

Genes that Affect the Look in Teens; Hereditary Gingival Fibromatosis: A Case Report

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Abstract: *Hereditary Gingival Fibromatosis (HGF) also referred to as idiopathic gingival hyperplasia is a rare type of slow growing gingival enlargement with great clinical and genetic heterogeneity inherited usually as Mendelian autosomal dominant trait. Occurring as an isolated trait (HGF) and/or as a component of a syndrome, the affected gingiva is characterized by firm, asymptomatic, nonhemorrhagic enlarged (hyperplastic) tissue with characteristic pale pink colour, covering most of the anatomic crown, involving usually all the quadrants. This paper presents a case report of a 16 year old male suffering from hereditary gingival fibromatosis with a positive family history. Periodontal management including gingivectomy (external bevel) was being undertaken after biopsy.*

Keywords: Hereditary Gingival Fibromatosis, Gingival Enlargement, Gingivectomy

1. Introduction

Hereditary gingival fibromatosis first reported by Goddard and Gross in 1856^[1], is a rare, benign, nonhaemorrhagic fibrous enlargement of gingival tissue. It was previously called elephantiasis gingivae, hereditary gingival hyperplasia and hypertrophic gingival^[2]. HGF is a rare disorder; phenotype frequency of 1:1,75000^[3], characterized by the proliferative fibrous overgrowth of the gingival tissue. It usually develops as an isolated disorder but can be one feature of several multi-system syndromes such as Zimmerman Laband, Rutherford, Jones, Cross and Prune-belly syndromes.

Hereditary gingival fibromatosis is usually identified as an autosomal dominant condition although recessive forms are described in the literature; however penetrance and expressivity vary considerably^[4]. The hyperplastic gingiva usually presents a normal colour and has a firm consistency with abundant stippling. This anomaly is classified in two types according to its form. The first, nodular form, localized, is characterized by the presence of multiple

enlargements in gingival papillae. The symmetric form, the most common type of the disorder, results in uniform enlargement of the gingiva. Gingival tissue enlargement usually begins with eruption of the permanent dentition but also can develop with the eruption of the primary dentition. It is rarely present at birth. According to a study of Brazilian patients, gingival enlargement occurs mainly in the mixed dentition and may worsen during puberty^[5].

HGF can potentially interfere with speech, lip competency and mastication resulting in both esthetic and functional problems^[2,6]. The most common effects related to gingival overgrowth are diastemmas, malpositioning of teeth and prolonged retention of primary teeth. Although gingival hyperplasia occurs alveolar bone is not affected^[7]. Parental consanguinity can be significantly seen in this disease. Hereditary gingival fibromatosis can occur as a solely manifestation affecting the gingiva only, with no other local or systemic involvement or is associated with certain syndromes; some of them are described below (Table 1)^[7,8].

Table 1: Syndromes Associated With Hereditary Gingival Fibromatosis

Syndrome	Features Apart From Gingival Fibromatosis	Inheritance
Gingival fibromatosis with hypertrichosis	Hypertrichosis, mental retardation	Autosomal dominant
Zimmermann-Laband	Ear and nose defects, dysplastic nails, terminal phalanges hypoplastic, joint hyperextensibility, and hepatosplenomegaly	Autosomal dominant
Murray-Puretic-Drescher (juvenile hyaline fibromatosis)	Multiple hyaline fibromas, osteolysis of terminal phalanges, recurrent infections, stunted growth, and premature death	Autosomal recessive
Rutherford	Corneal opacities and retarded tooth eruption	Autosomal dominant
Gingival fibromatosis with distinctive facies	Macrocephaly, hypertelorism, bushy eyebrows with synophrys, downslanted palpebral fissures, flat nasal bridge, hypoplastic nares, Cupid's bow mouth, and highly arched palate	Autosomal recessive
Ramon	Cherubism, hypertrichosis, mental deficiency, epilepsy, stunted growth, juvenile rheumatoid arthritis, and ocular abnormalities including pigmentary change in retina and paleness of optic disc	Autosomal recessive
Cross	Microphthalmia, mental retardation, athetosis, and hypopigmentation	Autosomal recessive
Jones	Progressive deafness, variant tendency to allergies or hypertelorism and supernumary teeth	Autosomal dominant
Prune-belly	Absence of abdominal muscles, abnormalities of urinary tract, cryptorchidism, and facial dimorphism, bilateral undescended testes	Unclear

Volume 5 Issue 7, July 2016

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This case report presents the clinical features and management of 16yr old patient who presented with classical features of hereditary gingival fibromatosis.

2. Case Description

A 16 year old male patient accompanied by his mother reported to the Department of Periodontics, Nair Hospital Dental College with a chief complaint of swollen gums. The patient revealed that he had noticed swelling of gums post eruption of his permanent teeth. The swelling slowly progressed involving the gingiva in both the arches and attained the current size [Fig 1]. The swelling caused difficulty in speaking, eating and also had obvious implications for his esthetic appearance that made the patient report for the treatment.



Figure 1: Generalized severe gingival overgrowth involving both the maxillary and mandibular arches

His medical history appeared to be non-contributory to the development of gingival enlargement. No significant drug history or personal history that may predispose to gingival enlargement. Patient had positive family history as his father also had presented with gingival features in form of gingival enlargement of maxilla and mandible to various extents with no syndromic association. [Fig 2&3]



Figure 2 & 3: Gingival enlargement in Patient's Father oral cavity

Intraoral examination revealed generalized severe gingival overgrowth involving both the maxillary and mandibular arches. The gingival tissue covered almost occlusal/incisal 2/3rd of the clinical crown illustrating Grade 3 gingival overgrowth [Fig 4 & 5].



Figure 4 & 5: Gingival tissue covered almost occlusal/incisal 2/3rd of the clinical crown illustrating Grade 3 gingival overgrowth

The gingiva was pale pink in colour with a firm, dense, fibrous consistency with no significant plaque deposition. The dental panoramic radiograph of the patient revealed no periodontal involvement except periapical involvement due to carious lesion in relation to 36 [Fig 6].



Figure 6: Dental panoramic radiograph of the patient revealed no periodontal involvement except periapical involvement due to carious lesion in relation to 36.

Biopsy samples were taken initially from lower anterior region and was sent for histopathological examination. Histopathological findings of fibroepithelial hyperplasia with numerous fibroblast in connective tissue [Fig 7] and positive family history led to the diagnosis of "Hereditary Gingival Fibromatosis."



Figure 7: Histopathological slide showing fibroepithelial hyperplasia with numerous fibroblast in connective tissue

Considering the size and extent of gingival enlargement a segment-wise external bevel gingivectomy was performed under local anesthesia. Following administration of local anesthesia, a periodontal probe was used to outline base of pockets [Fig 8] with series of bleeding points marked on both sides of gingival enlargement that helped in delineating the incision line. External bevel 45° incision was given with Kirkland knife & B.P blade no. 15 [Fig 9]; followed by gingivoplasty [Fig 10].



Figure 8: Probing shows presence of pseudopockets with adequate width of attached gingiva. Fig 9. External bevel 45° incision was given with Kirkland knife & B.P blade no. 15.



Figure 10: Segment-wise gingivectomy was done followed by gingivoplasty

Surgical site was given a dressing with Coe Pak periodontal dressing. Post-operative care included antibiotic and analgesic regimen for 3 days and 0.2% chlorhexidine rinse twice daily for 2 weeks. Post-operative healing was uneventful [Fig 11 & 12].



Figure 11&12: Post treatment visit after 2 months showing marked improvement.

Histopathological examination revealed stratified epithelium with hyperkeratosis and elongated rete pegs. The underlying connective tissue was abundant with dense fibrous tissue comprising of fibroblasts and collagen fibre bundles. The clinical and histopathological findings were consistent with Hereditary Gingival Fibromatosis. The post-operative course was uncomplicated and there was no recurrence of lesion.

3. Discussion

Gingival enlargement, either localized or generalized might be attributed to a number of reasons, ranging from inflammation, leukemic infiltration, association with use of medicines like phenytoin, cyclosporine, and nifedipine or due to genetic mutations^[9].

Idiopathic gingival fibromatosis may be congenital or hereditary. Although genetic mechanism is not well understood, majority of authors have attributed the condition related with hereditary factors. It is possible that isolated cases of gingival fibromatosis may arise from a single gene mutation, while generalized forms may result from alterations of multiple genes. Genetic studies have demonstrated that HGF is genetically heterogeneous. It

has been recently suggested that a mutation in the Son Of Sevenless1 (SOS1) gene, is responsible for the etiology of HGF^[10].

To date, we know three different loci associated with the isolated form of HGF: two map to chromosome 2 (GINGF on 2p21-22 and GINGF3 on 2p22.3-p23.3)^[11,12,13], which do not overlap, and one maps to chromosome 5 (GINGF2 on 5q13-q22)^[14]. Of these loci, only the SOS1 (son of sevenless one) gene underlying the Gingival Fibromatosis (GINGF) locus has been identified^[10]. Chromosomal abnormalities reported for syndromes with gingival fibromatosis include duplications, deletions, and/or other anomalies of chromosomes 2p13-16, 4q, 8, 14q, 19p, 19q, and Xq. Although the identification of SOS1 mutations in HGF patients is clear, further functional studies are needed to confirm this association with the HGF etiology.

The cellular and molecular mechanisms involved in HGF etiology are still not completely understood. HGF is characterized histologically by an accumulation of dense fibrous connective tissue. This is believed to be due to an imbalance between synthesis and degradation of extracellular matrix molecules or due to an alteration in fibroblast proliferation.

Research^[15] found that HGF fibroblasts are phenotypically distinct from normal human gingival fibroblasts in vitro and proliferate more rapidly and produce double the amount of type I collagen and fibronectin. Tipton, et al^[16], at the University of Tennessee, College of Dentistry demonstrated that autocrine stimulation of transforming growth factor (TGF- β) produced by HGF fibroblast contributes to this increased production. The excessive production of connective tissue products is directly related to the increase in gingival bulk.

Another possible mechanism of HGF pathogenesis is impairment in extracellular matrix degradation. Collagen turnover in gingival tissues is high and degradation occurs by two main pathways: fibroblast phagocytosis and degradation in the extracellular space by members of the matrix metalloproteinase (MMP) family of proteases. The MMP pathway is impaired in HGF: a decreased level of expression and activity of MMP-1 and MMP-2 has been described in HGF cells,^[17] resulting in collagen type I accumulation. In addition, MMP-2 inhibition results to an abnormal accumulation of glycosaminoglycans and fibronectin in the gingival tissues. It has been documented that TGF- β 1 downregulates MMP-1 and MMP-2 expression in an autocrine fashion, thus playing a key role in the biochemical mechanisms associated in the pathogenesis of gingival overgrowth. Furthermore, TGF- β 1 may induce fibroblast differentiation into myofibroblasts, which are considered predominant cells in matrix synthesis in interstitial fibrosis such as HGF. All of these actions of TGF- β 1 result in a dysregulation of the connective tissue homeostasis, leading to the accumulation of extracellular matrix which clinically results in gingival enlargement.

Numerous treatment modalities and time for surgical intervention have been proposed for excision of enlarged gingival tissues. However the optimal time for surgical

intervention is following eruption of permanent dentition because there is a higher risk of recurrence if performed in a mixed-dentition. Delay in treatment beyond this stage may have significant consequences for the patient, such as an altered eruption pattern of the permanent teeth, malposition of teeth, and malocclusion, difficulties in mastication and speech, gummy smile, esthetic problems with psychological consequences.

The treatment outcomes depend on the severity and extend of the gingival enlargement. When the enlargement is mild, thorough scaling of teeth and proper home care may be sufficient to restore good oral health and appearance. However, if scaling is proved to be ineffective and the gingival overgrowth continues to affect appearance and function, surgical intervention becomes mandatory. Gingivectomy and gingivoplasty^[18] with blades, surgical knives, laser^[19] or electrosurgery to restore normal gingival appearance and contours is the treatment of choice.

Recurrence of the gingival enlargement is unpredictable. It is most often seen in children and teenagers rather than adults. Review of literature suggests that, the psychological benefits resulting from cosmetic improvement far outweighs the risk of recurrence, which can be a major problem. However, in several reported cases there was no recurrence in a period of 2-14 years of follow-up.

For the present case, gingivectomy under local anaesthesia was the appropriate treatment as unesthetic appearance and impaired function demanded surgical intervention. Good esthetic result was achieved without recurrence of gingival overgrowth till date about at the end of 2yr.

4. Conclusion

HGF differs from other gingival enlargements because of its fibrous nature and high prevalence of recurrence post treatment. Maintaining good oral hygiene prevents reoccurrence of the overgrowth in most cases of HGF. However, gingival fibromatosis recurrence could occur in the presence of good oral hygiene due to multiple genetic predisposition.^[20] However the psychological benefits resulting from cosmetic improvement far outweighs the risks of recurrence. Therefore early treatment minimizes the displacement of erupting teeth, reduces malocclusion and thus overall improve esthetics diminishing psychological effects in young patients.

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