



Familial Hereditary Gingival Fibromatosis: A Rare Case Report

Ailesel Herediter Gingival Fibromatozis: Nadir Bir Olgu Sunumu

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Abstract

Hereditary gingival fibromatosis is a rare genetic condition characterized by varying degrees of growth attached gingiva. It usually develops as an isolated disorder but can be one feature of a multi systemic syndrome. In severe cases resective surgery of the fibromatosis excess tissue is the treatment available however, recurrence is a common feature. In this case a 28-year-old healthy male is reported who presented a familial hereditary gingival fibromatosis, characterized with severe gingival overgrowth, involving the maxillary and mandibular arches.

Key Words: Hereditary gingival fibromatosis, gingival enlargement, gingivectomy

Özet

Herediter gingivofibromatozis çeşitli derecelerde diş etinin büyüme gösterdiği nadir görülen genetik bir olgudur. Genellikle tek başına bir rahatsızlık olarak görülebildiği gibi multisistemik rahatsızlıkların bir bulgusu olarak da görülebilmektedir. Şiddetli vakalarda tedavi seçeneği büyümüş dokuların rezektif cerrahi yöntemle uzaklaştırılması iken diş eti büyümeleri tekrar görülebilir. Bu vakada 28 yaşında sağlıklı bir hastada ailesel olarak görülen alt ve üst çenede şiddetli diş eti büyümeleri ile karakterize herediter gingivofibromatozis vakası sunulmuştur.

Anahtar Kelimeler: Herediter gingivofibromatozis, diş eti büyümesi, gingivektomi

Introduction

Gingival enlargement describes gingival connective tissue cells that widen and increase in size over time, becoming larger than usual. There are various reasons for gingival enlargement, such as leukemia, inflammation, medications, and genetic factors. The most common causes are the antihypertensive nifedipine, the antiepileptic phenytoin and the systemic immunosuppressive cyclosporine (1). Characterized by the spontaneous and progressive enlargement of gingival tissue, hereditary gingivofibromatosis (HGF) is a rare disorder (1/750000) marked by proliferating, fibrous overgrowth of the gingival tissue, and is also known as hereditary gingival hyperplasia, gingival hypertrophy, elephantiasis gingiva, and familial gingival fibromatosis (1,2). Although recessive genetically inherited cases have been reported, HGF is thought to be autosomal dominant in generally. Recent studies suggest that 2 genetically distinct loci are responsible for autosomal-dominant hereditary gingival fibromatosis. The incidence of HGF is equal between the sexes (3). Although it presents alone, it may be accompanied by multi-systemic syndromes, such as Zimmermann-Laband, Murray-Puretic-Drescher, Rutherford, Cowden, Cross, Ramon, Jones, and Prune-belly syndromes. The most common characteristic findings of HGF are hypertrichosis, mental retardation, and epilepsy (4). Enlarging gingiva are reported clinically as having a normal appearance, firm consistency, and nodular form, and increased gingival

stippling can be seen. Gingival enlargement can be localized or generalized, and may affect both arches. Gum tissues in the tuber region of the maxilla and the molar region of the mandible are the most affected (3). The most common effects of gingival overgrowth are diastemata between the teeth, delays in tooth eruption, and malposition. The entire tooth is covered with enlarging gingiva in severe cases, which leads to aesthetic and functional problems. The alveolar bone is usually unaffected by overgrowth of the gums. Most cases of HGF do not require treatment; however, if it leads to functional difficulties in swallowing, speech, or aesthetic problems, surgical excision may be considered (5). This paper describes the clinical, familial findings and oral management of male HGF patient.

Case Report

A 28-year-old medically healthy man visited the periodontology clinic at Inonu University Faculty of Dentistry with complaints of gingival enlargement and difficulty in chewing and swallowing. He expressed that his gum enlargement had occurred over the past 5-6 years. While asymmetry was not detected during the patient's extra-oral examination, gingival overgrowth of both the mandible and maxilla were detected during his intra-oral examination. The gingival overgrowth was concentrated in the anterior region of the mandible and in the anterior and tuber regions of the maxilla. It was observed that the palatal mucosa of the maxillary

posterior palatal region had grown enough to affect the patient's chewing and swallowing. Teeth crowns were covered by gingival overgrowth of the posterior palate. There were diastema between the upper anterior teeth. The gingiva were pink in color, firm, and dense in consistency. There was no acute inflammatory response (Figure 1).



Figure 1. Intraoral view of the patient before surgery, showing severe gingival overgrowth.

The patient had no history of any endocrine disorder, hypertrichosis, mental retardation, blood pressure, or epilepsy controlled by medication. Assessment of the patient's family history showed that gingival overgrowth was present in the patient's sisters (Figure 2, 3) and also elder sister underwent a surgical treatment, other sister underwent both orthodontic and surgical treatment in other centers.



Figure 2. Intraoral view of the patient's elder sister.

Further treatment was rejected by these patients after the initial therapy, so these patients are followed up by us. Scaling was performed and the motivations for oral hygiene were explained to the patient in the first session.



Figure 3. Intraoral view of the patient's sister.

The patient's gingival overgrowth was slightly reduced after 4 weeks of oral care. Surgical treatments were performed four weeks apart in three separate sessions with the patient's approval. The surgical interventions were carried out under local anesthesia (Ultracain DS forte 2 mL, Sanofi Aventis / France, Articaine HCl: 40 mg/ mL Epinefrin HCl: 0,012 mg / mL). Classical hyperplastic tissue excision was performed for growth on the maxilla and mandible. External gingivectomy and gingivoplasty were performed for gum overgrowth of both jaws. Postoperative periodontal dressing was applied. An analgesic prescribed (*flurbiprofen*) twice a day for one week and 0,2 % chlorhexidine gluconate rinse prescribed twice a day for two weeks. Connective tissue proliferation was observed in the histopathological examination, which showed active fibroblasts beneath the ordered surface epithelium, but did not show any inflammatory cells. These results were compatible with a diagnosis of HGF.³ The patient was observed to be improving both aesthetically and functionally when he was examined after 12 weeks from operations (Figure 4).



Figure 4. Intraoral view of the patient 12 weeks after surgery. Aesthetic and functional requirements improved in the short term after surgical treatment.

Discussion

Gingival overgrowth can be caused by inflammation, leukemic infiltration, and medications such as phenytoin, calcium-channel blockers, and cyclosporine (4). HGF may present as the sole disorder, or it may be seen as an oral finding of another systemic disease (2,6,7). In this case report, no other symptom to prove that HGF was a symptom of another syndrome was observed. In this case, the diagnosis was based on clinical findings, family history, and histopathological results (3,4). HGF may present as an oral finding of many multi-systemic diseases, including Laband syndrome, Rutherford syndrome, and Cross syndrome. The most common comorbidities of HGF are hypertrichosis, epilepsy, and mental retardation (3). Gingival growth usually begins with the eruption of the permanent teeth, and is rarely seen with the eruption of the deciduous teeth. It can also cause delayed tooth eruption, orthodontic problems, and speech and chewing difficulties (5). In some cases HGF can be seen with amelogenesis imperfecta (8). Some hypocalcified teeth can be noticed at patient's elder sister. In this case, the patient said that his gingival enlargement started 5–6 years prior. The patient did not have any complaints regarding gingival overgrowth until it began to affect his chewing and swallowing functions. Gingival enlargement also leads to diastemata in patients with HGF (1). Typical clinical findings of HGF are compatible with diastemata presenting in the anterior maxillary region. HGF can be inherited as a dominant gene; however, it may also be inherited recessively (1,2). Genetic studies indicate that HGF has a genetically heterogeneous character (2,9). The patient's parents were normal and had no history of an endocrine disorder or medication use that could lead to gingival overgrowth in his family, and the patient and his sisters suggested that it was a recessive genetic transmission (10). Recent studies indicate that a mutation in the SOS-1 (son of sevenless homolog 1) gene is important in the etiology of HGF (9). SOS-1 is found in many tissues and cells, including the gingiva. It has been located in the basal and spinosum layers of the gingival epithelium and in the fibroblasts and vessels of gingival connective tissue (2). Casavecchia et al. could not find a genetic factor related to chromosomes 2p22 and 5q13q22 in their study of 3 individuals with HGF and aggressive periodontitis from the same family. They also reported that another gene may be important in the etiology of HGF (9). The histopathologic findings in this case showed increased connective tissue in which active fibroblasts were seen beneath the ordered surface of the epithelium, confirming the diagnosis of HGF. In the literature, there is no complete consensus on the cellular and molecular mechanisms of HGF. While some researchers have shown increased fibroblast proliferation in patients with HGF, others have suggested that the fibroblast proliferation is slower than normal (3). The histopathological diagnosis of this case is compatible with a greater amount of fibroblast proliferation than usual. Tipton et al. showed that the c-Myc gene can be effective in patients with HGF and increased fibroblast

proliferation (11). c-Myc is a nuclear proto-oncogene that plays a key role in the differentiation and proliferation of many cell types. The excessive presence of c-Myc can cause uncontrolled cell growth. A relationship has been demonstrated between increased fibroblast proliferation and the presence of increased and abnormal c-Myc in the skin of patients with systemic sclerosis and fibrotic scleroderma (2). Fatty acids are reported to play a role as anabolic enzymes in human malignancy. Almedia et al. demonstrated that higher fatty acid synthesis and androgen receptors enhanced HGF fibroblast proliferation; when fatty acid synthesis was blocked, a decrease was observed in both HGF fibroblast proliferation and normal gingival fibroblast proliferation (12). In recent studies, it has been reported that MMP1(matrix metalloproteinase), MMP2, TIMP1(tissue inhibitor metalloproteinase, the biological suppressor of MMP), and TIMP2 did not change the biological or cellular mechanisms of HGF. On the other hand, TGF- β (tissue growth factor) is seen twice as often as normal in fibroblasts with HGF (9). Drug-induced gingival hyperplasia occurs as a result of the excessive synthesis and accumulation of extracellular matrix components, which is stimulated by gingival fibroblast and cytokine growth factors (9). Increased levels of TGF- β produced by HGF fibroblasts contribute to an increase in the amount of type-1 collagen and fibronectin. An increasing number of molecules in the extracellular matrix can contribute to gum overgrowth, which is clinically expressed as HGF (2). However, the cellular mechanisms of HGF fibroblasts have still not been clarified (9). HGF is a disease that can cause serious problems, including delayed eruption of permanent teeth, retention of deciduous teeth, difficulties in speech and chewing, dental malposition, aesthetic disadvantages, and psychological problems for patients and their families (4,5). In this case, the patient's complaint was difficulty in swallowing and chewing. If the growth is not severe, scaling and proper hygiene can be enough to maintain oral health. In this case, slight decreases occurred in gum overgrowth in the anterior region as a result of the patient's care oral hygiene; however, if the growth is excessive and widespread, surgery is required. In all studies of patients with HGF, the recurrence rate after surgery is controversial. The recurrence rate is lower in treatments after the eruption of permanent teeth (1,5). Even if HGF treatment is usually performed during the period of permanent dentition, it can be done at an earlier stage if it is thought that the disease will lead to severe loss of function or psychological problems. A second surgical operation may be required, according to the degree of recurrence (2). Surgical treatment can be performed with external and internal bevel gingivectomy, gingivoplasty, an apically positioned flap, electrocautery, and carbon dioxide laser treatments. General anesthesia is the preferred method for severe and extreme cases. Chlorhexidine mouthwash is recommended postoperatively for 2 weeks. Recurrence is more common in children than in adults (1,4). In this case,

because of excessive hyperplastic tissues and the absence of periodontal tissue loss, conventional external gingivectomy and gingivoplasty were performed for growths in both jaw areas under local anesthesia.

Conclusion

In the present case, the clinical features and surgical treatment of familial, nonsyndromic, genetically inherited HGF are presented. Even though there was recurrence potential, the patient's aesthetic requirements, chewing, and swallowing functions improved in the short term after surgical treatment. The genetic and cellular mechanisms of HGF need to be examined in more detail.

Acknowledgments: We have not a financial relationship with the organization that sponsored the research

Note: The information presented here was reported at the 42th Annual Scientific Meeting of the Turkish Association of Periodontology, November 08 to 10, 2012, Ankara / TURKIYE.

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