Amlodipine induced gingival enlargement: A case report

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Abstract

Calcium channel blockers are one of the most prescribed antihypertensive drugs. Their major drawbacks is poor adherence resulting from headaches, pedal swellings, flushing, reflex tachycardia, erectile dysfunctions and rarely gingival enlargement. Gingival enlargement may lead to dental decay, painful mastication and loss of teeth if not detected and treated promptly. The usage of s-amlodipine has resulted in similar efficacy and less adverse effects. This is a case report of amlodipine-induced gingival enlargement that resolved completely on changing to s-amlodipine.

Hypertrophie gingivale induite par l'amlodipine : à propos d'un cas

Resume
Les inhibiteurs calciques sont l'un des médicaments antihypertenseurs les plus prescrits. Leurs inconvénients majeurs sont une mauvaise observance résultant de maux de tête, de gonflements des pédales, de bouffées vasomotrices, de tachycardie réflexe, de dysfonctions érectiles et rarement d'hypertrophie gingivale. L'hypertrophie gingivale peut entraîner des caries dentaires, une mastication douloureuse et une perte de dents si elle n'est pas détectée et traitée rapidement. L'utilisation de la s-amlodipine a entraîné une efficacité similaire et moins d'effets indésirables. Il s'agit d'un cas d'hypertrophie gingivale induite par l'amlodipine qui s'est complètement résolue lors du passage à la s-amlodipine.

INTRODUCTION

One of the major breakthroughs in the management of hypertension is the development of calcium channel blockers (CCBs). They have since become well established by guidelines as a first-line medication in the management of hypertension and angina pectoris (1-2). One of the major factors mitigating against patients' adherence to these drugs are the side effects of headache, ankle swelling, flushing, bradycardia, reflex tachycardia, erectile dysfunctions, etc (3). The CCBs, have other rare side effects which may be deleterious if not detected early and promptly treated. One of such adverse effects is gingival enlargement which may lead to dental decay and loss of teeth (4).Here is a case of Amlodipine-induced gingival enlargement in a 48-year old patient with hypertension.

CASE PRESENTATION.

A 48-year old man who is a known hypertensive for eight years but not regular on medication. He was referred from a Christian Mission Hospital where he presented a day earlier with headache, dizziness, blurring of vision and palpitations and was found to have markedly elevated blood pressure. At presentation in our facility, his blood pressure was 200/140mmHg and had normal heart sounds. His electrocardiogram, echocardiogram, urea, electrolytes and creatinine were essentially normal. He was placed on amlodipine 10mg 0nce daily, perindopril 10mg once daily, metoprolol succinate 50mg once daily and indapamide 1.5mg once daily. His blood pressure became 130/90mmHg and was completely asymptomatic after 2 months of treatment. At one year of treatment, his blood pressure was found to be 120/80mmHg but was noticed to have non-painful gingival enlargement which was first noticed when checking his teeth through the mirror (Figure 1). The amlodipine was then changed to doxazocin. One month later, the gingival enlargement was found to have regressed but blood pressure became elevated. This necessitated the change of doxazocin to S-amlodipine 5mg (chirally pure amlodipine). The gingival enlargement continued to regressed and resolved completely within 7 months (Figure 2) his blood pressure was maintained at 120/80mmHg.

DISCUSSION

Gingival enlargement, though a relatively rare adverse effect of C.C.Bs, may have deleterious effects of causing painful mastication, poor dental hygiene, and damaging cosmetic effects (4). Calcium channel blockers induced-gingival enlargement occurs most frequently with nifedipine (6 - 15%), then diltiazim (5 - 20%), verapamil (5%) and 1 - 3.4 % with amlodipine.[5] Calcium channel blockers with higher concentration in the gingival tissues when compared to plasma were found to have higher tendency of causing gingival overgrowth (4-5). Nifedipine tends to be more concentrated in the gingival tissue than amlodipine (4-5). This explained the reason for higher tendency of developing gingival enlargement with nifedipine even at lower dosage and shorter duration of intake than Amlodipine (4-5). The risk for developing CCBs induced gingival overgrowth is also increased in male gender, poor dental hygiene, high dose of medication, genetic susceptibility as well as long duration of drug usage (5). A pilot study in Lagos, Southwestern, Nigeria, reported a threefold likelihood of developing gingival enlargement among individuals on calcium channel blockers when compared to individuals that are not taking any of the CCBs (6).

The mechanism of CCBs induced gingival enlargement is not quite clear. However, some mechanisms have been proposed. Calcium channel blockage causes suppression of the calcium channel dependent aldosterone production from the adrenal cortex this results to increased pituitary gland production of adrenocorticotrophic hormone (ACTH) resulting in zona glomerulosa hyperplasia and consequently accumulation of androgenic steroid intermediates which leads to increased production of testosterone in the gingival cells causing gingival hyperplasia (7). Another proposed mechanism of CCBs induced gingival enlargement is CCBs- induced increased in the life span of the keratinocytes and reduction in collagen breakdown by suppression of apoptosis and decreased phagocytic activity respectively (4,8). This result in marked epithelial proliferation and accumulation of collagen in the connective tissues of the gingiva which manifest as gingival enlargement (4, 7). Gingival enlargement due to CCBs, has been hypothesized to be owing to stimulation of fibroblast growth on exposure to CCBs (8).The presence of bacterial plaques in the crevicular fluids of the gingiva has been assumed to caused increased in the production of proinflammatory cytokines like interlukein-1,interlukein-2, interlukein -6 as well as inflammatory cytokines like transformed growth factor-beta, platelet-derived growth factor and insulin-like growth factors (8). The non-inflammatory mechanism of gingival

overgrowth has also been proposed. This mechanism result from decreased collagenase activity owing decreased folic acid uptake that leads to increased accumulation of collagen (9). All these mechanisms result in imbalance between the anabolic and catabolic processes in the gingival tissue which makes the equilibrium to shift in favour of the anabolic processes leading to fibroblast proliferation, inhibition of apoptosis and increased collagen synthesis and accumulation.

Calcium channel blockers induced gingival enlargements have been reported to be more common in males in the ratio of 3 to 1 (10). This patient, being male, is not surprisingly predisposed to developing this side effect. While gingival enlargement from other drugs like phenytoin, ciclosporins tend to occur as early as one to three months, those induced by CCBs may take longer period to manifest (a median period of about 10 months) (11). The gingival overgrowth in our patient was first noticed at about 12 months of treatment which was not far from the median period of about 10 months. Though the ideal treatment of amlodipine-induced gingival overgrowth among other measures is switching to different class of drugs (12), after one month of losing control with the alternative drug (doxazocin) despite reduction in the size of gingival enlargement, chirally pure molecule (S-amlodipine) was introduced based on literature reports indicating that it had lower incidence of side effects and achieved similar blood pressure reduction when compared racemic amlodipine (13-14). The question whether using 10mg of S-amlodipine would have produced similar gingival enlargement cannot be ascertained because the maximum recommended therapeutic dose of S-amlodipine is 5mg which has been found to produce similar efficacy and better tolerated when compared with 10mg of racemic amlodipine (14).

CONCLUSION

Gingival overgrowth is an important side effect of amlodipine which if not early detected and promptly managed may result in adverse outcomes. Routine oral examination should be added to the routine evaluation at follow-up visits of all patients on calcium channel blockers. S-Amlodipine may be a suitable alternative in situations where racemic amlodipine is not tolerated owing to the fact that it will provide similar blood pressure control with lower incidence of adverse effects.

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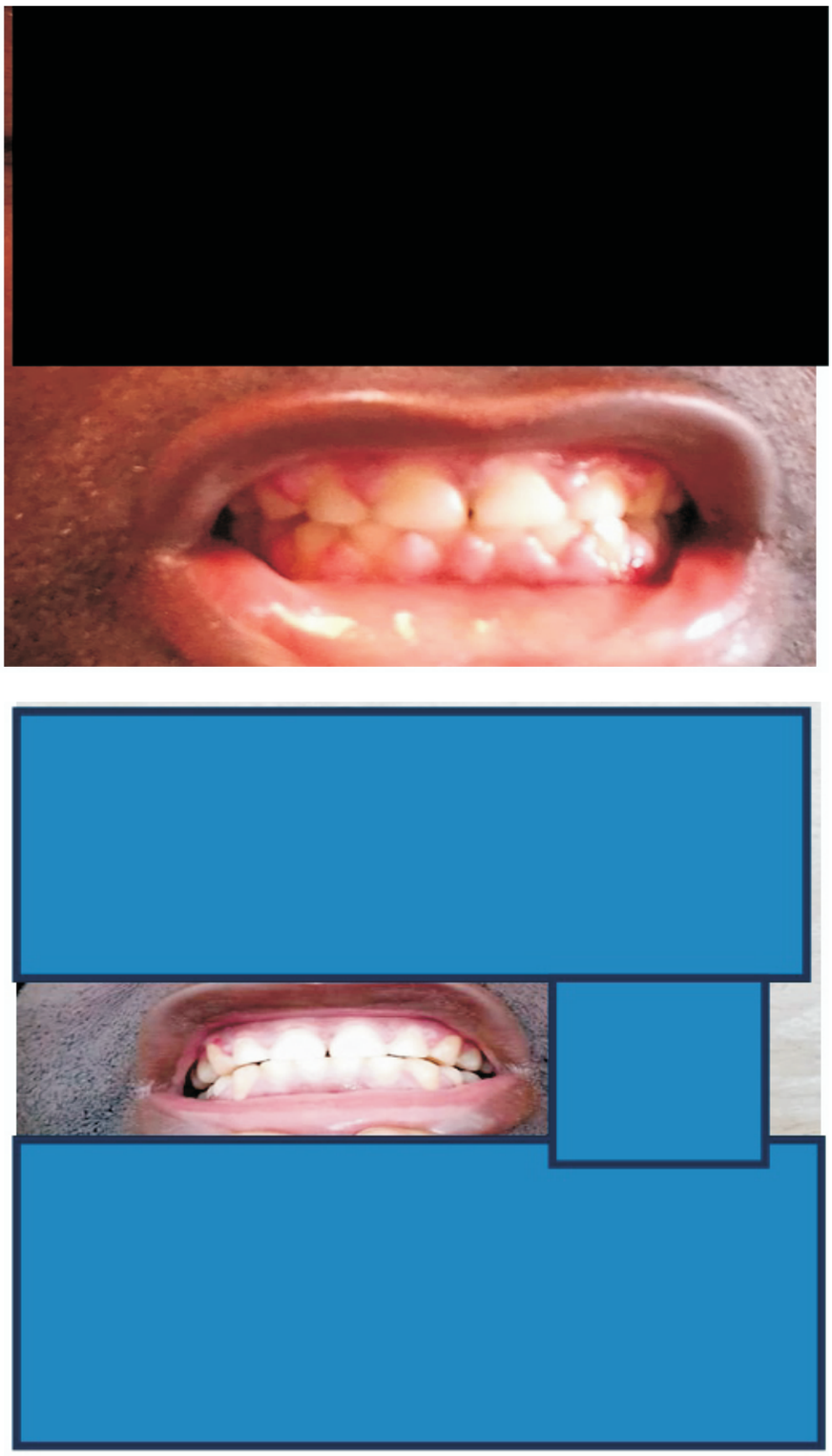

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