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Flunarizine-induced gingival hyperplasia?

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Introduction

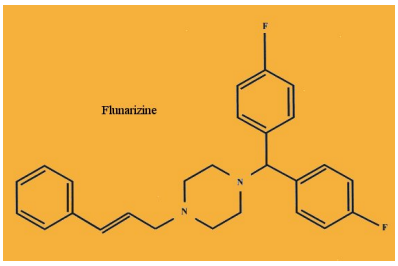
Gingival hyperplasia does not belong to the list of adverse reactions to flunarizine treatment. To the best of our knowledge only 2 cases of flunarizine-induced gingival hyperplasia have been previously reported.

Objectives

To report a case of gingival hyperplasia apparently caused by flunarizine, a calcium channel blocker indicated for prevention of migraine headaches.

Material and Methods

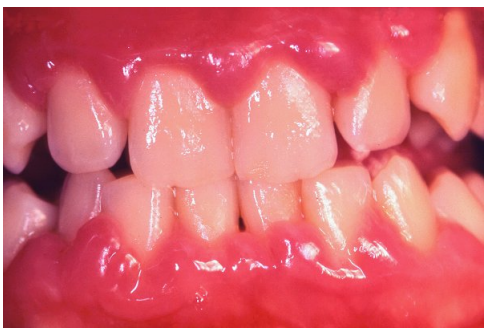
A 24 year-old healthy woman consulted for gingival bleeding. Periodontal examination showed a diffuse erythematous gingival hyperplasia predominating in the anterior part of lower gingiva, featuring a band-like growth 3 to 5 mm broad and 4 cm long in continuity with hyperplastic interdental papillae, masking the cervical part of canines and incisors, separated from the attached gingiva by a deep groove. The patient had suffered for 3 years of frequent migrainous attacks, and after numerous other unsuccessful drugs had taken for the last 1 year 5 mg per day of flunarizine, a calcium channel blocker devoid of any effect on the slow calcium channel of myocardium, indicated in prophylaxis of migraine attacks.



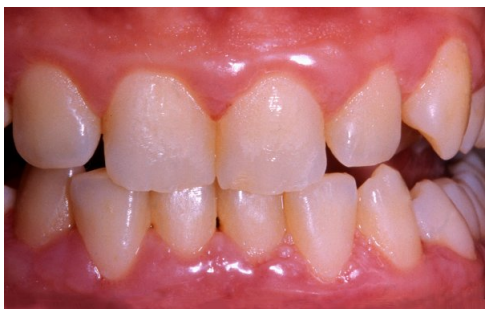
Flunarizine formula

Results

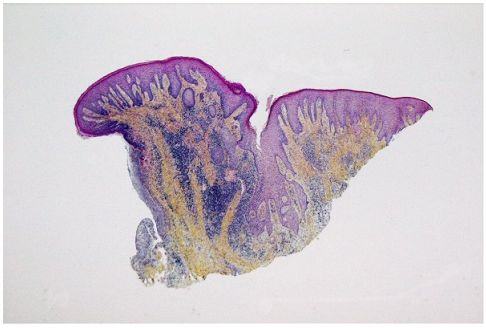
Biopsy of the gingival lesion showed a non specific pattern of fibro-epithelial hyperplasia, with a mostly perivascular infiltrate of lymphocytes and plasma cells, similar to the one observed in the well-known gingival hyperplasia induced by calcium channel blockers used in cardiology, like nifedipine.



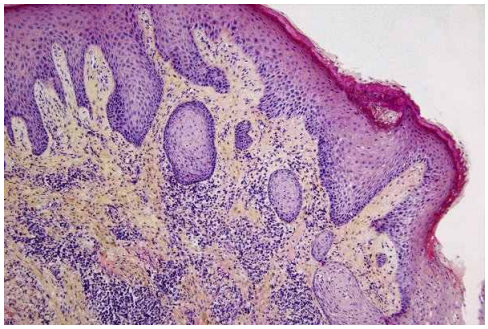
Hyperplastic gingivitis appeared 3 months after onset of flunarizine treatment for migraine.



Flunarizine could not be stopped. Status 5 months later, after non surgical periodontal treatment.



Low magnification of the mandibular gingiva biopsy showing dense inflammatory infiltrate and fibro-epithelial hyperplasia (HES, x 2)



High magnification showing the infiltrate of plasma cells and lymphocytes, and the hyperplastic epithelium (HES, x 10)

Discussion and Conclusions

The patient refused to stop flunarizine, the only effective drug for her migraine. Local treatment improved but did not heal the disease. Although imputability of flunarizine is possible in the development of gingival hyperplasia, it would be supported if withdrawal of this drug was followed by return to normal state.

Bibliography

- Hoppu K et al., "Flunarizine of limited value in children with intractable epilepsy", Pediatr Neurol 1995;13:143-147
- www4.jaring.my/madrac/interesting.htm

This Poster was submitted by PD Dr. Tommaso Lombardi.

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Poster Faksimile:

FLUNARIZINE-INDUCED GINGIVAL HYPERPLASIA ?

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A 24 year-old healthy woman consulted for gingival bleeding. Periodontal examination showed a diffuse erythematous gingival hyperplasia predominating in the anterior part of lower gingiva, featuring a band-like growth 3 to 5 mm broad and 4 cm long in continuity with hyperplastic interdental papillae, masking the cervical part of canines and incisors, separated from the attached gingiva by a deep groove. The patient had suffered for 3 years of frequent migrainous attacks, and after numerous other unsuccessful drugs had taken for the last 1 year 5 mg per day of flunarizine, a calcium channel blocker devoid of any effect on the slow calcium channel of myocardium, indicated in prophylaxis of migraine attacks.

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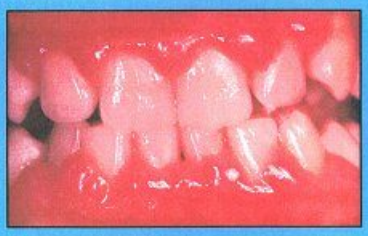
Although imputability of flunarizine is possible in the development of gingival hyperplasia, it would be supported if withdrawal of this drug was followed by return to normal state.

Flunarizine prevents the deleterious effects of cellular calcium overload by reducing excessive transmembrane fluxes of calcium. Flunarizine does not interfere with normal cellular calcium homeostasis. Flunarizine also has antihistaminic properties.

Flunarizine is indicated in the following diseases :
migraine prophylaxis
vertigo of vestibular origin
epilepsy unresponsive to conventional therapy

Flunarizine is contra-indicated in patients with known hypersensitivity to the drug, and in patients with a history of depression or pre-existing extrapyramidal disorders.
Side effects encountered in clinical trials include the following:
Gastrointestinal : heartburn, nausea, emesis, gastralgia;
Central Nervous System : insomnia and sleep change, anxiety, dizziness/vertigo.
Miscellaneous : dry mouth, asthenia, muscle aches, skin rash, lichenoid reaction

Proper name : flunarizine hydrochloride
Chemical Name : (E)-1-[bis(4-fluorophenyl)-Methyl]-4-(3-phenyl-2-propenyl) piperazine dihydrochloride.
Molecular Formula : $C_{26}H_{26}F_2N_2 \cdot 2HCl$
Molecular Weight : 477.41



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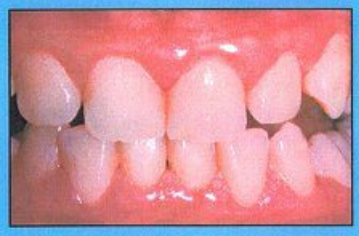

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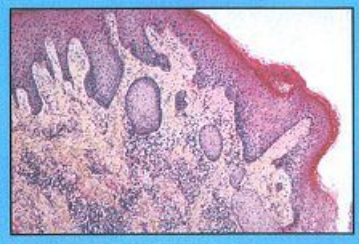

High magnification showing the infiltrate of plasma cells and lymphocytes, and the hyperplastic epithelium (HES, x 10)

Conclusion

- Gingival hyperplasia might be a side effect of flunarizine
- The mechanism of action of this drug on the periodontium needs to be investigated

References

- Hoppu K et al. Flunarizine of limited value in children with intractable epilepsy. Pediatr Neurol 1995;13:143-147.
- http://www4.jaring.my/madrac/interesting.htm