

Hereditary gingival fibromatosis: a 30 year follow up study in three generations

Banihashemrad SA. DDS¹, Tamizi M. DDS², Banihashem A.MD³

¹Assistant Professor of Periodontics, ²Professor of Periodontology,

³Associate Professor of Pediatrics

Introduction: Hereditary gingival fibromatosis [HGF] is a rare condition with undetermined etiology, thus is designated as idiopathic. Previous studies have revealed that the pattern of inheritance is autosomal dominant or (rarely) autosomal recessive.

Materials and Methods: In our study a group of family members in three generations were followed for 30 years. This clinical and histological study was initiated by the extraction of remaining teeth and excision of the enlarged gingiva of the oldest member of the group.

Results: No recurrence happened after 30 years of follow-up. The other cases were operated twice during the primary and permanent dentition periods. After the second surgery, so far there has been no recurrence in any of the patients.

Conclusions: In all cases the hyperplasia developed after the eruption of teeth and recurrence was observed after surgery in some of them who retained some teeth.

Keywords: Gingiva, Fibromatosis, Hereditary

Introduction

Generalized gingival enlargement can be caused by a variety of etiological factors. It can be inherited (hereditary gingival fibromatosis [HGF]) associated with other diseases characterizing a syndrome; or induced as a side effect of systemic drugs.

HGF, previously known as elephantiasis gingiva, hereditary gingival hyperplasia, and hypertrophic gingiva, is a genetic disorder characterized by a progressive enlargement of the gingival (1).

Genetic loci for autosomal dominant forms of HGF have been localized to chromosome 2p21-p22 (HGF1) and chromosome 5q13-q22 (HGF2).

To identify the gene responsible for HGF1, we extended genetic linkage studies to refine the chromosome 2q21-p22 candidate interval to approximately 2.3 Mb (2).

Increase in size of the gingival is a common feature of gingival disease. Accepted current terminology for this condition is gingival enlargement and gingival overgrowth. These are strictly clinical descriptive terms and avoid the erroneous pathologic connotations of terms used in the past such as hypertrophic gingivitis or gingival hyperplasia. The many types of gingival enlargement can be classified according to etiologic factors and pathologic changes as follows (3):

Banihashemrad SA. MD
Address: Dental School, Mashhad, Iran.
E-mail: s-a-banihashemrad@mums.ac.ir
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I- Inflammatory enlargement

A: Chronic B: Acute

II-Fibrotic enlargement(gingival hyperplasia)

A: Drug-induced B: Idiopathic

III- Enlargement associated with systemic diseases

A: Conditioned enlargement

(Pregnancy, Puberty, Vitamin C deficiency, Plasma cell gingivitis, Nonspecific conditioned enlargement).

B. Systemic diseases causing gingival enlargement.(Leukemia,Granulomatous disease)

IV-Neoplastic enlargement(Gingival tumors)

A: Benign tumors B: Malignant tumors

V- False enlargement

Gingival enlargement is a well-known consequence of the administration of some anticonvulsants, immunosuppressant, and calcium channel blockers and may creates speech, mastication, aesthetic problems and tooth eruption. Clinical and microscopic features of the enlargements caused by the different drugs are similar.

The term hyperplasia refers to an increase in the size of a tissue or an organ produced by an increase in the number of its component cells. Noninflammatory gingival hyperplasia is produced by factors other than local irritation. It is not common; and most cases occur after therapy with drugs such as phenytoin, cyclosporine and nifedipine (4).

Clinical Features

The enlargement affects the attached gingival, as well as the gingival margin and interdental papillae. The facial and lingual surfaces of the mandible and maxilla are generally affected, but the involvement may be limited to either jaw.

The enlarged gingival is pink, firm, and almost leathery in consistency and has a characteristic minutely pebbled surface.

In several cases the teeth are almost completely covered, and the enlargement projects into the oral vestibule.

The jaws appear distorted because of the bulbous enlargement of the gingival.

Secondary inflammatory changes are common at the gingival margin (3).

Histopathology

HGF fibroblasts are characterized by an increased production of collagen and transforming growth factor beta1 (TGF-beta) resulting in a fibrotic enlargement of the gingiva of affected patients.

A common feature of interstitial fibrosis is the occurrence of myofibroblasts, which are regarded as the predominant cells in matrix synthesis (5).

There is a bulbous increase in the amount of connective tissue that is relatively avascular and consists of densely arranged collagen bundles and numerous fibroblasts.

The surface epithelium is thickened and acanthotic with elongated rete-regs (4).

Etiology

The cause is unknown and thus the condition is designated as idiopathic.

Some cases have a hereditary basis, but the genetic mechanisms involved are not well understood.

A study of several families found the mode of inheritance to be autosomal dominant in others.

In some families the gingival enlargement may be linked to retardation of physical development. The enlargement usually begins with the eruption of the primary or secondary dentition and may regress after extraction, suggesting the possibility that the teeth (or the plaque attached to them) may be the initiating factors.

The presence of bacterial plaque is a complicating factor. The gingival enlargement may be present as an isolated finding or be associated with several more generalized syndromes (3).

Materials and Methods

This study has been performed on 13 patients who were members of a family in Khorasan and have referred to Mashhad Dental School for about 23 years.

The data consisted of: personal information, family history, dental and medical history, soft tissue, condition gingival overgrowth, OPG and periapical radiographic, intra and extraoral photography, hematology and biochemistry tests were recorded in their files.

Preliminary treatments such as: scaling, root planning, oral hygiene instructions and plaque control was done for each patient and their effects on disease was evaluated by reexamining the patients.

The surgical operations was done with patient permission after examination of the patients for their tissue response to the above treatments. The surgical treatment include gingivectomy, tooth extraction (for those which have no sufficient periodontal support or malalignment of teeth) and alveoplasty. The results of surgical operation and also the recurrence of the disease were noted.

Results

Here we reported a family with 13 affected individuals in three generations living in Iran. The proband, the oldest man in the family presented with a massive gingival overgrowth, at a regional dental clinic 30 years ago and was treated with extraction of all his teeth and gingival surgery to reduce the overgrowth. Recurrence was not observed (Fig.1).

Other members of his family (8 females and 4 males) who were also affected have been referred for assessment and treatment.

The interesting point in the study was that the disease had been occurred mostly in females (fig.2).

It has been reported that in most HGF, gingival enlargement has occurred in time of primary and permanently teeth eruption (fig.3).

Histological examination showed that the surface epithelium was thickened and acanthotic with elongated rete-regs (Fig.4).



Fig.1: A picture of the intra-oral aspect of both jaws belonging to a 40 year old male patient prior to surgery



Fig.2: Upper jaw of a patient with recurrence after surgery



Fig.3: The panoramic view of the same patient (fig.2) before the second surgery

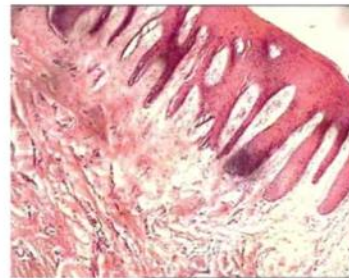


Fig.4: photomicrograph of the same patient

Discussion

However, there are some reports indicating that gingival overgrowth can occur after birth as well. Investigation in this family showed that gingival enlargement started at the time of teeth eruption. Examination of the family pedigree demonstrated an autosomal dominant trait of inheritance, and a sibling recurrence risk of 0.085 and an offspring recurrence risk of 0.078, indicating that HGF was a consequence of genetic alteration with low penetrance (6).

There are many reports indicating that tissue regeneration takes place after teeth extraction. These findings suggest that gingival sulcus slot environment has an important role in pathogenesis of this disease.

In recurrent HGF, the surgery is the least treatment which should be performed and if it takes place after tooth extraction the results will be satisfactory.

There are some reports showing that recurrent gingival hyperplasia has been observed around permanent teeth.

All these facts indicate that recurrent gingival hyperplasia cannot be predicted and every case should be treated individually.

In the cases studied, patients did not have any systemic problems and therefore the possibility of the induced hyperplasia by drug or disease was rejected. Treatment of patients with gingival hyperplasia should be based on a complete review of their medical history and physical examination. To confirm the diagnosis, a biopsy is necessary to distinguish it from neoplasm.

In fibrotic disorders excessive deposit of collagen is the first observable sign in the affected tissue and in HGF the gingiva has condensed collagen bundle due to increased collagen synthesis.

In this case degradation of collagen may be reduced as well. In HGF fibroblasts produce collagen type I almost two times more than normal gingiva.

These findings are in accordance with those reported by Shirasuna et al(7).

They reported that in fibrotic gingiva collagen synthesis was 2.2 times more than a normal gingiva (7).

Fibroblasts in HGF that induce gingival overgrowth show increased synthesis of sulfated glycosaminoglycans and may induce a decrease in collagen degradation as a result of the production of an inactive fibroblastic collagenase (3).

The result of our study showed that this disease has appeared mostly in girls and due to its effects on appearance, speech and chewing it might affect the psychiatric status of the patients and may result in depression. Therefore the proper treatment should be suggested. It seems that presence of teeth plays an important role in recurrence of gingival enlargement after surgery.

Conclusion

In all cases the hyperplasia developed after the eruption of teeth and recurrence was observed after surgery in some of them who retained some teeth.

Pedigree analysis suggested an autosomal dominant inheritance of gingival enlargement in this family. However, autosomal recessive inheritance cannot be ruled out due to consanguineous marriage in family who lived in small village in Khorasan, Iran, with possibility of maternal relationship between families, although the proband and his affected children were apparently from a non-consanguineous marriage, other affected individuals are clearly from consanguineous mating.

Further investigation on the chromosomal inheritance pattern is recommended.

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خلاصه

فیبروماتوزیس ارثی لته، مطالعه سی ساله در سه نسل

دکتر سید علی بنی هاشم راد، دکتر محمود تمیزی، دکتر عبدا... بنی هاشم

مقدمه: فیبروماتوزیس ارثی لته یک حالت نادر با اتیولوژی نامعین می باشد و به عنوان ایدئوپاتیک تعریف شده است. شکل توارث آن را از نوع اتوزومال مغلوب و اتوزومال غالب، ذکر کرده اند.

مواد و روش ها: در تحقیق ما که در دانشکده دندانپزشکی مشهد انجام شد یک گروه از اعضای خانواده را در سه نسل بررسی و برای مدت حدود سی سال پی گیری نمودیم، این پژوهش که به صورت کلینیکال و هیستولوژیکال بود، از مسن ترین عضو گروه با کشیدن دندان های باقیمانده شروع و لته اضافی نیز برداشته شد.

یافته ها: پس از سی سال پی گیری، هیچ گونه عودی مشاهده نگردید. سایر موارد، در طی دو مرحله که دارای دندان های شیری و دایمی بودند، جراحی شدند که بعد از جراحی دوم تا به اکنون هیچ مورد از عود بیماری مشاهده نشده است.

نتیجه گیری: در تمامی موارد هایپرپلازی پس از رویش دندان ها پیشرفت کرده و عود پس از جراحی در مواردی که دندان ها باقی مانده بود دیده شد.

واژه های کلیدی: لته، فیبروماتوزیس، ارثی