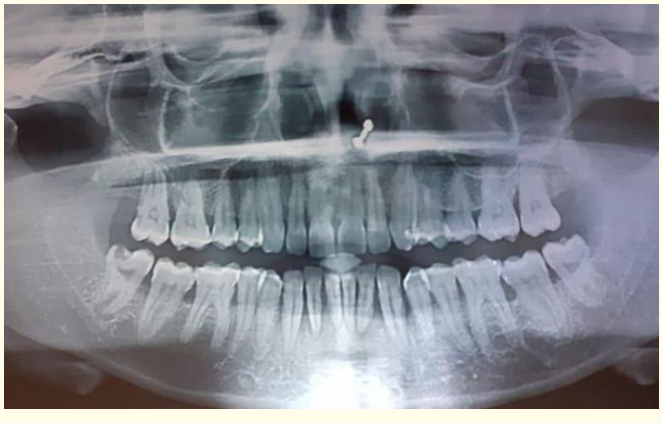

Figure 6: Orthopantomogram.

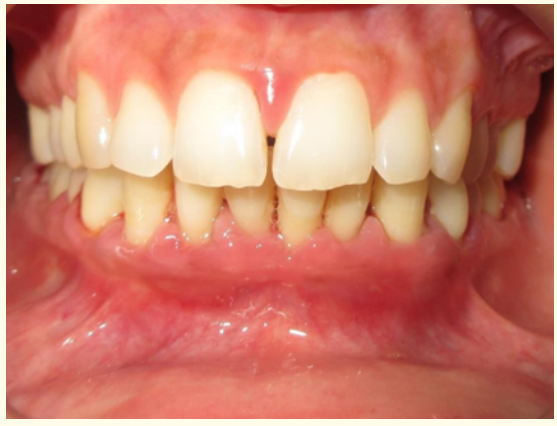

Figure 7: Post-operative Frontal View.

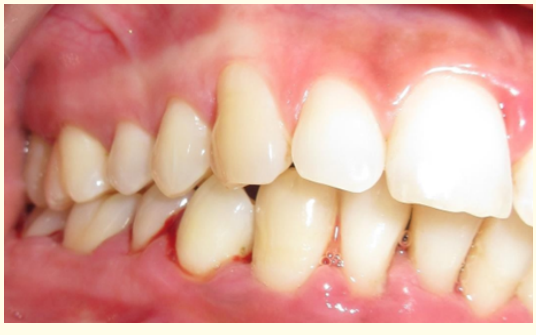

Figure 8: Post-operative Right Lateral View.

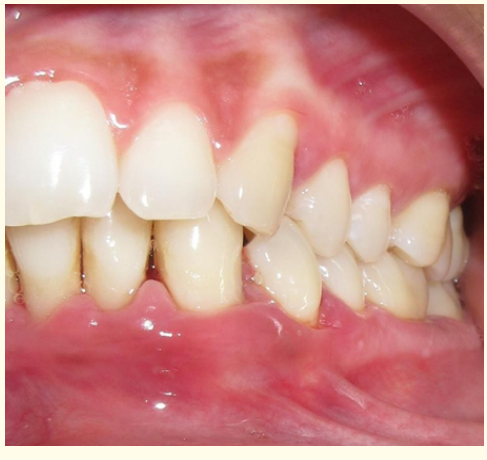

Figure 9: Post-operative Left Lateral View.

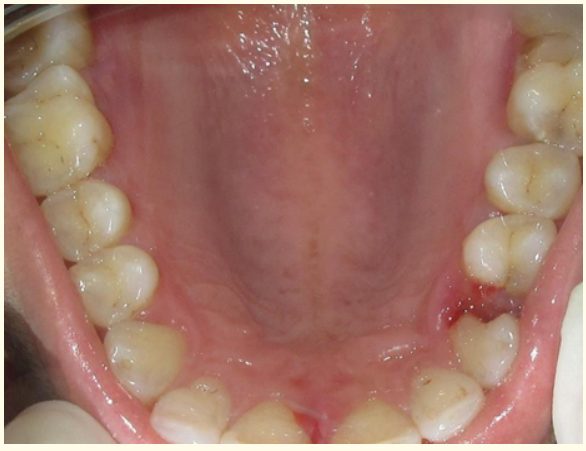

Figure 10: Post-operative Palatal View.

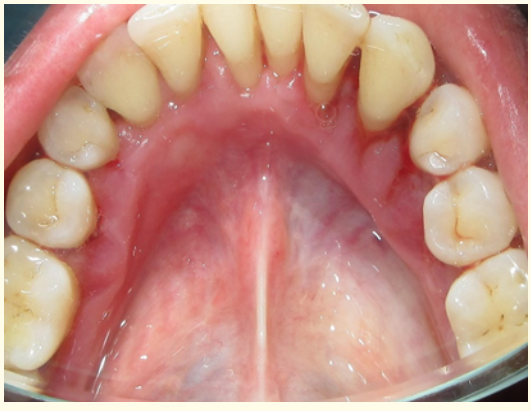

Figure 11: Post-operative Lingual View.

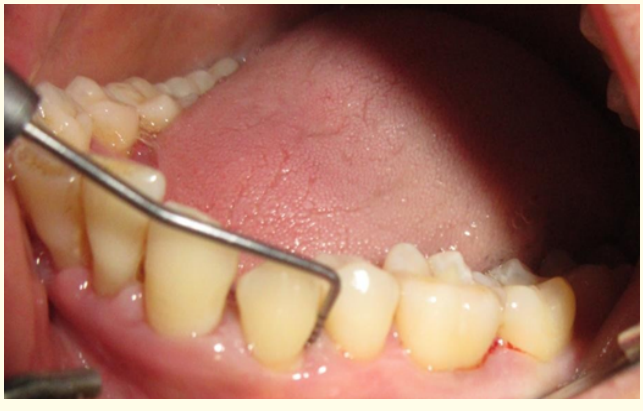

Figure 12: Pre-operative probing depth >5mm.

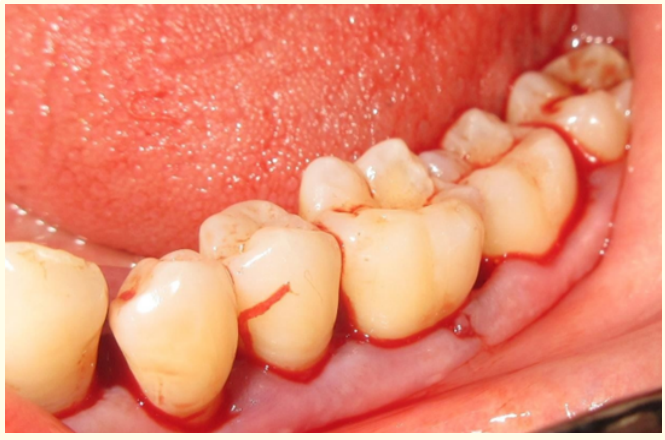

Figure 13: Crevicular Incision.

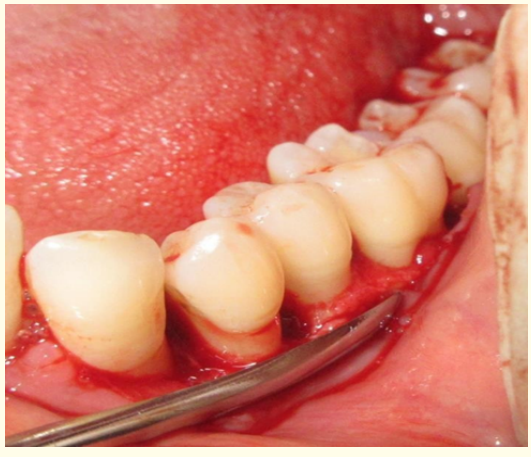

Figure 14: Full Thickness Mucoperiosteal Flap Reflection and Debridement Done.

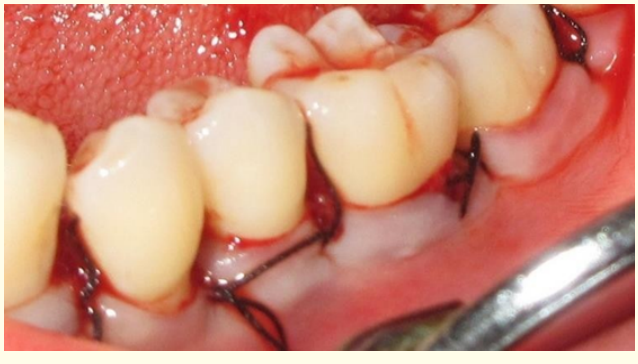

Figure 15: Sutures Placed.

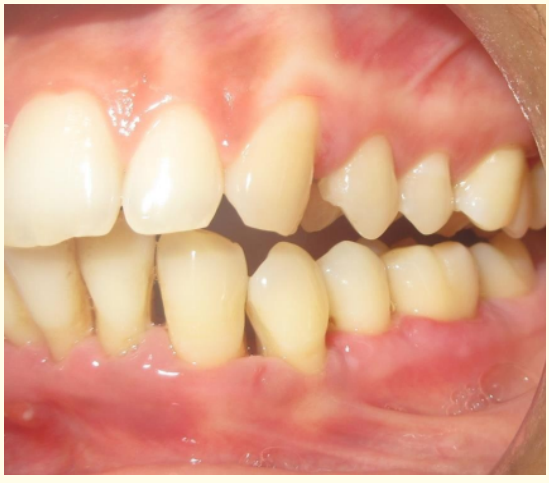

Figure 16: 2 Weeks Follow Up.

The patient was referred to physician for his consent and consideration on the drug substitution (Amlodipine) with the other anti-hypertensive drug and for the treatment of anemia. After the physician's consent, the anti-hypertensive drug was replaced with angiotensin receptor blockers (telmisartan) and along with this drug tablet Livogen, Alworm 400mg was prescribed.

The non-surgical periodontal therapy which include subgingival scaling and root planning were performed. The patient was advised to rinse with 10ml of 0.12% chlorhexidine mouthwash twice a day for a duration of 1 minute and to strictly maintain the oral hygiene. She was asked to report back after 2 weeks for a routine follow up. Meanwhile the gingiva had become fibrous and the inflammation had subsided. The pocket depths were retained at certain sites indicating surgical intervention. The patient was advised to report back after 1 month with her complete blood count report.

The gingival enlargement had almost subsided after 1 month. Her haemoglobin levels were back to normal and she was no more anemic. The pocket depth ≥5mm were treated with surgical periodontal therapy. Quadrant wise periodontal flap surgery under local anesthesia was performed for deeper pockets. The patient was prescribed antibiotics containing a combination of amoxycillin, clavulanic acid and anti-inflammatory drug for duration of 3 days to prevent infection after periodontal surgery. Along with these drugs the patient was prescribed 10 ml of 0.12% chlorhexidine mouthwash same as prescribed earlier. The mobility of the lower anterior didn't subside after non-surgical periodontal therapy, so due to poor prognosis of these teeth they were extracted. The patient was instructed to follow up for every 2 weeks for the first 3 months after the surgical periodontal therapy and later on every 3 months for a year.

Discussion

The classic sign of gingival inflammation is enlargement of gingiva. The causative factor for enlarged gingiva may be local, systemic, environmental or genetic. An increasing number of medications prescribed for the treatment of systemic conditions are associated with the gingival enlargement. Currently there are 20 drugs associated with gingival enlargement including oral contraceptive drugs [6]. Drugs that cause gingival enlargement are divided into 3 main categories they are anticonvulsants, calcium channel blockers and immunosuppressants [6]. The primary target tissue of these drugs is different but the secondary target tissue is the gingival connective tissue leading to common clinical and histological findings [6].

Calcium channel blockers are antihypertensive drugs that are mainly prescribed for elderly patients in case of angina or peripheral vascular disease [7]. Calcium channel blockers are divided into 2 main groups they are

- Dihydropyridine: Nifedipine, amlodipine
- Non-dihydropyridine: Diltiazem, verapamil, flunarizine [3].

The most frequent calcium channel blocker associated with GE is nifedipine and its prevalence rate is 6-15% [8,9] Whereas, the prevalence rate of amlodipine induced GE is about 3.3% which is less as compared to nifedipine [5].

Here, we present a case report of amlodipine induced gingival enlargement in a 42-year-old female hypertensive patient taking amlodipine 5 mg once a day for 3 years.

According to the research, the incidence of nifedipine induced GE is about 0.5% to 83% whereas amlodipine is rare [10]. However, currently a large number of amlodipine induced GE have been reported. The gingival contour is distorted in gingival enlargement leading to increased plaque accumulation. These changes seen in the gingival contour is further exacerbated with plaque induced gingival inflammation that results in edematous and inflamed gingiva. The gingival enlargement causes pain, tenderness, tooth mobility, aesthetic changes, speech disturbances, swelling, bleeding and occlusal disturbances [11]. In the present case the gingival contour was distorted with accumulation of subgingival plaque. Accumulation of plaque has led to the periodontal disease progression and destruction, further complicating the disease.

In the above case gingival enlargement was severe in the anterior region as compared to the posterior region. According to the research drug induced gingival overgrowth appears to be preva-

lent in children, adolescent and has predilection for the anterior gingival tissue [2]. Clinically the gingival changes occur within 3 months of consuming the medications. The pattern of overgrowth is different for each patient but it reaches a state of equilibrium within 1 year of commencement of the medication [2]. The present case is unique since the gingival enlargement was present from past 1 year, so this suggests that gingival overgrowth should also be considered for a late presentation.

It is always worth asking the physician for the drug substitution (Amlodipine in the present case). These drugs are prescribed for the debilitating systemic conditions so the dentist should always consult the physician and the decision of drug substitution should be left on the physician [11].

The treatment aspect of the present case involves non-surgical and surgical periodontal therapy. The non-surgical periodontal therapy involved subgingival scaling and root planning under local anesthesia. Patient was advised to follow intense oral hygiene practice to reduce the gingival inflammation. In the present case 0.12% chlorhexidine mouth rinse was recommended for maintaining the oral hygiene. The recommended periodontal maintenance therapy for drug induced gingival enlargement is of 3 months [12]. In this case the patient was asked to follow up after 2 weeks.

The surgical treatment for drug induced gingival enlargement was recommended by Thompson and Gillespie in 1941 [13]. According to the research factors that govern the surgical treatment aspect for drug induced gingival enlargement are : extent and grade of GE, amount of keratinized tissue present, location of the periodontal pocket in relation to mucogingival junction, type of bone defect present, and esthetic consideration. In the present case the patient was followed up after 1 month of drug substitution and non-surgical periodontal therapy. After 1 month the GE was almost subsided and her hemoglobin count was normal. The periodontal pocket didn't reduce and were ≥5mm, so quadrant wise periodontal flap surgery was planned with the physician's consent. Periodontal flap surgery was carried out under local anesthesia. Gingivectomy was performed in the 3rd quadrant to reduce the bulk of the tissue, followed by periodontal flap surgery. In this case there was severe generalized bone loss hence, the flap surgery was performed so that rapid reduction of inflammation takes place. Through non-surgical periodontal therapy, desired results are visible after 2 to 3 months [14]. The lower anterior 41, 42, 31, 32 were extracted due to poor periodontal prognosis.

According to Ilgenli., *et al*. the recurrence rate of severe drug induced gingival enlargement is 40% in 18 months after non-surgical periodontal therapy [15]. In this case there was substitution of the drug so the recurrence was not found even after 1 year follow up which otherwise would have been seen if the medication was continued.

The patient was advised strict oral hygiene measures and follow up of 3 months for 1year. No further periodontal treatment was required since the gingival enlargement had subsided completely. The patient was referred to the Department of Prosthodontics for the prosthetic rehabilitation with the lower anteriors.

Conclusion

Drug induced gingival over growth is caused due to three major class of drugs they are: Anticonvulsants, Calcium channel blockers and immunosuppressants. Evidence says that DIGO is caused by certain factors they are:

- Pharmacokinetic variables,
- Genetic variation leading to heterogenicity in fibroblast,
- Drug induced changes in the gingival connective tissue homeostasis,
- Plaque induced inflammatory changes
- Drug induced action on growth factors.

Thus, dentists should reflect on these factors and discuss with the medical practitioner to consider the side effect of these drug before prescribing it.

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