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Gingival Hyperplasia Secondary to Everolimus Therapy

Hiperplasia gingival secundaria a everolimus

To the Editor:

We present the case of a 34 year-old woman with type 1 diabetes with onset 20 years earlier who consulted for thickening of the gums. The patient had a history of diabetic retinopathy and nephropathy that led to a kidney transplant 3 years ago. Graft function was normal at the time of presentation. Other relevant history included hypertension, migraine, and surgery for a pituitary adenoma 10 years earlier. She reported intolerance to enalapril and mycophenolate-mofetil and she was therefore being treated with injectable insulin, tacrolimus, calcitriol, pantoprazole, and everolimus. The patient had noted progressive thickening of the gums, erosive lesions on the oral mucosa and on the borders of the lips, and intense halitosis following introduction of the everolimus treatment 4 months prior to the present consultation (the other treatments had been employed for several years). She consulted as the condition was causing her considerable discomfort. Examination revealed gingival hyperplasia predominantly of the maxillary gingiva (Figure), accompanied by ulceration of the lips and gums. Severe pyorrhea was also observed.

A diagnosis of gingival hyperplasia secondary to everolimus therapy was made on the basis of the clear temporal relationship reported by the patient. Withdrawal of the drug was not considered appropriate as the kidney transplant was well controlled by the agent, meaning the only recommendation made was for rigorous oral hygiene and regular dental check-ups.

Drug-induced gingival hyperplasia is an adverse drug reaction of unknown etiology that could be related to changes in calcium metabolism and other local factors. The drugs most commonly associated with the condition include anticonvulsants, immunosuppressants, and calcium antagonists.[1,2]

In 1939, phenytoin was the first drug to be associated with the disorder and it is still the most common associated anticonvulsant. Ciclosporin[3] stands out in the literature as the leading immunosuppressant related to the condition and nifedipine is the most commonly cited calcium antagonist.[4]

Gingival hyperplasia tends to appear a few months after starting treatment with the drug, and in general

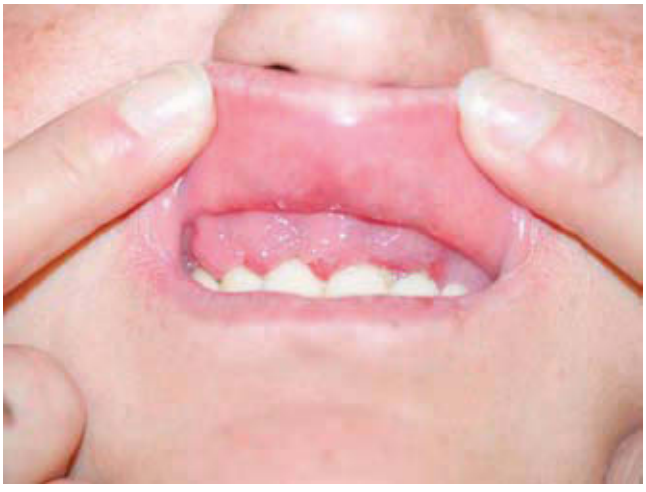

Figure Marked maxillary gingival hyperplasia. Erosions on the lips and gums.

it is reversible. The principle approach is to avoid or substitute the drugs wherever possible, and to maintain strict dental hygiene regimes. Antibiotics can also be used (metronidazole, clarithromycin, azithromycin), and in resistant cases a gingivectomy may be performed by means of scalpel, electrosurgery, cryosurgery, or carbon dioxide laser, although the condition tends to recur within 3 to 12 months.[1,2]

Everolimus is a new sirolimus derivative immunosuppressant with a better bioavailability and shorter half-life. It is a potent proliferation signal inhibitor operating via the m-TOR receptors. It is used in prophylaxis to prevent rejection of solid organ transplants in adult recipients with a low to moderate immunological risk.[5]

The most common adverse reactions associated with this group of drugs are hyperlipidemia, thrombocytopenia, delayed healing, delayed recovery from acute tubular necrosis in kidney transplantation, reduced testosterone levels, increased proteinuria, pneumonitis, headache, asthenia, joint pain, lymphocele and, in combination with cyclosporine, an increase in hemolytic uremic syndrome, nephrotoxicity, and systemic hypertension.

Use of the drug has also been associated with adverse skin reactions: mouth ulcers (60%), gingivitis (20%), chronic labial fissures (11%), epitaxis (60%), acneiform rashes (46%), folliculitis of the scalp (26%), suppurative hidradenitis (12%), chronic edema and sclerodermiform changes (55%), angioedema (15%), nail disorders (74%), and periungual infections (16%).[6]

We consider this case worthy of discussion as we have found no other reports of gingival hyperplasia secondary everolimus amongst the many descriptions of such drug reactions in our review of the literature.

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Contact Allergic Dermatitis to Quinine in an Anti-hair Loss Lotion

Dermatitis alérgica de contacto a quinina por una loción capilar anticaída

To the Editor:

The use of anti-hair loss lotions for treating androgenic alopecia can occasionally cause pruritus and desquamation of the scalp. The most common causes include irritant contact dermatitis, allergic contact dermatitis, and even exacerbation of seborrheic dermatitis. Allergic contact dermatitis caused by anti-hair loss lotions has been widely described in the literature and is generally associated with the use of minoxidil or propylene glycol used as excipients, the latter being the causative allergen in most cases.[1] Allergic contact dermatitis to the quinine contained in anti-hair loss lotion, as in the present case, is much less common.

The patient was a 73-year-old woman with no relevant personal history, referred by her health-area dermatologist for a highly pruritic and impetiginous papulovesicular dermatitis of the scalp, ears, and face that had begun several days earlier (Figure 1). The patient reported the topical application of Bio-anagenol shampoo, Lacovin (2% minoxidil), and Kavel anti-hair loss lotion over a period of 13 years for androgenic alopecia. She denied having used other topical, cosmetic, or therapeutic products, did not associate her symptoms with any occupational activity, and had no history of atopy or other skin diseases. Treatment was prescribed with corticosteroid solution (clobetasol propionate twice a day), prednisone (30 mg/d), antihistamines, and oral antibiotics for a week, leading to complete resolution of the symptoms. An open test subsequently performed on the patient's forearm with Lacovin (2% minoxidil) was negative, while Kavel anti-hair loss lotion was positive (++) on the third day. A patch test with Kavel anti-hair loss lotion applied to the back was positive (++). The other patch tests with a standard series from the Spanish Contact Dermatitis