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The effect of Mitomycin C on inhibition of long-term Cyclosporin A induced gingival overgrowth

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As a powerful immunosuppressive agent, Cyclosporin A(CsA) has a significant impact on transplant medicine and in the therapy of autoimmune diseases. One of the most commonly observed adverse effects of CsA is the development of gingival overgrowth(GO). A number of treatment options are utilized in the treatment of GO, including CO2 laser surgery, improved oral hygiene, the use of antibiotics and surgical intervention. Nevertheless, the treatments still have problems need to be worked out. In this case, Mitomycin C(MMC) was tried to investigate whether MMC could inhibit proliferation of connective cells through apoptosis of fibroblast, which have antiproliferative or cytotoxic effects on fibroblasts. Two healthy 2-year-old mixed breed dogs had renal transplantation. The dogs were given daily oral CsA dose of 20mg/kg of body weight for the prevention of acute renal allograft rejection. They also have had no evidence of a chronic allograft rejection episode. The dogs had moderate to severe GO as a side effect of CsA. Prior to the gingivectomy, teeth were scaled and brushed in order to improve and standardize the oral health. Maxillary gingiva was excised anteriorly and laterally. However, 4 weeks after the 1st gingivectomy, GO reoccurred and developed to a similar degree as before the surgery. To prevent reoccurrence of GO, topical MMC were applied with 2nd gingivectomy. The occurrence and severity of gingival alterations were documented weekly. Histopathological examination was performed at every surgery and the levels of transforming growth factor-beta 1 (TGF-β1) in tissue were measured by ELISA kits. After topical MMC was applied, gingival overgrowth has not occurred for 3 months post surgery. The levels of TGF-b1, which is known to have a major influence to CsA induced GO, was still elevated after MMC treatment. However, in histopathologic examination, apoptosis of fibroblast was increased significantly. Density of fibroblasts also decreased. Apoptotic fibroblast is characterized by mitochondrial shrink. This case shows that topical application of MMC may inhibit CsA-induced GO following organ transplantation, and the effects may be based on inhibition of collagen deposition by apoptosis of fibroblast.

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