

Gingival Hyperplasia Associated with Cyclosporin A

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A 45-year-old woman presented in 1992 with symmetrical polyarthritis affecting the small joints of the hands and wrists bilaterally. The diagnosis of rheumatoid arthritis (RA) was made and she was given methotrexate and small doses of prednisone, with significant improvement. In 1997 she experienced a flare of the synovitis and cyclosporin A (CSA) (3 mg/kg/day), equivalent to 200 mg/day, was added. Six months later the synovitis had improved¹. At that time she presented with mild hypertrichosis involving the areas of the arms and forearms bilaterally, followed by progressive gingival hyperplasia (GH) (Figure 1)². In 1998, the dose of CSA was decreased to 100 mg/day and one year later the GH had decreased. Clinical manifestation of CSA induced GH begins within the first 6 months after initiation of CSA therapy. Its incidence ranges from 8 to 85%. However, part of this variability probably results from many of the patients receiving CSA concurrently taking other medications such as calcium channel blockers, which can contribute to GH³. CSA induced GH has been reported to be less common in treated patients with RA than in transplant recipients. Concerning the pathogenetic mechanisms underlying GH, it seems that CSA regu-

lates cytokine expression in gingival tissue, especially interleukin 6 and keratinocyte growth factor^{4,5}. Azithromycin or metronidazole can effectively treat GH³. However, complete resolution cannot be expected unless CSA is stopped. In this case the GH might disappear over a period of a few months to one year.

REFERENCES

1. Tugwell P, Pincus T, Yocum D, et al. Combination with cyclosporine and methotrexate in severe rheumatoid arthritis. *N Engl J Med* 1995;333:137-41.
2. Drosos AA, Voulgari PV, Katsaraki A, Zikou AK. Influence of cyclosporin A on radiological progression in early rheumatoid arthritis patients: a 42-month prospective study. *Rheumatol Int* 2000;19:113-8.
3. Meraw SJ, Sheridan PJ. Medically induced gingival hyperplasia. *Mayo Clin Proc* 1998;73:1196-9.
4. Myrillas TT, Linden GJ, Marley JJ, Irwin CR. Cyclosporin A regulates interleukin-1 beta and interleukin-6 expression in gingiva: implications for gingival overgrowth. *J Periodontol* 1999; 70:294-300.
5. Das SJ, Parkar MH, Olsen I. Upregulation of keratinocyte growth factor in cyclosporin A-induced gingival overgrowth. *J Periodontol* 2001;72:745-52.



Figure 1. A 45-year-old woman with progressive gingival hyperplasia.