Histopathological Variations in Generalized Inflammatory Gingival Enlargements and Normal Gingiva: A Randomized Case-Control Study

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ABSTRACT

Introduction: The healthy gingiva almost completely accommodates the interproximal spaces between teeth in the oral cavity. But sometimes, there is frequent increase in the size of the gingiva, which is called gingival enlargement. It mainly occurs as inflammatory, noninflammatory (fibrous), any drug induced (Cyclosporine A, Phenytoin, Amlodipine, Nifedipine), and mixed type (systemic diseases and conditions like in leukemia, vitamin C deficiency). The aim of this study is to compare the histopathological changes in gingival enlargement with normal gingiva.

Materials and methods: The study was conducted on 40 subjects divided into two groups of 20 each. Group I was the study group with gingival enlargement patients, and group II was the control group with normal gingiva. The gingiva of all the subjects was surgically excised, fixed, stained, and examined under the microscope to study the histological features.

Results: Microscopically, the tissue samples of gingival enlargements showed markedly thickened epithelium with hyperkeratinization in the spinous layer. The connective tissue contains collagen fibers, plumped to spindle fibroblast and numerous blood vessels with extravasated red blood corpuscles. Chronic dense inflammatory infiltrate was also evident.

Conclusion: The persistent clinical manifestation of gingival enlargements and its early histopathological diagnosis can help the clinician to prevent further severity of the disease.

Keywords: Chronic dense inflammatory infiltrate, Gingival enlargements, Hyperkeratinization, Spinous layer.


Source of support: Nil

Conflict of interest: None

INTRODUCTION

Gingival enlargements can be defined as pathology which is characterized by an excessive growth of the periodontal tissues and it mainly occurs as inflammatory, noninflammatory (fibrous), any drug induced (Cyclosporine A, Phenytoin, Amlodipine, Nifedipine), and mixed type (systemic diseases and conditions like in leukemia, vitamin C deficiency).1 The healthy gingiva almost completely accommodates the interproximal spaces between teeth in the oral cavity. But sometimes, there is frequent increase in the size of the gingiva, which leads to its protrusion into the oral cavity. This protruded growth of gingiva may be localized to one papilla or may involve whole of the gingival papillae in the oral cavity.2 Clinically, the consistency of gingival enlargements may vary from firm and fibrous, to edematous and bleeding tissue.3

Inflammatory gingival enlargements mostly occur due to local irritants, such as dental plaque and calculus which are accumulated due to poor oral hygiene. This may cause discomfort, interfere with speech or chewing, resulting in halitosis.2 The enlargement in hereditary gingival fibromatosis most commonly occurs in the interdental areas on palatal and lingual gingiva along with labial and buccal gingiva. The enlargements may be so florid that the teeth involved are almost completely covered by gingiva (pseudoanodontia). The enlargements are rounded, smooth, firm, and pale-colored. Drug-associated gingival hypertrophy occurs due to antiepileptic drug phenytoin for long-term treatment, Cyclosporine and calcium channel blockers, such as Nifedipine, Amlodipine, and Verapamil. The enlargement affects the interdental areas on the labial aspect. The gingiva tends to enlarge laterally and this growth pattern may result in the formation of vertical clefts between adjacent enlargements. The normal gingival stippling may be enhanced, producing an orange-peel appearance. The treatment of gingival enlargements can be done by controlling the inflammation by scaling, root planing, and good oral hygiene measures. The small growth of drug-induced enlargement can be treated by early withdrawal of the drug while large growths are treated by surgical excision procedures like gingivectomy.4
MATERIALS AND METHODS

Source of Data

A total of 40 subjects were selected for the study, from the outpatient Department of Institute of Dental Sciences, Bareilly, Uttar Pradesh. Ethical approval was obtained from the Institutional Ethical Committee, prior to the commencement of the present study. Signed written informed consent was obtained from every individual after explaining the procedures and the outcomes in their vernacular language. The study subjects were divided into two groups of 20 each. Group I as the study group and group II as the control group.

Inclusion Criteria

The patients diagnosed clinically with generalized gingival enlargements while normal individuals without any obvious gingival enlargements were included for the study.

Exclusion Criteria

The patients with localized and drug-induced enlargements, patients on antibiotic therapy, diabetics, and smokers were excluded.

Procedure

The case history was recorded, including the patient’s biodata, such as name, sex, age, address, marital status, occupation, and personal history. Both the groups had undergone phase I therapy, including scaling and root planing prior to excision of gingival tissue. Gingival tissues of study group were excised with the bard parker blade 15 during gingivectomy procedure, while gingival tissues of control group were excised during extraction of tooth with poor prognosis, or tooth undergone extraction during orthodontic treatment, or during crown lengthening procedure (Fig. 1).

All the excised tissues were fixed in 10% formalin. After grossing, all the tissues were placed in the cassettes and processed in the automatic processor unit. The 2 to 4 μm thick sections were cut under microtome and dipped in warm water for the ease in placing over the slide. The slides were then allowed to be dried and stained with hematoxylin and eosin for the microscopic evaluation.

Statistical Method

The statistical data was obtained and entered in Microsoft Excel sheet for comparing the gingival changes between study group and control group via chi-square test.

RESULTS

The histopathological parameters, such as nature of epithelium, intensity of inflammatory infiltrate, number of blood vessels, and fibroblast and collagen activity within the connective tissue were assessed. Microscopically, the gingival tissues of study group show histological alterations in gingival epithelium. There was highly significant difference in hyperparakeratinization and inflammatory cells between the study and control group, and significant differences in hyalinization and blood vessels between study and control group (Table 1).

The epithelium of study group was markedly thickened. The three layers – basal, spinous, and superficial are seen, whereas in the spinous layer hyperkeratinization

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Gingival overgrowth group</th>
<th>Control group</th>
<th>$\chi^2$ value</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Keratinization</td>
<td>(a) Hyperkeratinized 11</td>
<td>0</td>
<td>15.172</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td></td>
<td>(b) Parakeratinized 9</td>
<td>20</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 Hyalinization</td>
<td>9</td>
<td>2</td>
<td>6.144</td>
<td>0.013*</td>
</tr>
<tr>
<td>3 Blood vessels with extravasated red blood cells</td>
<td>12</td>
<td>4</td>
<td>6.667</td>
<td>0.010*</td>
</tr>
<tr>
<td>4 Inflammatory cells</td>
<td>(a) Mild 0</td>
<td>18</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(b) Moderate 13</td>
<td>1</td>
<td>32.786</td>
<td>&lt;0.001**</td>
</tr>
<tr>
<td></td>
<td>(c) Severe 7</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 Collagen fibers</td>
<td>(a) Loose to dense 16</td>
<td>11</td>
<td>4.859</td>
<td>0.008NS</td>
</tr>
<tr>
<td></td>
<td>(b) Loose 2</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(c) Dense 2</td>
<td>8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 Fibroblasts</td>
<td>(a) Plump 3</td>
<td>3</td>
<td>0.654</td>
<td>0.721NS</td>
</tr>
<tr>
<td></td>
<td>(b) Spindle 5</td>
<td>3</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>(c) Plump to spindle 12</td>
<td>14</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

p > 0.05: Nonsignificant (NS); *p < 0.05: Significant; **p < 0.001: Highly significant
was detected. The thickening of epithelium was due to the acanthosis process of spinous layer and vacuolation of the suprabasal epithelium. The underlying cause of this condition appears to be a mutation affecting the structure of CKI3 and/or CK4. The connective tissue of study group was highly hyalinized. The gingival connective tissue contains moderate inflammatory cell infiltration, loose to dense collagen fibers, plumped to spindle fibroblast, with increase in number of blood vessels (Figs 2A and B).

Comparing with that of control group, the gingival tissue was found to be parakeratinized, with mild inflammatory cells infiltration, which contains increased number of collagen and fibroblasts with fewer blood vessels. The connective tissue was hyalinized (Fig. 3).

DISCUSSION

The enlargement of oral mucosa is characterized by the formation of exuberant granulation tissue, which occurs due to chronic inflammation. The enlargements can arise in any part of oral mucosa, but when arise from gingiva, it is called Epulides. Epulides are hyperplastic tumor-like gingival enlargements, but they are not neoplastic. They may arise from interdental area of gingival tissue due to subgingival plaque and calculus or any trauma. They affect the females more than the males, particularly in pregnancy (epulis and pyogenic granuloma). The lesion mostly occurs in maxillary intercanine area, anterior to the molar teeth. The localized gingival enlargements lesions are fibrous epulis, pyogenic granuloma, pregnancy epulis, peripheral giant cell granuloma, giant cell fibroma, peripheral ossifying fibroma, and denture irritation hyperplasia.

Fibrous epulis is the most common Epulides, firm in consistency with color similar to adjacent gingiva. The growth may be pedunculated or sessile, covered by yellowish fibrous exudates. Histologically, the growth contains rich network of cellular fibroblast and mature collagen fibers with variable inflammatory cell infiltration. Pregnancy epulis and pyogenic granuloma are vascular Epulides, soft in consistency, deep reddish purple in color. Spontaneous bleeding may occur on minor trauma. The lesion occurs in first trimester of pregnancy. The growth increases in size during this period and regresses after delivery. Histologically, both appear as solid sheets of endothelial cells with numerous small vessels or large dilated thin-walled vascular space with edematous cellular stroma. The infiltratory cell infiltration is variable.

The peripheral giant cell granuloma is ulcerated, dark red, pedunculated, or sessile swelling in the interdental area of dentate. Histologically, the epithelium is stratified squamous. The lesion consists of multinucleated osteoclasts cells rich in vascular cellular stroma with dilated blood vessels. Giant cell fibroma is pink, painless, pedunculated, or sessile swelling occurring in cheek near occlusal line, lips, and tongue. It is also known as leaf trauma.
Histologically, it contains dense, avascular, and acellular fibrous tissue with thick interlacing collagen bundles with scanty plump fibroblasts. Hyperplastic stratified squamous epithelium is seen with mild inflammatory cell infiltration. Dental irritation hyperplasia contains hyperplastic mucosa with single or multiple leaf-like lesion in vestibular sulcus area, also involve the inner cheek, lip, and palate. The lesion is firm in consistency, with moderate inflammation and may be ulcerated. The true fibroma of mouth is rare and it cannot be distinguished with certainty from non-neoplastic fibrous hyperplastic lesions.

The histopathological changes in the epithelium of gingival enlargements patient were found to be acanthotic and parakeratinized. The inflammatory cell infiltration was found to be severe with increased number of blood vessels in connective tissue stroma. In our study, the epithelium was also found to be acanthotic, hyperparakeratinized with moderate infiltration of inflammatory cells with increased blood vessels. According to Chaturvedi in 2009, the epithelium was found to be parakeratinized and acanthotic with mild inflammatory cell infiltration. The number of blood vessels was found to be decreased in the connective tissue. In our study, the epithelium was found to be acanthotic and hyperparakeratinized with moderate inflammatory cells and increased blood vessels. According to Omori et al. in 2014, the gingival epithelium was found to be hyperparakeratinized, which was due to an increase and thickening of mature collagen bundles in the connective tissue stroma, with moderate inflammatory cell infiltration in connective tissue stroma which was similar to our study. According to study in 2013, the gingival epithelium was found to be hyperparakeratinized and acanthotic, with severe inflammatory cell infiltration and decreased number of blood vessels unlike to our study. According to Coletta and Graner, in 2006, they found mild inflammatory cell infiltration in subepithelial connective tissue unlike our study.

CONCLUSION

Gingival enlargements are characterized by an excessive growth of the periodontal tissues. To understand the nature of cells, responsible for enlargements, is always a challenging task. Cells have certain typical characteristic features which get activated in response to enlargements, such as hyperkeratinization in the spinous cell layer. The mechanism behind the enlargements has to be evaluated and further studies should be done to understand the ultrastructural changes in gingiva.

REFERENCES