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內文：

Introduction

- Gingival fibromatosis(GF) is a rare, benign, slowly-growing fibrous overgrowth of the gingiva, with great genetic and clinical heterogeneity
- GF can be
  - Inherited as an isolated trait (idiopathic gingival fibromatosis)
  - Inherited as a component of a syndrome,
  - Induced by drugs(e.g., cyclosporin, nifedipine, phenytoin)
  - Caused by Inflammation, leukemia, and neurofibromatosis I (von Recklinghausen disease)
- Hereditary GF (HGF) was probably first reported by Cross in 1856
- The clinical and genetic expressions of HGF are highly heterogenous, especially if presented as a manifestation of a syndrome
- Usually, the isolated form is inherited in an autosomal-dominant manner
- It seems that HGF males and females are equally affected

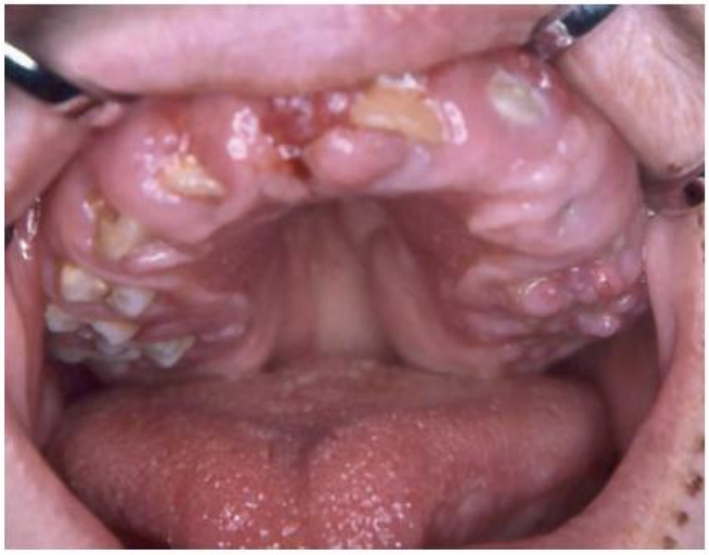

Figure 1. Gingival fibromatosis is presented as a gradually slow-growing overgrowth of the gingival tissue of the maxilla and mandible.

Clinical Features

- Enlarged gingivae might be erythematous or normal in color, non-hemorrhagic and asymptomatic
- Consistency feels firm and nodular on palpation
- The onset of overgrowth usually coincides with the eruption of permanent dentition
- Complications of GF
  - mainly functional and esthetic, such as diastemas, cross- and open bites
  - prolonged retention of primary dentition and delayed eruption of permanent dentition
  - abnormal occlusion,
  - prominent lips, open-lip posture
  - disabilities with eating and speech
  - Bacterial plaque accumulation/poor hygiene can induce periodontitis, bone resorption, and halitosis

Histological features

- collagen-fiber bundles running in all directions (usually types I and III)
- numerous fibroblasts, and mild chronic inflammatory cells
- The overlying epithelium is squamous, hyperplastic, acanthotic, and parakeratinized with thin, elongated rete ridges in the connective tissue
- Fibroblasts are flat or star shaped, with slender cytoplasmic processes, irregular nuclei, and a well-developed Golgi apparatus

- Myofibroblasts (exception of fibroblasts)

Pathogenesis

- HGF
  - Isolated trait is transmitted in an autosomal-dominant pattern
  - To the genetic mechanism to the isolated form, Son of sevenless-1 (SOS-1) is a bifunctional guanine nucleotide factor that regulates the activity of **Ras, Rac, and Rho** which are responsible for cell differentiation and proliferation
  - Syndromic form is transmitted in an autosomal-dominant or an autosomal-recessive manner, or as even an X-linked inheritance
  - Chromosomes 2, 4, and 5 seem to include the most important and known genetic loci, including 2p21-p22, 2p13-p16, 5q13-q22, 4q21, and 4q that enable **mutations, duplications, deletions**
  - The specific mutation is localized In three genetic loci: two maps to **chromosome 2** (GINGF1 2P21-22 and GINFG3 2p22.3-p23.3), which do not overlap, and one map to **chromosome 5** (GINGF2 5q13-q22)
- The relationship between sex hormones, gingival overgrowth, and fibroblast proliferation is obvious
  - **C-myc proto-oncogene** expression has been demonstrated to specifically induce the increased proliferation of HGF fibroblasts
  - **testosterone** induces the production of interleukin-6 by HGF fibroblasts
- The accumulation of collagen and fibronectin in the extracellular matrix (ECM) is caused by the lack of balance between metalloproteinases and their inhibitors
- Decreased degradation of ECM due to a genetic defect.
- Finally, impaired collagen phagocytosis was proposed as a possible mechanism of fibrosis

Syndromes

- GF is most common in younger patients
- Both autosomal-dominant and autosomal-recessive forms of this disorder have been described in GH related syndromes

Zimmermann–Laband syndrome[27–29]	–	135500	GF–hypertrophy, absence/dysplasia of the terminal phalanxes or nails of the hands or feet and thick lips, bulbous soft nose, thick floppy ears, mental retardation, hepatosplenomegaly, hypertrichosis, hyperextensibility of the joints, ocular symptoms
Ramon syndrome[6,30]	AR	266270	GF, cherubism, seizures, mental deficiency, hypertrichosis, stunted growth, juvenile rheumatoid arthritis
Congenital generalized hypertrichosis[6]	X-linked AD/AR	307150	Hypertrichosis Affected females have asymmetric, patchy hirsutism

Rutherford syndrome–gingival hypertrophy with corneal dystrophy[6,16]	AD	180900	Gingival hypertrophy, corneal opacity, mental retardation, failure of tooth eruption, aggressive behavior
Cross syndrome[9,16]	AR	257800	Hypopigmenation/silver grey hair color, microphthalmia with cloudy corneas, mental retardation/spasticity, athetoid movements/ growth retardation

- The gingival enlargement
  - usually begins at the time of eruption of the permanent dentition
  - but can develop with the eruption of the primary dentition.
  - It is rarely present at birth.
- In a case report, HGF, generalized hypertrichosis, mental retardation,and epilepsy are considered to resemble to Zimmermann–Laband, Ramon, and Cantu syndromes
- The coexistence of gingival hypertrophy, hypertrichosis, mental retardation, and brachymetacarpia in two sisters is another example
- The coexistence of GF and mental retardation does not comprise a distinct syndrome, but provides direct evidence of genetic heterogeneity for HGF

Differential diagnosis

- The diagnosis is based on the patient's medical and family history, the clinical presentation, the pattern of recurrence, and the characteristic microscopic features of the histology samples
- Elements from the medical history indicate or exclude the implication of drugs responsible for GF (antiseizure drugs, antihypertensives, immunosuppressives)
- Laboratory and clinical examinations and microscopic findings indicate or eliminate gingival enlargement as part of leukemia or the presence of an acute or chronic dento-alveolar abscess.
- The detection of specific mutations, including duplications, deletions, and/or other anomalies of chromosomes
- The characteristics most often associated with HGF are hypertrichosis, mental retardation, and epilepsy

Treatment

- The treatment of HGF patients is conservative
- Surgical excision of the hyperplastic tissue to restore the gingival contours
  - external or internal bevel gingivectomy in association with gingivoplasty,
  - apically-positioned flap, electrosurgery, and
  - carbon dioxide laser
- The best time is when all of the permanent dentition has erupted, because the risk

of recurrence is greater before eruption

- delay in the surgical treatment might cause significant consequences for the patient
  - primary dentition retention
  - permanent teeth delay in the eruption
  - difficulties in mastication and
  - phonation
  - malpositioning of teeth
  - aesthetic effects
  - psychological problems
- Conservative treatment that consists of quadrant by-quadrant **internal bevel gingivectomy** in association with **gingivoplasty**, followed by 0.12% chlorhexidine oral rinse twice a day for 2 weeks after each surgery
- Recurrence is most often seen in **children and teenagers**, rather than adults
- Normally recurrence is minimal or delayed if good oral hygiene is achieved by a combination of monthly examinations with professional cleaning and oral hygiene instructions
- The advantages of CO_2 consist of limitations in bleeding, pain, and treatment duration, as well as allowing treatment of all quadrants in one visit with minimal discomfort, which is an important consideration in children's therapy.
- The suppression attempt of TGF-β1 could become a future treatment aim to inhibit myofibroblasts activity
- γ-interferon might be clinically effective in attenuating excessive accumulation of the ECM produced by myofibroblasts

題號	題目
1	下列哪一種症候群與 Gingival Fibromatosis 較無關? (A)Zimmermann–Laband syndrome (B) Ramon syndrome (B)Rutherford syndrome (D) Eagle syndrome
答案 (D)	出處：Oral and Maxillofacial Pathology, 3rd ed, p.166
題號	題目
2	下列何者不是 Gingival Fibromatosis 的病理組織特徵? (A) Densely-arranged collagen-fiber (B) Numerous fibroblasts (C) Parakeratinized epithelium (D)Otrhokeratinized epithelium
答案 (D)	出處： Oral and Maxillofacial Pathology, 3rd ed, p.168