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Drug Induced Gingival Enlargement-A Review

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Abstract: Enlargement of gingiva can occur by taking any medications which leads to problems of speech,mastication and aesthetics. Drug induced gingival enlargement manifests as abnormal growth of gingiva due to adverse drug reactions. The key drugs are anti convulsants, immunosuppressants and calcium channel blockers. It commonly affects the oral hygiene and interfere with masticatory functions. This article relates the various gingival enlargement caused by drugs and its pathogenesis and clinical manifestations.

Keywords: Gingival enlargement, drug induced gingival enlargement, drugs, anticonvulsants, calcium channel blockers, phenytoin, pathogenesis.

1. INTRODUCTION

Drugs are the most common cause of gingival hyperplasia. Drug induced gingival enlargement also known as drug induced gingival hyperplasia is a side effect of certain drug and the overgrowth cannot be explained[1]. It is seen in patients having drugs such as anticonvulsants, immunosuppressants, calcium channel blockers.

2. DRUGS CAUSING GINGIVAL OVERGROWTH[1-5]:

Anticonvulsants: Phenytoin, Sodium Valproate, Phenobarbitone, Vigabatrin, Primidone, Mephenytoin, Ethotoin, Ethosuximide, Methosuximide,

Immunosupressants: Cyclosporin, Tacrolimus, Sirolimus,

Calcium Channel Blockers: Nifedipine, Nitrendipine, Felodipine, Nicardipine, Manidipine, Amlodipine, Nimodipine, Nisoldipine, Verapamil, Diltiazem.

3. ANTICONVULSANTS

These drugs cause overgrowth of gingival tissue. Phenytoin is the drug of choice for the treatment of grand mal etc and is the most common drug that induce gingival enlargement[6]. Phenytoin was introduced in 1938 as an antiepileptic drug. Literature suggest that these drugs cause gingival growth in fetus as well as congenitally[7].

3.1 Clinical Changes

The gingival growth appears 2-3months of drug use and increases after 12-18months[8]. It is more common in young people. The phenytoin can cause megaloblastic anemia[9].

3.2 Histopathologial Feature

Proliferation of fibroblasts is seen but fibroblast to collagen ratio is similar[9].

3.3 Pathogenesis

Molecular-cellular studies showed the increased expression of TGFB in lamina propria. Increased PDGF-BB as a mitogenic factor and chemotaxis of gingival fibroblasts as well as the increasedIL1B and IL6 resulting in the increased synthesis of collagen and glycosoaminoglycans were reported. Phenytoin-induced reduction of folic acid leads to degenerative changes in the epithelium exacerbated in the presence of inflammatory factors. The increased synthesis of testosterone metabolite by fibroblasts can cause gingival enlargement in people who take phenytoin [8-10].

3.4 Treatment

After stopping the drug, the enlargement disappears spontaneously in 4months. Then periodontal therapy is advised and follow up is recommended first six months and then once in 3 months. Topical folic acid has shown little improvement since it gives fibroblasts with higher concentration of folate[8,9].

4. IMMUNOSUPPRESSANTS

Cyclosporin is the most commonly used immunosuppressants . They are given after organ transplantation like renal transplants and in treatment of rheumatoid arthritis.Tacrolimusor FK506 is less toxic than cyclosporine[6,11,12]. Cyclosporine have side effects such as nephrotoxicity, hepatotoxicity, hypertension, and gingival overgrowth[13]. Synergistic effects have been reported when cyclosporin is administered concurrently with calcium channel blockers of dihydropyridine derivatives[14].

4.1 Clinical Appearance

It is associated with hyphal candida having pebbly or papillary appearance invading the gingival epithelium and the people taking immunosuppressants are more hyperemic and prone to bleeding on probing[15]. It is predilected in both men and women[9]. Occurrence of Age is between 20-40years of age.

4.2 Histopathology

It is often seen in connective tissue wand secularization as well as focal inflammatory cells particularly plasma cells. It is due to epithelial acanthosis and accumulation of extracellular matrix[16].

4.3 Pathogenesis

Blood and cellular immunity response has been influenced by selective and reversible inhibition of T helper cells[17]. Secretions of the enlarged gingiva contain more IL6 compared to normal gingiva. IL6 increases the proliferation of fibroblasts and synthesis of glycosoaminoglycans[9].

4.4 Treatment

The enlargement progresses to 12months after starting the drug and regresses after stopping of the dosage.

5. CALCIUM CHANNEL BLOCKERS

Antihypertensive drugs in the calcium channel blocker group are used extensively in elderly patients who have angina or peripheral vascular disease[6]. It includes nifedipine, felodipin, verapamil,diltiazem, amlodipine and isradipine. CCB are administered for the treatment of cardiovascular diseases which includes hypertension, angina pectoralis, arrhythmia and coronary artery spasm[15,17]. The use of calcium channel blocker in conjunction with cyclosporin can also affect the prevalence or severity of gingival enlargement.

5.1 Clinical changes

The changes in gingiva appears 1-3months after administration. It is more common in men than women. In addition to gingival enlargement, tachycardia and facial redness can be seen[9].

5.2 Histopathology

The gingival epithelial proliferation was more responsible for gingival enlargement than connective tissue proliferation[18].

5.3 Pathogenesis

Calcium channel blockers affects the Calcium metabolism by decreasing the intracellular Calcium flow and limiting the production of active collagenase. The inflammatory cytokines such as IL6 and IL1b also plays an important role in physiological response to calcium channel blockers. Thenifedipine which is lipophilic easily penetrates into the cells when compared to the polarized amlodipine and this structural difference plays an important role in drug-induced gingival enlargement. A large portion of amlodipine remains in the tissue and it is not observed freely in the circulation. Amlodipine rarely reaches the threshold required to cause gingival enlargement[9].

5.4 Treatment

Full recovery of gingival enlargement occurs at 4months after stopping the drug. If no abnormality develops, isradipine is replaced by following the protocol[9].

6. CONCLUSION

Gingival enlargement can cause problems in controlling plaque, chewing, teething, speech and aesthetics (1).Treatment is based on the administered drug and clinical characteristics and it can include non-surgical treatments, surgical treatments as

drug replacement. Gingival enlargement is an under recognized effect of calcium channel blockers, immunosuppressants and anticonvulsants. Doctors can identify the problem by looking in thepatients mouth and refer for further treatment.

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