Hereditary gingival fibromatosis: report of three cases

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Three cases of generalized and severe HGF in young patients of the same family without other features are reported. The purpose of this article is to present documented cases and discuss the identification, treatment, and control of the disease. The histopathological characteristics of HGF are emphasized.
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INTRODUCTION

Hereditary gingival fibromatosis (HGF) is a rare oral disease characterized by a slowly and progressive enlargement of both the maxilla and mandible gingiva.[1] Males and females are equally affected as a phenotype frequency of 1:175,000.[2] The enlarged gingiva is of normal color, firm consistency, nonhemorragic and assymptomatic. The hyperplasia gingival may be generalized or partial, involving only localized portions of maxilla and mandible, and the degree of enlargement may vary from mild to severe, same between individuals within the same family.[3] Most cases are seen from birth or it may not be noted until later childhood, at the time of eruption of deciduous or permanent teeth.[4,5] Histologically, HGF tissues are composed mainly of dense connective tissue rich in collagen fibers; the epithelium is hyperplasic with long rete pegs.[6] Small calcified particles, islands osseous metaplasia, ulceration of the overlying mucosa and inflammation can also be seen occasionally.[7]

A number of reports have documented in HGF an increased synthesis of extracellular matrix (ECM) including collagen, fibronectin and glycosaminoglycans.[8-11] Although the exact genetic alteration leading to the increased accumulation of the collagen remains unclear, our previous investigations showed that, *in vitro,* HGF fibroblasts proliferate more rapidly and produce lower amounts of matrix metalloproteinases-1 and -2 (MMP-1 and MMP-2, respectively), the major enzymes associate with the degradation of[12,13] HGF may seen as an isolated findings or in association with other features, as part of a syndrome. HGF has been reported in association with hypertrichosis[14], mental retardation[4], epilepsy[15], progressive sensorineural hearing loss[16] and abnormalities of the extremities, particularly of fingers and toes.[17] Of these ancillary features, hypertrichosis is the most commonly associated feature.[14,18] The HGF has an autosomal dominant mode of inheritance with variable penetrance and expressivity, however, the disease may be found as an autosomal recessive mode of inheritance.[19] This article describes the identification, treatment and control of three cases of HGF without any associated findings, affecting young patients of a same family.

CASE REPORTS

CASE I

An eight-year-old Caucasian boy was referred to the Orocentro - Center for the Study of Oral Disease at University of Campinas Dental School, Piracicaba-SP, due to pronounced fibrous gingival overgrowth. Clinical examination revealed generalized and severe gingival hyperplasia involving both the maxillary and mandibular arches, with morphologically normal teeth. In region of mandibular incisors the overgrowth was the most severe (Figure 1). The gingiva was pink, and its firm, dense, fibrous consistency caused difficulty in tooth eruption. The patient had difficulty maintaining

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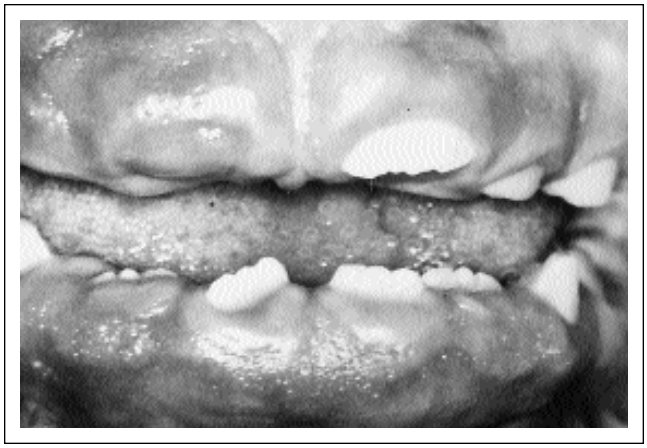

Figure 1. Case 1. Clinical photograph of maxillary and mandibular arches in an eight-year-old boy with HGF. Note the greatly thickened gingiva and the malpositioning of the teeth.

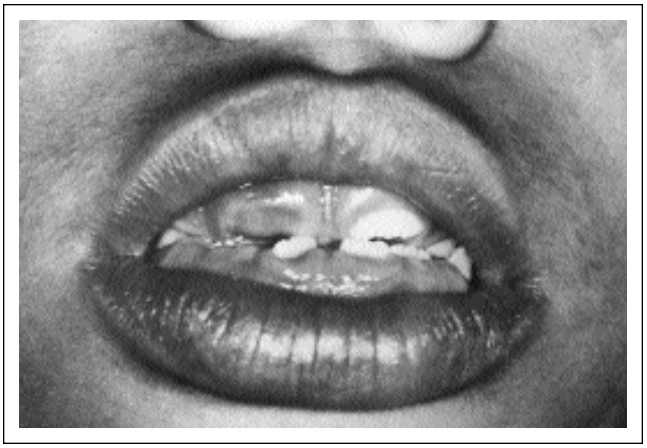

Figure 2. Case 1. Marked cross bite with dramatic flaring caused by gingival overgrowth, preventing closure lip closure.

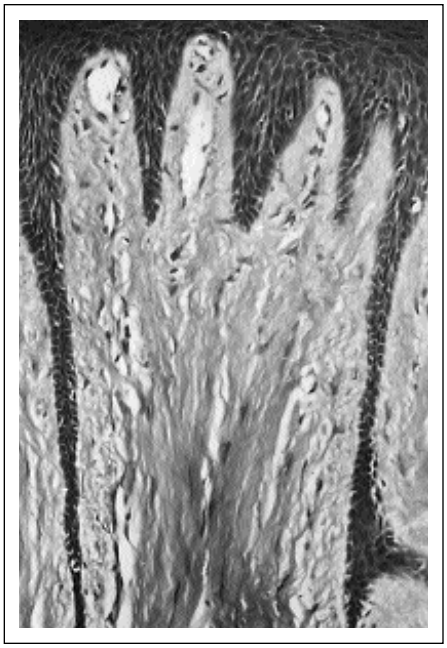

Figure 3. Case 1. Histologically, the HGF is characterized by a mucosa in which the epithelium contains long slender rete pegs that extend into a dense connective tissue that is rich in collagen fibers.

adequate oral hygiene. Gingival enlargement had first been noticed months after birth, but it was most intense during the period of primary dentition.

Panoramic radiograph did not reveal any bone lesion. He had a marked cross bite with dramatic flaring prevented normal lip closure (Figure 2). The patient was a mouth breather and manifested a tongue thrust during swallowing.

The mother described the pregnancy as normal, without risk of fetal loss or use of medications. His medical history was unremarkable. He confirmed toxoplasmosis at the age of 5 years. He denied taking any medications and his weight and height were considered to be within normal limits. He did not appear to have any mental impairment. The patient was unhappy with the appearance of his gingiva. His mother had several gingival excisional surgeries because of unpredictable, slowly progressing hyperplasia. His mother had not had epilepsy or any type of seizure disorder, nor had she taken any medications associated with gingival hyperplasia. This family had absence of a relevant medication history.

The treatment consisted of quadrant-by-quadrant gingivectomy/gingivoplasty technique with periodontal pack placement for four days, followed by 0.25% chlorhexidine oral rinses twice a day for two weeks after each surgery. After the last gingivectomy and post-surgical follow-up visit, the patient returned periodically for observation. Scaling and prophylaxis are performed every six months.

The tissues removed during gingivectomy were examined. The microscopy showed mild epithelial hyperplasia with longs rete pegs and marked increase in the dense fibrous connective tissue. A mild chronic inflammatory cells infiltrate was observed around junction epithelial (Figure 3).

CASE 2

A twelve-year-old Caucasian girl, cousin of the first patient, was referred to our service because of pronounced generalized symmetric gingival hyperplasia affecting buccal and lingual/palatal aspects, involving both the maxilla and mandible. Gingival excess was most evident in the anterior region (Figure 4a and 4b). Oral malformations were not found. The level of oral hygiene was good. The lips were prominent and she had a cupid bow mouth. The panoramic radiographic does not show any missing or malformed teeth.

The mother stated that the condition became evident with the emergence of the permanent dentition. The systemic exploration was normal. Her medical history was unremarkable and she never taken any medication associated with gingival overgrowth. The girl

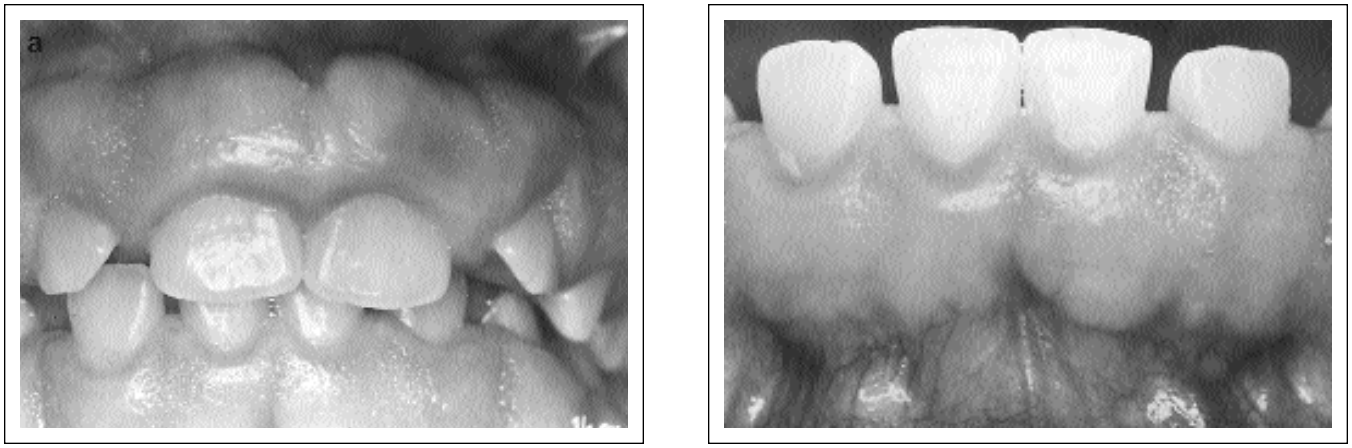

Figure 4. Case 2. Clinical view showing a pronounced gingival hyperplasia. A -maxilla. B - mandible.

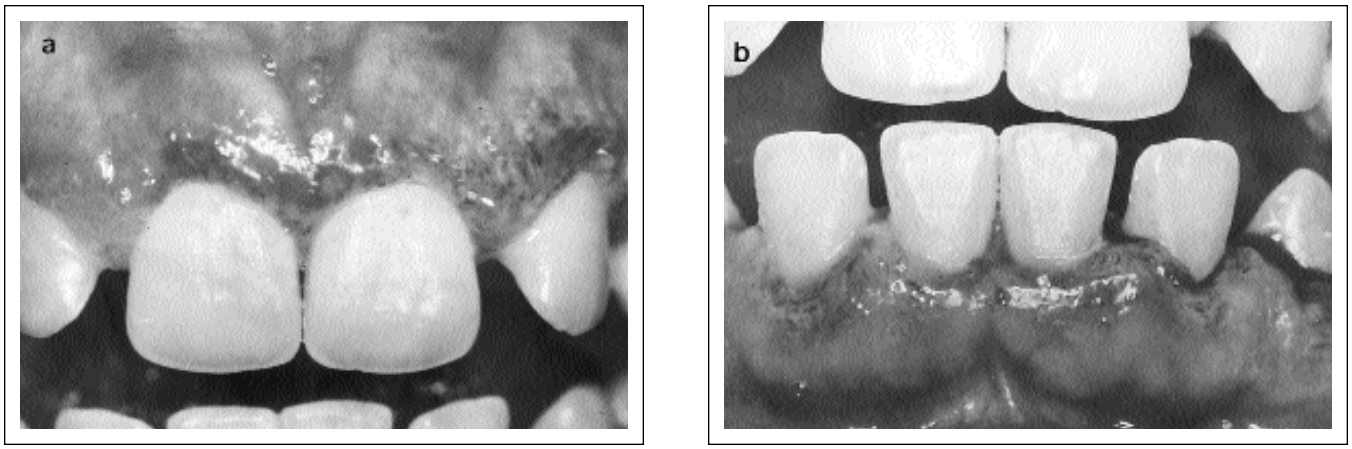

Figure 5. Case 2. Photograph taken 2 weeks after surgical procedure, followed by 0.25% chlorhexidine oral rinses. A - maxilla. B - mandible.

had chicken pox at the age of 6 years. She did not appear to have any mental impairment or hypertrichosis. The mother described the pregnancy as normal. Her father and her sister have the same problem. This family had absence of a relevant medication history.

She was treated by conventional gingivectomy/gingivoplasty procedure at the age of 12 years (Figure 5a and 5a). She is now aged 15 years and has developed, rather rapidly, marked gingival hyperplasia around upper incisors (Figure 6). The tissue removed showed histological characteristics similar of the case 1. The epithelium displays a moderate hyperplasia with elongation of the rete pegs, but the increased tissue mass is primarily the result of a marked increase in the dense fibrous connective tissue. There was marked infiltration of chronic inflammatory cells in the region of the gingival sulcus and close to surface, whereas the remainder of the tissue is relatively free of inflammatory elements.

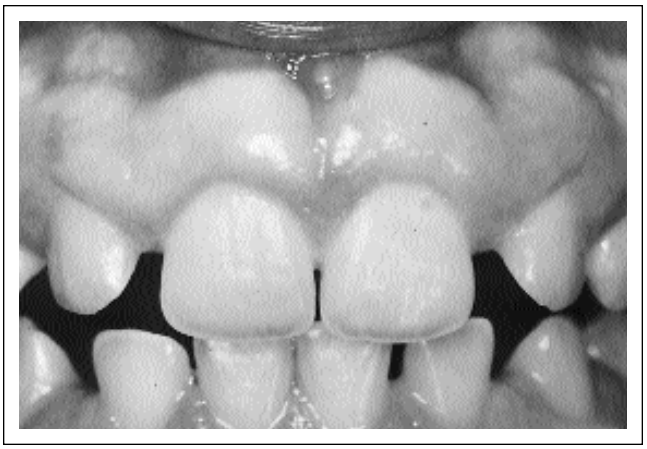

Figure 6. Case 2. Regrowth of tissue gingival two years later. Note excellent healing and more normal oral appearance.

CASE 3

An eight-year-old Caucasian boy, also cousin of the first and second patients, was seen at the Orocentro for investigation of gingival hyperplasia. The dental arches were broad and rounded anteriorly and were characterized by generalized attached gingival hyperplasia affecting both the buccal and lingual/palatal regions in the maxilla and mandible (Figure 7). The mucosa was pink and firm to probing. The hyperplasia gingival caused difficulty with dental plaque removal and in

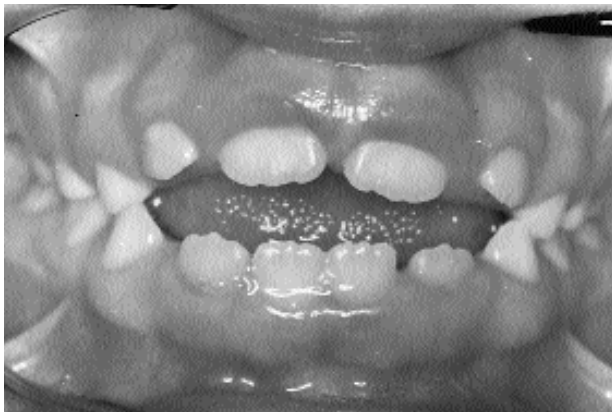

Figure 7. Case 3. Clinical photograph showing enlargement of upper and lower incisors' gingiva. Note the spacing of the upper and lower incisors and the prominent open bite.

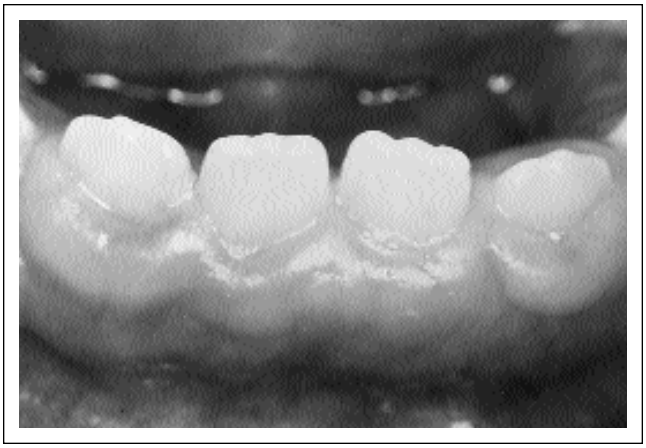

Figure 8. Case 3. Regrowth of gingival tissue around the lower incisors two years later the last surgical procedure.

these areas were observed signals of inflammation. There was generalized spacing of the upper and lower labial segments with a prominent median diastema. The permanent dentition showed incomplete eruption into the mouth due to the hyperplasic gingival tissue. Occlusal features of note included an open bite and a non-displacing crossbite. The overgrowth had been present since the age of 12 months and the gingiva was noted to grow fastly. All physical findings were within normal limits. His father has the same problem, but his brother is entirely normal. The affected boy was of normal intelligence, had no associated syndromic features and was not on medication known to induce gingival hyperplasia.

The treatment consisted of gingivectomy/gingivoplasty with periodontal pack placement for one week, followed by 0.25% chlorhexidine oral rinses twice a day for two weeks. The tissue obtained was histologically quite similar to that observed in case 1 and case 2. Epithelial hyperplasia was well marked with long rete pegs. The predominant feature, however, was the fibrosis of connective tissue, in which collagen fibers were disposed in parallel strands form the greatest bulk. The immediate result therapy was a dramatic cosmetic improvement.

By 5 months, a definite recurrence in the growth gingival tissue was apparent around the lower incisors. At two years postoperatively, a gingivectomy localized to the lower incisors was performed (Figure 8). Posterior areas have shown only minimal regrowth. The patient is now 11-year old and he has placed under periodic review to monitor occlusal and gingival development. It is planned to carry out corrective orthodontic treatment on establishment permanent dentition.

DISCUSSION

This report documents three cases of HGF affected young patients of the same family without association with other features, in which HGF was apparently transmitted by mean of an autosomal dominant trait with a high degree of penetrance. There was no history of consanguinity to suggest autosomal recessive inheritance. Additional information about autosomal dominant inheritance has been published.[1] Nevertheless, the features observed were similar in every way to those described by other authors.

HGF may occur as an isolated feature or rarely as part of a syndrome. The cases presented had a previously few described condition with distinctive oral features, such as cross bite and open bite in case 1 and case 3 respectively, lips prominent in all three cases, and open lip posture in case 1, in association with the oral signs of HGF. The syndromic characteristic most commonly seen in association with HGF is hypertrichosis[10], which is occasionally associated with mental retardation and epilepsy.[16,20] Our patients showed no hirsute but as some authors have shown, this feature does not appear until after puberty.[21]

These manifestations and other rare associations such as multiple hyaline fibromas, osteolysis of terminal phalanges and recurrent infections (Murray-Peretuc-Drescher syndrome), corneal opacities and retarded tooth eruption (Rutherford syndrome), ear, nose, bone and nail defects with hepatosplenomegaly (Zimmermann-Laband syndrome), progressive deafness (Jones syndrome), microphthalmia, mental retardation, athetosis and hypopigmentation (Cross syndrome) and giant fibroadenoma of breast, hypertrichosis and multiple hamartomas (Cowden syndrome) were not observed in either of the three children who were of normal intellect (for review: Gorlin, Cohen and Levin[15]).

Oral manifestations of HGF can vary from focal sites of gingival hyperplasia to generalized involvement, and the degree of hyperplasia may vary from slight to severe, that can as in the described cases

inhibit the complete eruption of the primary or permanent dentition into the oral cavity. All three patients exhibited generalized and severe gingival enlargement, whereas the anterior region of both maxilla and mandible were most severely affected.

It is known from previous reported cases that the condition usually begins at the time of eruption of the permanent dentition[3], but can develop with the eruption of the primary dentition and rarely is present at birth.[22] Fletcher[2] reported that the enlargement seems to progress rapidly during "active" eruption and decrease with the end of this stage. This author also reported that the presence of teeth appears to be necessary for HGF to occur, because the condition is not seen before eruption of the teeth and disappears or recedes with the loss of the teeth. In our case 1 and case 3, HGF was present shortly after birth, and in case 2 at the time of eruption of the permanent teeth. This may represent further clinical heterogeneity of HGF; however, a conclusion based on these cases is tenuous.

It is accepted that HGF is a disease of genetic origin, but the mechanism by which leads to the accumulation of excessive amounts of gingival tissue is unknown. The abnormal accumulation of connective tissue has traditionally been regarded to result from local increases in matrix collagen synthesis, which is consistent with the histological evidence.[8,10,23] However, recent study have recognized the equally important role of mechanisms of connective tissue degradation in excess accumulation of ECM in the gingival tissue of patients affected by HGF.[13]

HGF can not be cured, but can be controlled with varying degrees of success. When the enlargement is minimal, good scaling of teeth and homecare may be all that is required to maintain good appearance. As the excess tissue increases, appearance and function, as regards eating and speech, indicate need for surgical intervention. Several authors have reported the recurrence of hyperplasic tissue in HGF following gingivectomy, however, the psychological benefits of even temporary cosmetic improvement must not be underestimated and may outweigh the probability of recurrences in such a severe case. Cuestas-Carneiro and Bornancini[14] and many other authors recommend excision of the excess tissue combined with removal of all teeth in severe chronic cases, because it appears that permanent cure is most likely to be obtained.[24] In all three cases, we trended toward a more conservative approach. This option was based in studies of hereditary generalized gingival fibromatosis reported by Fletcher,[2] who observed in patients over 30 years of age, no detectable change in size during his period of observation. Other methods of removing large quantities of gingival tissue has been used in a number of studies, such as carbon dioxide laser[25] and electrocautery.[26] Emerson[17] emphasizes the importance of obtaining correct physiological contour of the gingiva an of maintaining good surgical after care it recurrence is to be prevented. He has also demonstrated that the degree of enlargement did not appear to be related to the oral hygiene or to the amount of calculus present.

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REFERENCES

1. Bozzo L, Almeida OP, Scully C, Aidred MJ. Hereditary gingival fibromatosis report of an extensive four-generation pedigree. Oral Surg Oral Med Oral Pathol 78: 452-454, 1994.
2. Fletcher JP. Gingival abnormalities of genetic origin: a preliminary communication with special reference to hereditary generalized gingival fibromatosis. J Dent Res 45: 597-612, 1966.
3. Singer SL, Goldblatt J, Hallam LA, Winters JC. Hereditary gingival fibromatosis with a recessive mode of inheritance. Case reports. Aust Dent J 38: 427-432, 1993.
4. Araiche M, Brode H. A case of fibromatosis gingivae. Oral Surg 12: 1307-1310, 1959.
5. Becker W, Collings CK, Zimmerman ER, La Rosa MD, Singdahlsen D. hereditary gingival fibromatosis. J Oral Path 24: 313-318, 1967.
6. Gunhan 0, Gardner DG, Bostanci H, Gunhan M. Familial gingival fibromatosis with unusual histologic findings. J Periodontol 66:1008-1011, 1995.
7. Farrer-Brown G, Lucas RB, Winstock D. Familial gingival fibromatosis: an unusual pathology. J Oral Pathol 1: 76-83, 1972.
8. Shirasuna K, Okur M, Watatani K, Hayashido Y, Saka M, Matsuya T. Abnormal cellular property of fibroblasts from congenital gingival fibromatosis. J Oral Pathol 7: 381-385, 1989.
9. Oikarinen K, Salo T, Kaar M-L, Lahtela P, Altonen M. Hereditary gingival fibromatosis associated with growth hormone deficiency. Br J Oral Maxillofac Surg 28: 335-339, 1990.
10. Tipton DA, Dabbous MKh. Autocrine transforming growth factor j3 stimulation of extracellular matrix production by fibroblasts from fibrotic human gingiva. J Periodontol 69: 609-619, 1998.
11. Coletta RD, Almeida OP, Ferreira LR, Reynolds MA, Sauk JJ. Increase in expression of Hsp47 and collagen in hereditary gingival fibromatosis is modulated by stress and terminal procollagen N-propeptides. Conn Tis Res, 1999. (IN PRESS)
12. Coletta RD, Almeida OP, Graner E, Page RC, Bozzo L. Differential proliferation of fibroblasts cultured from hereditary gingival fibromatosis and normal gingiva. J Periodont Res 33: 469-475, 1998.
13. Coletta RD, Almeida OP, Reynolds MA, Sauk JJ. Alteration in expression of MMP-1 and MMP-2 but not TIMP-1 and TIMP-2 in hereditary gingival fibromatosis is mediated by TGF-pI autocrine stimulation. J Periodont Res 34:1-7,1999.
14. Cuestas-Carneiro R, Bornancini CA. Hereditary generalized gingival fibromatosis associated with hypertrichosis: report of five cases in one family. J Oral Maxillofac Surg 46: 415-420, 1988.
15. Ramon Y, Berman W, Bubis JS. Gingival fibromatosis combined with cherubism. Oral Surg 24: 435-448, 1967.
16. Hartsfield JK, Bixler D, Hazen RH. Gingival fibromatosis with sensoneural hearing loss: an autosomal dominant trait. Am J Med Genet 22: 623-627, 1985.
17. Skrinjaric I, Bacic M. Hereditary gingival fibromatosis: report on three families and dermatoglyphic analysis. J Periodont Res 24: 303-309, 1989.
18. Winter GB, Simpkiss JJ. Hypertrichosis with hereditary gingival hyperplasia. Arch Dis Child 49: 394-399, 1974.
19. Gorlin RJ, Cohen MM, Levin LS. Syndromes of the head and neck, 3rd Ed. New York, Oxford University Press; 847-858, 1990.

20. Nevin NC, Scally BG, Kemohan DC, Dodge JA. Hereditary gingival fibromatosis. J Ment Defic Res 15: 130-135, 1971.
21. Emerson TG. Hereditary gingival fibromatosis: a family pedigree of four generations. Oral Surg Oral Med Oral Pathol 19: 1-9, 1965.
22. Ball El. Case of gengivoma, or elephantiasis of the gingiva. J Periodont 12: 96-100, 1941.
23. Tipton DA, Howell KJ, Dabbous MK. Increased proliferation, collagen, and fibronectin production by hereditary gingival fibromatosis fibroblasts. J Periodontol 68: 524-530, 1997.
24. Mclndoe A, Smith BO. Congenital familial fibromatosis of the gums with the teeth as a probable etiological factor: report of an affected family. Brit J Plast Surg 11: 62-71,1958.
25. Bakaeen G, Scully C. Hereditary gingival fibromatosis in a family with the Zimmermann-Laband syndrome. J Oral Pathol Med 20: 457-459, 1991.
26. Zackin SJ, Weisberger D. Hereditary gingival fibromatosis: report of a family. J Oral Pathol 14: 828-836, 1961.