EJPD 2022 CLINICAL FOCUS

Periodontology Part 3: Hereditary Gingival Fibromatosis (HGF): from diagnosis to treatment in the paediatric age

E. Carli, L. Lardani, R. Fitzgibbon*, E. Fambrini, S. Bagattoni*

Department of Surgical Medical Molecular Pathology and Critical Area, Dental and Oral Surgery Clinic, Unit of Pediatric Dentistry, University of Pisa, Pisa, Italy
**Department of Biomedical and NeuroMotor Sciences (DiBiNeM), Unit of Dental Care for Special Needs Patients and Paediatric Dentistry, University of Bologna, Bologna, Italy*

e-mail: simone.bagattoni2@unibo.it

DOI: 10.23804/ejpd.2022.23.03.13

Abstract

Hereditary Gingival Fibromatosis (HGF) is a challenging condition that paediatric dentists may face during clinical practice. In the present article, etiopathology, diagnosis and treatment options are discussed offering a paediatric dentistry-oriented overview of HGF.

KEYWORDS Hereditary gingival fibromatosis; Gingival overgrowth; Fibroblastic proliferation; Genetic analysis.

Introduction

Gingival overgrowth is the enlargement of the attached gingiva due to an increased number of cells [Doufexi et al., 2005]. Gingival tissue diseases can be classified in two main aetiological categories: dental plaque-induced and non-dental plaque-induced [Chapple et al., 2018]. Non-dental plaque-induced gingivitis include genetic and developmental disorders forms, of which Hereditary Gingival Fibromatosis (HGF) is the most prevalent condition during childhood [Doufexi et al., 2005; Holmstrup et al., 2018; Bagattoni et al., 2022; Mummolo et al., 2022]. The aim of the present focus is to summarise the latest knowledge on HGF during childhood.

HGF: Inheritance and pathogenesis

HGF is a rare condition that can occur as an isolated disease, chromosomal abnormality, or as part of a number of syndromes [Chaurasia, 2014], and is the most common syndromic gingival hyperplasia in growing patients. Its aetiology is complex, involving both genetic factors and biochemical mechanisms. HGF penetrance is variable, it may appear as an autosomal dominant disease (in Rutherford or Laband syndromes); or more rarely, as an autosomal recessive tract (Murray-Puretic-Drescher, Cross or Ramon syndrome or lysosomial storage disease) [Coletta and Graner, 2006]. Hypertrichosis, intellectual disability or epilepsy are the most common associated features [Mangino et al., 2003; Poulopoulos et al., 2011]. A wide spectrum of clinical and genetic heterogeneity is described in literature [Takagi et al., 1991]. Members of the same family can exhibit different phenotypes as a result of a variable penetrance of HGF [Nofal et al., 2009].

Several biochemical mechanisms may cause collagen accumulation in HGF: reduced degradation in extracellular-matrix proteins, MMP-1 and MMP-2 lower expression and/or genetic defects impairing MMPs and TIMPs functions, and an altered collagen phagocytosis [Coletta et al., 1999]. Finally, genetic mutations localised on 2p21-p22 (HGF1) and 5q13-q22 (HGF2), of "Son of Sevenless" (SOS 1, SOS 2) and REST genes can cause HGF [Bayram et al. 2017; Strzelec et al. 2021].

HGF: Diagnosis and clinical features

HGF diagnosis is based on clinical presentation, patient's medical and family history, recurrency pattern and characteristic microscopic features. HGF is a rare disease, presenting a prevalence of 1:175,000 [Kather et al., 2008].

Clinically, HGF presents either as a generalised or a localised painless non-haemorrhagic gingival hyperplasia, pale pink attached gingiva of a firm and lobular consistency, in the absence of inflammatory signs (Fig. 1) [Ercoli et al., 2015]. It typically develops during the eruption of the permanent dentition. Few cases report an early detection in primary dentition and it is rare at birth [Doufexi et al., 2005; Coletta and Graner, 2006]. The gingival overgrowth causes dental crown partial or total coverage, affecting firstly frontal, then lateral and posterior sectors of the dental arches (Fig. 2–5). Its clinical expression is heterogeneous: it is detected upon front teeth interdentally and labially, with a higher prevalence on the maxillary arch, maxillary tuberosities and labial gingiva around lower molars [Ercoli et al., 2015]. Diagnosis is mainly clinical and may be confirmed by the histological analysis, that typically reports epithelium hyperplasia and, within the connective tissue, collagen accumulation in addition to fibroblast and blood vessel shortage. The main differential diagnosis is with drug-induced gingival hyperplasia, namely associated with phenytoin, cyclosporine and nifedipine intake [Doufexi et al. 2005]. The pathognomonic gingival tissue excess may provide new ecological niches for microorganisms, determining plaque accumulation and pseudo-pockets assessment [Lindhe, 2006; Gawron et al., 2016; Casavecchia et al., 2004]. The most common clinical effects in children are diastemas, prolonged retention of primary or impacted teeth, teeth mispositioning, delayed eruption, pseudo-pockets without attachment loss, prominent lips, open and cross bites, and labial incompetence. Moreover, halitosis and incipient periodontal disease are found. HGF patients may show difficulties in speech, chewing, swallowing, in addition to the negative relational life impact of the poor aesthetics [Coletta and Graner, 2006; Sfasciotti et al., 2017; Gawron et al., 2016; Henefer and Kay, 1967; Ferro et al., 2017; Millet et al., 2012; Giuca et al.,2020]. Labial incompetence together with open and/or cross bites due to HGF can cause difficulties in breathing, snoring and a higher risk for obstructive sleep apnea episodes [Giuca et al.,2021; Marchetti et al., 2020; Giuca et al., 2021].

HGF: treatment in the paediatric population

HGF treatment options in children include hyperplastic gingival tissue removal, usually through multiple surgical gingivectomies in association with gingivoplasty, mini-invasive periodontal surgery by apically repositioned flaps, electrocautery, and/or carbon dioxide laser. Treatment choice depends on HGF severity [Ramer et al., 1996; Howe and Palmer, 1991; Caprioglio et al., 2017; Olivi et al., 2017]. Critical treatment aspects are surgical timing as well as its recurrence. It has been hypothesized

FIG. 1 A child presenting HGF on the anterior teeth.

FIG. 2 Clinical records of a child with HGF. Front view of both dental arches.

FIG. 3 Clinical records of a child with HGF. Intra-oral view of partial crown covering of front teeth.

FIG. 4 Clinical records of a child with HGF. Detail of the severe crown covering of the lower molars.

FIG. 5 Detail of the partial crown covering of the upper and lower frontal teeth.

that the best treatment timing may be after completion of permanent dentition, due to a high recurrence risk in growing patients (children and teenagers) than in adults [Coletta and Graner, 2006; Fletcher, 1966; Takagi et al., 1991; Ramer et al., 1996]. A recent paper reports that after surgical treatment, the rate of gingival enlargement recurrence is around 35% within 12 months, while after 3 years from surgery less than 50% of operated patients result free from relapse [Boutiou et al., 2021]. On the other hand, the psychological and local benefits of early treatment, even if temporary and with a possible relapse risk, are fundamental to prevent long-lasting effects on the paediatric patient and to the permanent dentition. In addition, a correct oral hygiene regimen is fundamental to prevent recurrence, which has been demonstrated to appear faster in poor oral hygiene sites [Arduino et al., 2011; Bello et al., 2020; Berta et al., 2021].

Conclusions

HGF is a clinical condition that paediatric dentists may detect on growing patients during routine intraoral examinations. The complexity of HGF's aetiologic background must be known, requiring multidisciplinary evaluation of the child, with possible need for multi-specialists' referral, as the geneticist, to confirm the diagnostic suspicion of syndromic diseases. HGF treatment prognosis is sometimes unpredictable, therefore clinicians should consider the psychological and social discomfort of the patient, as well as the level of cooperation and the fact that a good oral hygiene is a key to prevent recurrence.

References

- Arduino PG, D'Aiuto F, Cavallito C, Carcieri P, Carbone M, Conrotto D, Defabianis P, Broccoletti R. Professional oral hygiene as a therapeutic option for pediatric patients with plasma cell gingivitis: preliminary results of a prospective case series. J Periodontol. 2011 Dec;82(12):1670-5. doi: 10.1902/jop.2011.100663. Epub 2011 May 12. PMID: 21563944
- Bayram Y, White JJ, Elcioglu N, Cho MT, Zadeh N, Gedikbasi A, et al. REST fnal-exon-truncating mutations cause hereditary gingival fibromatosis. Am J Hum Genet 2017;101(1):149–56.
- Bagattoni S, Lardani L, Ligori S, Fitzgibbon R, Carli E. Periodontology. Part 2: Localised Juvenile Spongiotic Gingival Hyperplasia: histopathological and clinical features. Eur J Paediatr Dent 2022 Jun;23(2): 163-165.
- Bello L, Romano F, Gaido C, Defabianis P The effect of an oral spray containing an aqueous extract of Triticum vulgare on dental plaque and gingival inflammation in schoolchildren: A randomized controlled trial Eur J Paediatr Dent 2020 June;21(2):110-114 ISSN (Online): 2035-648X
- Berta G, Romano F, Vallone R, Abbadessa G, Di Scipio F, Defabianis P An innovative strategy for oral biofilm control in early childhood based on a resveratrol-cyclodextrin nanotechnology approach. Materials 2021;14(14): 3801.
- Boutiou E, Ziogas IA, Giannis D, Doufexi AE. Hereditary gingival fibromatosis in children: a systematic review of the literature. Clin Oral Investig 2021; 25(6): 3599-3607.
- Caprioglio C, Olivi G, Genovese MD. Paediatric laser dentistry. Part 1: General introduction. Eur J Paediatr Dent 2017; 18(1): 80-82.
- Chapple ILC, Mealey BL, Van Dyke TE, et al. Periodontal health and gingival diseases and conditions on an intact and a reduced periodontium: Consensus report of workgroup 1 of the 2017 World Workshop on the Classification of Periodontal and Peri-Implant Diseases and Conditions. J Periodontol 2018; 89 Suppl 1: S74-S84.
- Chaurasia A. Hereditary gingival fibromatosis. Natl J Maxillofac Surg 2014;5(1):42-46.
- 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-beta 1 autocrine stimulation. J Periodontal Res 1999; 34(8): 457-463.
- Coletta RD, Graner E. Hereditary gingival fibromatosis: a systematic review. J Periodontol 2006; 77(5): 753-764.
- Doufexi A, Mina M, Ioannidou E. Gingival overgrowth in children: epidemiology, pathogenesis, and complications. A literature review. J Periodontol 2005; 76(1): 3-10.
- Ercoli C, Bartolino M, Montesani L, Docimo R. Gingival fibromatosis: a case report. Eur J Paediatr Dent 2015; 16(3): 233-235.
- Lindhe J. Clinical periodontology and implant dentistry 2006; 286-287.
- Ferro R, Pasini M, Fortini A, Arrighi A, Carli E, Giuca MR. Evaluation of maxillary and mandibular arch forms in an Italian adolescents sample with normocclusion. Eur J Paediatr Dent 2017; 18(3):193-198.
- Gawron K, Łazarz-Bartyzel K, Potempa J, Chomyszyn-Gajewska M. Gingival fibromatosis: clinical, molecular and therapeutic issues. Orphanet J Rare Dis 2016; 11:9.
- Casavecchia P, Uzel MI, Kantarci A, Hatice Hasturk H, Dibart S, Hart TC, et al. Hereditary gingival fibromatosis associated with generalized aggressive periodontitis: a case report. J Periodontol 2004; 75: 770–78.
- Giuca MR, Carli E, Lardani L, Pasini M, Miceli M, Fambrini E. Pediatric Obstructive Sleep Apnea Syndrome: Emerging evidence and treatment approach. ScientificWorldJournal 2021; 2021:5591251.
- Giuca MR, Pasini M, Drago S, Del Corso L, Vanni A, Carli E, Manni A Influence of Vertical Facial Growth Pattern On Herbst Appliance Effects In Prepubertal Patients: A Retrospective Controlled Study International Study of Dentistry 2020.
- Giuca MR, Lardani L, Ligori S, Carli E,Giuca G, Miceli M. Oral manifestations in paediatric patients with hepatobiliary diseases: A review Journal of Biological Regulators and Homeostatic Agents 2021;35(3):117–125.
- Henefer EP, Kay LA. Congenital idiopathic gingival fibromatosis in the deciduous dentition. Report of a case. Oral Surg Oral Med Oral Pathol 1967; 24(1): 65-70.
- Holmstrup P, Plemons J, Meyle J. Non-plaque-induced gingival diseases. J Clin Periodontol 2018; 45 Suppl 20: S28-S43.
- Kather J, Salgado MA, Salgado UF, Cortelli JR, Pallos D. Clinical and histomorphometric characteristics of three different families with hereditary gingival fibromatosis. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2008 Mar;105(3):348-52.
- Mangino M, Pizzuti A, Dallapiccola B, Bonfante A, Saccilotto D, Cucchiara E. Hereditary gingival fibromatosis (HGF) with hypertrichosis is unlinked to the HGF1 and HGF2 loci. Am J Med Genet A 2003; 116A(3): 312-314.
- Marchetti E, Petro E, Gaggioli F, Lardani L, Mancini L, Marzo G. The dentist's role in diagnosis and treatment of obstructive sleep apnea syndrome: a literature review. J Biol Regul Homeost Agents 2020; 34 (3 Suppl. 1).
- Millet C, Rodier P, Farges JC, Labert N, Duprez JP. Surgical and prosthetic treatment in an elderly patient affected by unilateral idiopathic gingival fibromatosis: a case report. Gerodontology 2012; 29:e 1185–89.
- Mummolo S, Cirillo E, Ciribè M, Manenti RJ, Galeotti A. Periodontology. Part 1: Gingivitis in adolescence. Review of the literature and case reports. Eur J Paediatr Dent 2022 Mar;23(1):79-82.
- Nofal A, Sanad M, Assaf M et al. Juvenile hyaline fibromatosis and infantile systemic hyalinosis: a unifying term and a proposed grading system. J Am Acad Dermatol 2009; 61: 695–700.
- Olivi G, Caprioglio C, Olivi M, Genovese MD. Paediatric laser dentistry. Part 4: Soft tissue laser applications. Eur J Paediatr Dent 2017; 18(4): 332-334.
- Poulopoulos A, Kittas D, Sarigelou A. Current concepts on gingival fibromatosis-related syndromes. J Investig Clin Dent 2011;2:156-161.
- Ramer M, Marrone J, Stahl B, Burakoff R. Hereditary gingival fibromatosis: identification, treatment, control. J Am Dent Assoc 1996; 127(4): 493-495.
- Sfasciotti GL, Di Carlo G, Marini R, Colaci R, Solidani M, Polimeni A. Surgical management of impacted primary teeth: report of two cases. Eur J Paediatr Dent 2017; 18(1):19-22.
- Strzelec K, Dziedzic A, Łazarz-Bartyzel K. et al. Clinics and genetic background of hereditary gingival fibromatosis. Orphanet J Rare Dis 2021;16:492 .
- Takagi M, Yamamoto H, Mega H, Hsieh KJ, Shioda S, Enomoto S. Heterogeneity in the gingival fibromatoses. Cancer 1991; 68(10): 2202-2212.