Summary

Hypertrophic human gingiva is frequently found in case of therapy with certain medication, such as Calcium antagonists, used to treat arterial hypertension.

Material and method. The current study has been carried on 11 cases of hypertrophic gingiva in 6 men and 5 women, aged 40-65 years, who followed treatment with Calcium antagonists over a period of 16-60 months. First, the samples of hypertrophic gingiva resulting from surgery (gingivectomy) were analyzed, in order to establish the histopathological diagnosis. Once the clinical diagnosis was confirmed, the samples were investigated by means of immunohistochemical method, using the ABC (avidin-biotin-peroxidase complex) indirect trisradial technique. The type IV collagen, which, along with laminin constitutes the main component of the basal membrane in human organism, was thus assessed. The basal membranes at the epithelium-chorion border and the subepithelial basal membranes of the blood capillaries were investigated.

Results. Immunostaining for type IV collagen in basal membranes of gingival mucosa and blood capillaries evidenced chemical changes of these structures.

Conclusions. The facts suggest that the factor triggering gingival hyperplasia deteriorated the chemical structure of basal membranes, and altered the local tissular interdependence, processes which led to gingival hypertrophy.

Keywords: hypertrophic human gingiva, immunohistochemical study, calcium antagonists.

Introduction

Gingival hypertrophy is a pathological state, found in dental practice, being the consequence of medical therapy administered by general practitioners. Certain medicines based on calcium antagonists, used to treat arterial hypertension, chest angina and arrhythmia (such as nifedipine, verapamil, and diltiazem) can trigger gingival hypertrophy [1]. These drugs are largely prescribed in cardiology therapy, but the pathogeny of gingival hypertrophy they induce is unknown [2,3].

In order to clarify the action mechanism, various studies are being performed, but it seems their results will no longer be justified, as Calcium antagonists tend to be currently replaced by new medicines even more effective, with no adverse reactions, gingival hypertrophy included [1].

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Material and method

The patients involved in the study were selected from 201 persons treated for arterial hypertension, with Calcium antagonists (nifedipine, verapamil, diltiazem), in the Clinic of Cardiology and its ambulatory, of the Craiova University of Medicine and Pharmacy.

The study was run over a period of 16-60 months. Of the total number of patients, 28 manifested gingival hypertrophy, and 11 (6 men and 5 women, aged 45-60 years) agreed to surgical therapy through gingivectomy.

Tissue samples from the surgical site were harvested and fixed in 10% formalin, embedded in paraffin and the histopathological diagnosis of gingival hypertrophy was put.

The immunohistochemical study of tissue sections was made by the ABC avidin-biotin-peroxidase tristadiial method. Type IV collagen was assessed in the basal membranes at epithelium-chorion borderline in hypertrophic gingiva and in the basal membranes of blood capillaries of subepithelial chorion.

Results and discussions

Microscopical examinations of tissue samples of hypertrophic gingiva of the study patients displays histological alterations of hypertrophic type, both in gingival epithelium and chorion (Figure 1). The epithelium was markedly thickened, but with preservation of its non-keratinized stratified structure. The three layers: basal, spinosum and superficial are seen, whereas in the spinosum layer hyperkantosis is detected (an increase of spiky-type cells).

The gingival chorion consists of connective tissue with rich ground substance, numberless collagen fibers and connective cells, with hyperplasia of fibrocytes. Small blood vessels (capillaries, arterioles and venules) are in high numbers, hyperplasia being significantly noted in blood capillaries (Figure 2).

Comparing the gingival chorion in our study with that of normal gingiva, our tissue sections evince a great number of fibrocytes in the hypertrophic chorion. It is important to underline the fibrocyte hyperplasia, knowing the role that fibrocytes play in the histogenesis of the other components of connective tissue [4]. We did not find any differences in the histological items assessed relating to age and sex, our findings being similar to literature data [2,5,6].

Type IV collagen immunostaining evidenced chemical alterations in basal membranes of hypertrophic gingiva, both at epithelium-chorion level and in blood capillaries (Figure 3). Type IV collagen is afibrillar, constituting the main component of basal membranes, along with laminin [7]. In consequence, antibodies to this type of collagen are the most effective in demonstrating the presence of basal membranes and of other aspects [8]. Antibodies to laminin, even existent, are less useful, as laminin is less represented in the basal membranes as compared to type IV collagen [9].

All basal membranes in the study had a positive reaction to type IV collagen antibodies (Figure 4). The intensity of the positive reaction was different in terms of case and area. The delicate basal membrane of blood capillaries, perfectly marked by these antibodies, easily allowed the detection of doubling and thinning in its structure. The reactivity with uneven intensity at the level of basal membranes was also signaled by Barsky et al., 1991, who stated that the use of antibodies to basal membrane demonstrates its active alteration. Immunostaining in the previous pattern detected in our research samples suggests that the factor triggering gingival hyperplasia, by aggressing the chemical structure of basal membranes, leads to alteration of its functions of active and selective filter in the transit of
metabolical products from the internal medium towards tissues and of tissular products toward the internal medium. This transport alteration affects local tissular interdependence, having as consequence gingival hypertrophy.

**Conclusions**

Microscopical research of histological samples with gingival hypertrophy, consecutive to therapy with Calcium antagonists, demonstrates alterations of epithelium and chorion, found in all study cases. Epithelium is thickened due to akantosis process of spinosum layer and the chorion is increased in volume due to all tissular components, blood capillaries included, but especially through fibrocyte hyperplasia.

Immunostaining to type IV collagen is positive in hypertrophic gingiva consecutive to Calcium antagonists therapy, evidencing different staining intensities, thus demonstrating alterations of the chemical structure of basal membrane, both at epithelium-chorion level and in the chorion capillaries. This alteration entails changes in the function of active and selective filter, modifying the tissular interdependence.
References


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