

Case Report**Cyclosporine Induced Gingival Enlargement in Renal Transplant Patient: A Case Report**

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Abstract: Kidney transplantation is considered the best therapeutic option for end stage renal disease (ESRD). Cyclosporine is a potent immunosuppressive drug used to prevent graft rejection. Gingival hyperplasia is one of the collateral effect of cyclosporine, the exact pathogenesis of cyclosporine induced gingival hyperplasia is uncertain, and it may interfere with normal oral functions causing unpleasant appearance, carry psychological impacts and leads to difficulty in maintaining good oral hygiene. Here we report a case of 54 year old male renal transplant patient who was suffering from cyclosporine induced gingival enlargement.

Keywords: Cyclosporine; Gingival Enlargement; Renal Transplant; Immunosuppressive Drug.

INTRODUCTION

Kidney transplant (KT) is the most efficient renal replacement therapy for a significant number of patients with end stage renal disease (ESRD). Survival of KT patients has increased because of improvements in candidates selection and study process, surgical techniques, immunosuppressive drugs and protocols, and a better surveillance and management of extra-renal risk factors.¹

Cyclosporine-A (CsA) is a drug used to prevent rejection of the kidney graft. It is a cyclic polypeptide calcineurin inhibitor. Its administration prevents the expression of genes for several cytokines whose activity is critical for lymphocyte T activation, including interleukins 2 and 4, gamma interferon, tumor necrosis factor and others, thus preventing lymphocyte proliferation. The drug is used either alone or combined with other immunosuppressor drugs.^{1,2} Its use causes collateral effects, such as nephrotoxicity, hirsutism, arterial hypertension, dermatosis² and lymphoproliferative diseases. Gingival hyperplasia is a collateral effect of Cyclosporine A use.¹

Gingival enlargement or gingival overgrowth are the current terms for all medication-related gingival lesions, previously known as gingival hyperplasia or gingival hypertrophy.³ Gingival enlargement is usually caused by local conditions such as poor oral hygiene, food impaction or mouth breathing. Systemic conditions such as hormonal changes, drug therapy or tumor infiltrates may complicate the process or

even set the stage for the development of unfavorable local conditions that lead to food impaction and difficulty with oral hygiene.^{3,4} The variability of clinical expression of Cyclosporine A -related gingival hyperplasia implies a multifactorial pathogenesis. Cyclosporine A blood concentration, plaque/gingivitis level, bacterial lipopolysaccharides, and alteration of calcium ion cellular influx have been suggested as possible factors.¹

CASE REPORT

A 54 year old male patient reported to the Dept of Oral Medicine and Radiology with the chief complaint of overgrowth of gums from last eight months. Patient gave the history of sudden increase in gum growth which was painful and patient was unable to eat. Patient was known case of renal transplant from last 10 years and on medication (cyclosporine 20mg/BD). Upon oral examination there was fibrotic gingival enlargement seen in upper and lower jaw. Gingival enlargement was up to the coronal 1/3 of teeth in both upper and lower jaw extending till molars (Fig 1&2).



Figure 1: Fibrotic gingival enlargement in upper and lower arches



Figure 2: Fibrotic gingival enlargement in upper and lower arches extending upto molar region

Gingiva was inflamed; pinkish red in color with irregular margins (Fig-1). Bleeding on probing with scalloping of the interdental gingival was present. Local accumulation of calculus was present with gingival recession even though the overall oral mucosa was healthy. Based on medical history and local examination provisional diagnosis was given as Cyclosporine induced gingival enlargement. Routine blood test came within the normal limit and no bony changes were seen in OPG. All local irritants were removed and gingivectomy was advised along with the Nephrologist consultation for alternate drug regime.

DISCUSSION

Cyclosporine A (CsA) is a powerful immunosuppressant widely used for prevention of transplant rejection as well as for management of a number of autoimmune conditions such as rheumatoid arthritis.^{1,2} Cyclosporine A is usually administered orally. The oral therapeutic dose for immunosuppression is 10 to 20 mg/kg body weight/day, which results in a serum concentration of 100-400 ng/ml. The major adverse reactions to cyclosporine therapy are nephrotoxicity, hepatotoxicity, tremors, hirsutism, hypertension, mild anemia, gingival overgrowth and, in rare instances, lymphoma. Gingival enlargement (GE) is an abnormal growth of the periodontal tissue. Several cause of gingival enlargement is known, and the most recognized is drug induced gingival enlargement. The drug-induced gingival enlargement is a side effect of some immunosuppressive drugs such as cyclosporine A, which is the drug of choice in kidney transplant patients.^{3,4} Factors

affecting the occurrence of GE may include gender with males being three times as likely to develop the overgrowth. Children (52%) and adults younger than 30 years of age are more susceptible.^{1,3,5} There is no clear-cut correlation between the plasma concentration and gingival enlargement.³

The precise mechanism of cyclosporine induced gingival overgrowth is uncertain. Various investigations for pathogenesis of gingival overgrowth support the hypothesis that it is multifactorial. Overgrowth in cyclosporine treated patients is dependent upon the interaction of several factors.^{1,5} These include plaque control, the level of gingival inflammation and extent of periodontal destruction; the dosage and duration of cyclosporine therapy; plasma and tissue concentrations of the drug and metabolites; age of the patient and perhaps the underlying medical condition.^{3,6,7}

Cyclosporine-induced gingival overgrowth commences as a papillary enlargement which is more pronounced on the labial aspects of the gingival than the palatal or lingual surfaces.^{1,2} The papillary enlargement increases and adjacent papillae appear to coalesce. This gives the gingival tissues a lobulated appearance. Overgrowth is restricted to the width of attached gingiva, but can extend coronally and interfere with the occlusion, mastication and speech. Cyclosporine induced gingival overgrowth has not been reported in edentulous subjects.^{2,7}

Histologically, it is not known for sure if Cyclosporine A-induced gingival hyperplasia is a true hyperplasia because enlargement may not result simply from an increase in the number of cells but from the increase in extracellular tissue volume. The overlying epithelium is of variable thickness, irregular, and multilayered, with acanthosis, parakeratosis and pseudoepitheliomatous proliferation. The epithelial ridges penetrate deep into the subepithelial connective tissue. Microscopic examination shows sparsely vascular fibrous connective tissue with thick, dense, interlacing bundles of collagen fibers with an inflammatory infiltrate, primarily plasma cells.^{1,2}

The most effective treatment of drug induced GE is substitution of medication, which should be done in conjugation with patient's physician.^{1,2,4} Drug substitution or reduction in the dose of cyclosporine has been shown to be beneficial in drug induced GE.^{1,3,5}

However the nature of organ transplant often means that alternative therapy or dose reduction is not available. Some patients can use more conventional immunosuppressant such as steroid and azathioprine but survival rate are not as good new immunosuppressant such as tacrolimus (FK 506) (Prograf), rapamycin and mycophenolate mofetil (MMF) Cell Cept may offer some hope,² as to date these have not been reported in association with gingival overgrowth. Presence of drug induced gingival enlargement is associated with pseudo-pocket formation.^{1,7} Although the treatment of gingival overgrowth can be complicated due to the intense inflammation of the fibrotic tissue.^{5,8}

Therefore the possibility of periodontitis to develop due to plaque accumulation exists.³ Professional debridement with scaling and root planning has been shown to offer some relief in gingival enlargement patients.^{1,10} Recurrence of drug induced GE is a reality in surgically treated cases. Meticulous home care, chlorhexidine gluconate rinses and professional cleaning can decrease the rate and degree at which recurrence occurs.^{1,2,5}

CONCLUSION: Gingival overgrowth is one of the most frequent side effects in renal transplant patients associated with assumption of cyclosporine A. Poor oral hygiene and dental plaque are considered important risk factors in pathogenesis of gingival enlargement. Every case of gingival enlargement should be treated in a stepwise manner inclusive of consultation with patient's physician, substitution of the drug, non-surgical and surgical therapy.

Additionally the encouragement and maintenance of proper periodontal hygiene has an important and decisive role in its prevention.

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