Use of minocycline as systemic antimicrobial therapy in refractory periodontitis with chronic gingival enlargement

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Abstract
Periodontal disease is a multifactorial disease having various risk factors, but a dynamic interaction between bacterial products and host response in association with genetic and environmental factors is considered as the primary cause for periodontal tissue destruction in periodontitis. This bacterial-host interaction which is ever-so-present in periodontitis directs us toward utilizing antimicrobial agents along with the routine mechanical debridement. This case report presents a case of a female patient with recurrent periodontal infections with gingival enlargement treated with systemic minocycline in conjunction with the conventional non-surgical approach.

Key words: Gingival enlargement, minocycline, refractory periodontitis, systemic drug therapy

INTRODUCTION
Periodontal disease is a multifactorial disease, characterized by periodontal pocket formation, loss of clinical attachment, and alveolar bone resorption. Various risk factors have been described for the onset and progression of periodontal disease. However, dynamic interactions between bacterial factors and host response with genetic and environmental factors are considered as the primary cause for tissue destruction in periodontitis. In consideration to this bacterial-host response, treatment approach to periodontitis should be conventional mechanical debridement and the use of pharmacotherapeutic agents.

Antibiotics can often be prescribed to the patients who are non-responsive to conventional mechanical therapy, for patients with acute periodontal infections associated with systemic manifestations, as a prophylactic agent in medically compromised patients and as an adjunct to mechanical therapy. Tetracyclines are broad-spectrum antibiotics which inhibit ribosomal protein synthesis and may also serve as a bacteria-reducing and host-modulating agent.

Minocycline is a semi-synthetic derivative of tetracycline. This drug is mainly used for the treatment of acne, chronic respiratory diseases, and rheumatoid arthritis. Minocycline has many advantages over other tetracyclines, e.g., both anti-inflammatory as well as antibiotic properties, better absorption, increased antimicrobial activity, and negligible or no phototoxicity. Being lipid soluble, minocycline can easily penetrate into various body fluids, such as saliva and Gingival Crevicular Fluid, and can act locally at the site of infection.

CASE REPORT
A 28-year-old female patient reported with complaints of generalized swollen gums since last one year, preventing proper speech, articulation, and mastication causing inadequate lip apposition and poor aesthetics. Detailed case history disclosed that in last six years, she has been operated for the same problem four times; once full mouth open flap debridement and three times gingivectomy was performed...
but again causing the recurrence of gingival enlargement within 4 to 5 months. She did not give any history of drugs intake, fever, anorexia, weight loss, seizures, hearing loss, nor having any physical or mental disorder. Also, family and postnatal history was non-contributory.

**Examination**
Extra oral examination revealed that patient has incompetent averted lips and convex profile.

An intraoral examination revealed generalized diffused, nodular enlargement of gingiva, more on the right side. Gingiva was fiery red in color with soft and spongy consistency and bleeding on slightest of provocation. The teeth were covered with enlarged gingiva till the middle one third, with some teeth showing grade I mobility [Figures 1a-d].

**Investigations**
Panoramic radiograph revealed generalized bone loss [Figure 2] and, teeth no. 11, 21, 45, and 46 were root canal treated with crowns on them. Hematological investigations showed all the blood elements to be within normal limits.

**Diagnosis**
On the basis of detailed case analysis and clinical and histological findings, the case was diagnosed as refractory periodontitis with chronic inflammatory gingival enlargement.

On the basis of clinical features and history of the patient, the diagnosis of refractory periodontitis with gingival hypertrophy was made, not responding to various periodontal surgical procedures. Thus, non-surgical periodontal therapy was chosen as the mode of therapy along with systemic administration of minocycline for which a written informed consent was signed from the patient. Minocycline 100 mg one a day was advised to start with for 1 week. At the end of 1 week on examination, patient showed dramatic improvement in gingival health, so the same medication was continued for another 1 week and on re-examination, gingival tissues showed overall reduction in gingival hypertrophy, inflammation, and pocket depth [Figures 3a-d].

For the better maintenance and to reduce plaque deposition,
scaling and root planning was performed to remove local irritating and aggravating factors at the end of 2 weeks and medication was continued till 4 weeks.

On recall visits at the end of 4 weeks, patient showed great improvement with disappearance of gingival enlargement completely with gingiva showing coral pink color, firm and resilient consistency and no bleeding on probing [Figures 4a-d]. Also, patient could maintain oral hygiene procedure routinely without any discomfort, pain, or bleeding. Patient was advised to stop medication after 4 weeks and was kept on regular follow-up for next six months with every month check-up.

**DISCUSSION**

This case report presents a case of a female patient with severe gingival inflammation, bleeding gums even on the slightest provocation, and generalized deep periodontal pockets. In addition to mechanical instrumentation, minocycline had been prescribed for 4 weeks. This non-surgical approach resulted in improved periodontal health of the patient.

The conventional periodontal therapy is the removal of bacterial biofilm and supra- and subgingival calculus, as much as possible. But, because of the lack of visibility to the subgingival areas, complete plaque and calculus removal is difficult to achieve. Waerhaug described that
non-surgical scaling and root planing is not capable of removing subgingival deposits in sites with probing depths exceeding 5 mm.[7] Therefore, the use of antimicrobial agents in conjunction with periodontal therapy was proposed.

In the present case, there were significant improvements in all clinical parameters on follow-up visits. This is the expected outcome in association with non-surgical periodontal therapy.[8] These results were also consistent with previous studies where minocycline was administered systemically. Basegmez et al. also found reduction in gingival inflammation and probing pocket depth in the minocycline group and they suggested that additional use of systemic minocycline demonstrated improvement on MMP-8 and PGE-2. They also speculated that minocycline has a kind of host-modulating capacity when used systemically for 2 weeks.[9] Studies also evidenced that tetracycline accumulates within phagocytes. This accumulation could potentially improve the intracellular killing of the bacteria. Migration of neutrophils with tetracycline to the infected site could potentially boost the concentration of tetracycline at local sites. Neutrophils' tendency to penetrate site of infection in great numbers could result in enhanced tetracycline action.[10]

Systemic administration of antibiotics has certain advantages over topical administration such as penetration of the drug to multiple sites of disease activity and effect on extra dental sites, e.g., tongue and tonsillar areas. This enhances elimination of microorganisms from the entire mouth and decreases the risk of reinfection from the other sites. Disadvantages of systemic administration of antibiotics are the increased of drug reactions,[11] increased selection of multiple antibiotic-resistant microorganisms, and chances of lower concentration of the drug in the Gingival Crevicular Fluid.[12]

**CONCLUSION**

Even though recurrence cannot be predicted, psychological and functional benefits far outweigh the recurrence. Oral hygiene maintenance and the plaque accumulation have a very crucial effect on prognosis of any periodontal therapy. Long-term follow-up will be required to evaluate the predictability of the therapy carried out.

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