An unusual case report of gingival overgrowth associated with the use of leflunomide

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To the editor,

We report the case of a 38-year-old woman with rheumatoid arthritis (RA) who developed gingival overgrowth whilst taking leflunomide. The patient was diagnosed with RA 9 months ago and was initially treated with methotrexate at a dose of 20 mg daily. After 6 months of the initial treatment, she was switched to leflunomide 20 mg daily because of failure to come under control the disease activity level. Two months later, her disease activity score in 28 joints (DAS-28) was < 3.2 which indicates mild disease activity level for RA. Her erythrocyte sedimentation rate (ESR) reduced from 58 mm/hr to 26 mm/hr. 3 months after starting leflunomide, she complained of pain and gingival swelling in both maxillary and mandibular arch and consequent difficulty of eating. The patient was consulted to a periodontist. Oral examination revealed gingival overgrowth involving the both maxillary and mandibular arch (Figure 1). Since the gingival overgrowth was assumed to be due to leflunomide, the patient ceased leflunomide temporarily and gingival overgrowth markedly improved within 3 weeks after drug cessation but her arthritis worsened. On restarting leflunomide, gingival overgrowth recurred. She switched to biologic therapy. There was no recurrence of the gingival overgrowth after switching to biologic therapy.

Gingival overgrowth is one of the most common adverse effects of systemic drugs on the periodontal tissues. The well-known drugs causing gingival overgrowth are the anticonvulsant phenytoin, antihypertensive calcium channel blockers, and the immunosuppressant cyclosporine[1]. Although it is known that there are some oral mucosal lesions such as aphthous stomatitis, oral mucosal ulcers and oral monoliasis associated with the use of leflunomide, no case with gingival overgrowth due to the use of this drug has been reported previously. In addition, the most common side effects of leflunomide are hepatotoxicity, immunosuppression, skin reactions, peripheral neuropathy, hypertension, diarrhea, interstitial lung disease, and rarely oral mucosal lesions[2].

Although the exact pathogenesis of drug-induced gingival overgrowth is not known, two major theories including inflammatory and non-inflammatory pathways have already been suggested. In non-inflammatory pathway, deficiency of collagenase activity is supposed to play a role in the pathogenesis of drug-induced gingival overgrowth. An inflammatory mechanism suggests that direct toxic effects of concentrated drug in gingival crevicular fluid may be cause gingivitis[1]. The best treatment for drug-induced gingival overgrowth is the discontinuation of the problematic drug. Usually, surgical approach is not needed. If the surgery is indicated, gingivectomy or periodontal flap can be performed[3].

We believe that this is the first description of gingival overgrowth following treatment with leflunomide.

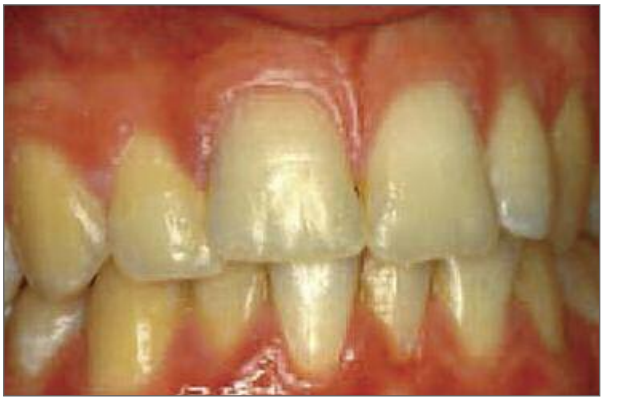

FIGURE 1. Gingival overgrowth involving the both maxillary and mandibular arch

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Gingival overgrowth is an unusual side effect of leflunomide and may require cessation of the treatment.

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