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Hereditary Gingival Fibromatosis – the current problem

Dziedziczna włókniakowatość dziąseł – problem wciąż aktualny

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ABSTRACT

Hereditary Gingival Fibromatosis (HGF) poses a complex interdisciplinary challenge, necessitating collaboration among genetics, dentistry, and pathology. Its genetic basis involves mutations in specific genes and disrupted cellular processes leading to excessive fibrous tissue growth in the gums. Clinical symptoms vary from facial/oral to oral symptoms, including a slow but continuous enlargement of the gingiva, which can eventually cover the teeth to varying extents. HGF require a thorough diagnosis and treatment. Diagnosis typically involves a combination of clinical evaluation and genetic testing, while management demands a comprehensive approach encompassing both non-surgical and surgical interventions. Given the risk of recurrence, diligent post-operative monitoring is essential. Through interdisciplinary teamwork, precise diagnosis, a proper dental treatment and ongoing care can be provided, ultimately enhancing the quality of life for individuals with HGF.

Keywords: Hereditary Gingival Fibromatosis, genetic disorders, periodontology.

STRESZCZENIE

Dziedziczna włókniakowatość dziąseł (HGF) stanowi złożone wyzwanie interdyscyplinarne, wymagające współpracy między specjalistami z zakresu genetyki, stomatologii i patomorfologii. Jej podłoże genetyczne polega na mutacjach w określonych genach i zakłóceniu procesów komórkowych prowadzących do nadmiernego rozrostu tkanki włóknistej dziąseł. Klinicznie w jamie ustnej objawia się wolnym, ale ciągłym powiększeniem dziąseł, które może ostatecznie w różnym stopniu pokryć zęby pacjenta. HGF wymaga przeprowadzenia dokładnej diagnostyki i wdrożenia specjalistycznego leczenia. Diagnoza zazwyczaj obejmuje połączenie oceny klinicznej i badań genetycznych, podczas gdy leczenie wymaga kompleksowego podejścia, obejmującego zarówno interwencje niechirurgiczne, jak i chirurgiczne. Ze względu na ryzyko nawrotu niezbędne jest stałe monitorowanie efektów leczenia. Dzięki interdyscyplinarnej pracy zespołowej można zapewnić precyzyjną diagnozę, właściwe leczenie stomatologiczne i stałą opiekę, co ostatecznie istotnie przyczyni się do poprawy jakości życia osób z HGF.

Słowa kluczowe: dziedziczna włókniakowatość dziąseł, choroby genetyczne, periodontologia.

Introduction

Hereditary Gingival Fibromatosis (HGF) is a rare genetic disorder characterized by an abnormal and progressive overgrowth of the gum tissue [1–3]. According to genotype, it has a prevalence of 1:350,000 and does not depend on gender [1]. This condition, while benign, can lead to significant oral and cosmetic challenges. It is commonly inherited in an autosomal dominant manner, meaning a single copy of the mutated gene can cause the condition [4].

Clinical features of HGF include a slow but continuous enlargement of the gingiva, which can eventually cover the teeth to varying extents [5–7]. This overgrowth often appears in childhood and can persist or exaggerate over time [1]. The enlarged gingival tissue is typically firm, fibrous, and non-painful [1, 5, 6, 8]. Although it is not harmful in itself, the excessive gum tissue can hinder normal oral activities such as eating, speaking, and oral hygiene maintenance [1, 5–9]. It can also cause dental problems like misalignment of the teeth [1]. In ad-

vanced cases, the condition may significantly impact appearance and lead to psychological distress [1].

HGF is an interdisciplinary challenge, as its complex nature demands collaboration among specialists in the field of genetics, dentistry, pathology, and psychology to understand its genetic basis, accurately diagnose, and develop effective treatment strategies, due to its multifaceted etiology and diverse clinical manifestations [1, 10].

This review aims to provide a thorough understanding of HGF, exploring its genetics, clinical features, diagnostic methods and treatment strategies.

Genetic basis and pathophysiology

The pathophysiology of HGF involves a complex interplay of genetic factors, cellular processes and tissue changes that lead to the characteristic fibrous overgrowth of the gingiva [4, 11, 12]. HGF can be inherited either through autosomal dominant or autosomal recessive patterns, where mutations in specific genes are implicated in its development [6, 13–15]. Studies have pinpointed loci on chromosomes 2, 5, 11, and 4 associated with non-syndromic HGF. Notably, mutations in genes such as SOS-1 on chromosome 2 and REST on chromosome 4 have been linked to the condition [6, 13–15]. The pathogenic variant of SOS-1 is related to increased fibroblast proliferation. The REST gene is a transcriptional repressor [6] during embryogenesis and neurogenesis and plays and important role in several cellular mechanisms [6].

Abnormalities in fibroblast function within gingival tissues are pivotal in HGF pathogenesis, with dysregulated collagen metabolism leading to excessive collagen production and fibrosis [16]. Furthermore, alterations in the expression of matrix metalloproteinases (MMPs) and tissue inhibitors of metalloproteinases (TIMPs) have been noted in individuals with HGF [13]. This dysregulation results in reduced degradation of extracellular matrix proteins, alongside altered MMP-1 and MMP-2 expression and impaired MMP and TIMP functions, all contributing to the fibrotic changes observed in the gingiva [12, 13]. Autocrine stimulation of transforming growth factor-beta 1 (TGF-β1) signaling pathways has also been implicated, exacerbating the fibrous overgrowth of the gingiva by further alteration in the expression of MMP-1 and MMP-2 [17]. Moreover, various mechanisms, including genetic defects affecting MMPs and TIMPs functions, can lead to collagen accumulation in gingival tissues, thus contributing to the observed fibrotic phenotype in HGF [6].

Clinical manifestations

Clinical Manifestations of HGF presents a wide range of clinical symptoms, involving both facial/oral and oral findings [5, 6, 8]. Among the facial/oral symptoms, individuals with HGF may encounter discomfort in the facial or oral region, alterations in facial profile leading to convexity and distortion of jaw structures, potentially causing issues with lip closure and lip positioning [1]. Additionally, facial muscles may appear tense or drawn, resulting in a distinctive "cupid bow" mouth shape [1]. Challenges related to chewing, speech articulation and swallowing are prevalent, compounded by difficulties in maintaining oral hygiene due to the characteristic dense and fibrotic nature of the gingiva [1, 7, 8].

Within the oral cavity, gingival overgrowth may manifest as nodular, pigmented, ulcerated or bleeding tissue, often accompanied by the formation of pseudopockets and deposits of calculus [1, 5, 6, 8]. This overgrowth can cover teeth partially or entirely, resulting in irregular spacing, crowding, protrusion, and misalignment of teeth, as well as delayed eruption or loss of primary or permanent teeth [1, 5, 6, 8, 18]. Malocclusion, open bite and/or cross bite and a narrow palate are frequent observed, impacting chewing function and the alignment of the teeth [1, 7–9]. Restricted tongue movement and limited oral space cause further difficulties in oral function [1, 7].

Indirectly associated clinical manifestations, though less directly related to the oral cavity, contribute to the complexity of HGF [1, 8, 9]. These encompass nasal deformities, excessive hair growth (hypertrichosis), skeletal anomalies and respiratory infections [1]. Despite their indirect association, these manifestations may ipse an impact on oral health and treatment outcomes [1, 7, 19]. HGF presents a multifaceted clinical profile and diverse array of symptoms affecting both the facial/oral region and the oral cavity itself [5, 7–9]. Understanding the nuances of these symptoms is pivotal for thorough diagnosis and management of individuals affected by HGF, requiring interdisciplinary collaboration for optimal treatment outcomes [1, 5, 7, 9].

Diagnosis

HGF diagnosis necessitates both clinical assessment and genetic testing [5, 6, 9]. Key clinical indicators used in diagnosing HGF involve generalized gingival enlargement characterized by a firm, dense, or fibrotic texture [5, 6].

It is crucial to differentiate HGF from drug-induced gingival hyperplasia, often associated with medications such as phenytoin, cyclosporine, and nifedipine [7, 9]. Though both conditions present with similar gingival overgrowth, drug-induced hyperplasia stems from pharmacological effects rather than genetic factors [7]. Thus, accurate differentiation between HGF and drug-induced hyperplasia is imperative for tailored management and treatment planning [5, 6].

Genetic analysis serves as a pivotal tool in confirming the diagnosis of HGF by identifying specific genetic mutations associated with the condition [4]. This testing aids in elucidating the mode of inheritance, whether autosomal dominant or recessive, and proves especially valuable in cases with atypical clinical presentations or when differentiation from similar conditions is necessary [1, 4, 9]. Furthermore, genetic testing facilitates genetic counseling, enables family screening, and informs personalized management strategies related to the genetic profile of individuals affected by HGF [1, 7, 8].

Management and treatment

In the comprehensive management of HGF, an interdisciplinary approach incorporating both non-surgical and surgical interventions is essential to address gingival overgrowth and optimize oral health outcomes [10].

Non-surgical approaches

Fundamental oral hygiene play a crucial role in managing HGF, aiming to reduce gingival inflammation and minimize the risk of recurrence [1, 7, 9]. Research underscores the significance of maintaining optimal oral hygiene through regular brushing with a soft-bristled toothbrush, meticulous flossing to remove interdental plaque and scheduling regular professional cleanings to control plaque accumulation [4, 10]. Effective plaque control is particularly essential among individuals with HGF, as it can exacerbate gingival overgrowth and predispose to periodontal complications [5, 8, 9]. Studies highlight that inadequate oral hygiene significantly accelerates the recurrence of gingival enlargement, emphasizing the indispensable nature of meticulous oral care in managing HGF [1, 7, 8].

Integral to HGF management is periodontal maintenance therapy, involving regular appointments with a dental professional for thorough supra- and subgingival scaling, root planing, and plaque control [1, 4, 7, 11, 18–20]. These interventions aim to mitigate gingival inflammation, promote periodontal health, and reduce the risk of recurrence post-surgical intervention [4, 5, 10, 20]. Topical medications, particularly corticosteroids like triamcinolone acetonide, serve as adjunctive therapies to manage gingival overgrowth by reducing inflammation and promoting tissue regression [1]. Administered under professional supervision, these medications contribute to an improvement in periodontal health and minimize gingival enlargement [1].

Orthodontic treatment plays a role in conjunction with non-surgical and surgical approaches to address malocclusion and optimize occlusal function in individuals with HGF [5, 8, 21]. By aligning teeth properly and enhancing overall dental esthetics, orthodontic treatment contributes to stabilizing gingival tissues and maintaining long-term periodontal health [1].

Surgical approaches

Surgical intervention is pivotal in cases of significant gingival overgrowth where non-surgical measures alone may be insufficient [5, 6]. Gingivectomy in a primary surgical procedure, involving precise excision of excess gingival tissue under local anesthesia to restore gingival contour and improve periodontal health [5]. Gingivoplasty complements gingivectomy by reshaping and refining gingival architecture to enhance esthetics and oral function [6]. This technique involves contouring and sculpting gingival tissues to create smoother margins and improve symmetry, with laser-assisted options offering precision and post-operative comfort [6].

Periodontal flap surgery addresses underlying periodontal issues accompanying gingival overgrowth, such as pocket formation and bone loss [5–8]. Therefore, by elevating a surgical flap to access periodontal structures for thorough debridement and root surface decontamination, this procedure aims to eliminate pockets, reduce inflammation, and promote healing of periodontal tissues [5].

Guided Tissue Regeneration (GTR) represents an advanced surgical approach for HGF-associated periodontal defects, utilizing barrier membranes to prevent epithelial downgrowth and facilitate periodontal tissue regeneration [22, 23]. This technique promotes soft tissue healing, supports long-term stability, and may be used alongside conventional periodontal flap surgery to optimize treatment outcomes [10, 22, 23].

Carbon dioxide laser therapy has emerged as a promising modality for managing gingival over-

growth in HGF, offering precise tissue ablation with minimal trauma and enhanced post-operative comfort [1, 5, 24]. Laser-assisted procedures, such as gingivectomy or periodontal therapy, allow for selective removal of excess gingival tissue, improved contouring and accelerated tissue healing [6, 8, 25].

Potential for recurrence and management

Recurrence of gingival overgrowth poses a significant challenge in the management of HGF, even following surgical intervention [1, 5, 10, 11]. Research indicates that the rate of recurrence after surgical treatment for HGF can be approximately 35% within 12 months, with less than 50% of patients remaining free from relapse after 3 years [1]. The risk of recurrence is higher in growing patients, such as children and teenagers, compared to adults [4, 10]. To effectively manage recurrence, close post-operative monitoring is required [10, 20]. Emphasizing good oral hygiene practices, regular follow-up dental appointments and potential adjunctive orthodontic treatment can reduce the risk of recurrence [1, 10, 20]. In case of recurrence, additional surgical procedures may be performed to address the overgrowth and restore oral health [5, 10].

Interdisciplinary perspectives

To comprehend and effective management of HGF, a multidisciplinary approach is imperative, engaging various fields such as genetics, dentistry, and pathology. Each discipline contributes distinct expertise crucial in addressing different facets of HGF [10].

Geneticists play a pivotal role in unraveling the intricate genetic mechanisms underpinning HGF [10]. They delve into inheritance patterns, gene mutations, and genetic determinants affecting HGF development [1, 4]. Through genetic analyses, they unveil specific gene mutations associated with HGF, furnishing invaluable insights into its hereditary nature and familial transmission [10]. This understanding not only aids in precise diagnosis but also informs genetic counseling and lays groundwork for potential targeted therapeutic interventions in the future [8].

Dentists, particularly pediatric dentists and periodontists, are frontline practitioners in diagnosing and managing HGF in clinical symptoms [1]. They posse expertise in recognizing the clinical features of HGF, conducting meticulous oral examinations and implement treatment plans including patient's individual requirements [10, 22]. Dentists perform surgical interventions like gingivectomy and gingivoplasty to address gingival overgrowth, restoring oral health and function [23]. Furthermore, they emphasize the significance of proper oral hygiene practices to reduce post-operative complications and prevent recurrence of gingival enlargement [7].

Pathologists contribute significantly in elucidating HGF by scrutinizing the histological attributes of affected gingival tissues [11, 21]. Through meticulous histopathological analysis, they discern the fibrous enlargement of gingiva, deposition of collagen and alterations in connective tissue architecture [11, 21]. This histopathological comprehension is important in diagnosis confirmation, distinguishing HGF from other gingival pathologies and guiding treatment strategies [10, 11, 21].

This multidisciplinary collaboration not only facilitates accurate diagnosis but also determines proper treatment approaches and long-term management strategies, ultimately enhancing the quality of life for individuals grappling with this rare genetic disorder [10, 26].

Conclusions

HGF is a genetic disorder that requires a a complex interdisciplinary diagnosis and treatment. A proper maintenance of the disease remains crucial for enhancing the quality of life for individuals diagnosed with the disease. Therefore, further research is required to develop the most effective therapeutic options.

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Conflict of interest statement

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