DISPLACEMENT OF MAXILLARY LATERAL INCISOR CAUSED BY IDIOPATHIC GINGIVAL FIBROMATOSIS

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Abstract

Idiopathic gingival fibromatosisrarely occurs, but frequently recurred after surgical removal. It usually occurs in generalized symmetrical pattern but sometimes in localized unilateral pattern. The localized pattern usually affects the maxillary molar and tuberosity area. This disease usually causes tooth migration, malocclusion, and problems in eating, speech, and esthetics. A boy showed dense gingival fibromatosis localized at primary maxillary right lateral incisor area at the age of 5 years, and his maxillary right lateral incisor become severely displaced at the age of 9 years. He had no medical and hereditary factors relevant to the gingival fibromatosis. However, the dense fibrous tissue was dominant in his labial gingiva of maxillary right incisors. In order to realign the displaced incisors by orthodontic treatment, the dense fibrous tissue covered the defect space between the central incisor and the displaced lateral incisor was surgically removed. The removed specimen was examined by simple immunohistochemical(IHC) array method. IHC array showed increased expression of CTGF, HSP-70, MMP-1, PCNA, CMG2, and TNF-α in keratinocytes, fibroblasts, endothelial cells, and macrophages of gingival fibromatosis tissue. Therefore, it was suggested that the gingival fibromatosis be caused by the concomitant overexpression of CTGF, HSP-70, MMP-1, PCNA, CMG2, and TNF-α,and resulted in the fibroepithelial proliferation and the inflammatory reaction of gingival tissue.

Key words: Gingival overgrowth, Idiopathic gingival fibromatosis, Tooth displacement, Immunohistochemical array method

Ⅰ. Introduction

Gingival fibromatosis is characterized by localized or generalized fibrous enlargement of the gingivae, usually around permanent teeth. This disease causes aesthetic-changes and clinical symptoms such aspain, speech disturbances, abnormal toothmovement, dental occlusion problems,enhanced risk of caries and periodontaldisorders[1)]. Gingival fibromatosis isassociated with multiple factors includinginflammation, drug uses[2-4)], neoplasia, hormonal disturbancesand hereditary factors. However,its pathogenesisremains unknownin some idiopathic cases[1,5)].

Gingival tissue enlargement usually begins withthe eruption of the permanent dentition, although itmay also develop with the eruption of primary teethbut it is rarely present at birth. Enlargement seemsto progress suddenly during the eruption of both primaryand permanent teeth, and decrease upon completionof eruption[6)].

The gingival tissues are usually pink butnonhemorrhagic, and have a firm and fibroticconsistency[7)]. Histopathologically, the bulbous increasedconnective tissue is relatively avascular and has densely arranged collagen fiber bundles, numerous fibroblastsand mild chronic inflammatory cells. The overlyingepithelium is thickened and acanthotic withelongated rete ridges[8)]. In

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general, the histological features are relatively nonspecific, and therefore, the definitediagnosis of gingival fibromatosis is mainly basedon family, medical and dental history, and on clinicalfindings.

We report here an unusual case of nonsyndromic,idiopathic gingival fibromatosis associated with displaced maxillary lateral incisor. We have discussed aboutthe clinical findings, histopathologicevaluation, andtreatment procedures.

Ⅱ. Case report

A 5-year-old boy visited the Department of Pediatric Dentistry, Gangneung-Wonju National University Dental Hospital, due to the slight gingival bulging in the maxillary right lateral incisor area. During the follow-up period for 3 years, gingival bulging was slightly increased. In gross and radiological observation the maxillary right lateral incisor was ectopically erupted in maxillary right canine area (Fig. 1). The gingival tissue was firm with tiny round eruptions, and was also pale, but non-painful and non-hemorrhagic. He did not complain of any other medical problem nor familial disease history.

The enlarged gingival lesion was treated by surgical removal of gingival excess (Fig. 2). The removed specimenwas immediatelyfixed in 10% buffered formaldehyde solution andprocessed for histopathologicmethod (Fig. 3). Briefly, the specimen wasembedded in paraffin wax. Multiple5-㎛m serial sections were prepared, stained with hematoxylinand eosin, and viewed under lightmicroscopeat 40×, 100× and 400× magnification.The microscopic evaluationrevealed a moderate hyperplasia, hyperkeratosis, and severe elongation of the rete peg in the epithelial layer, and also the marked increase and thickening of the collagenous bundles in the connective tissue stroma with a marked infiltration of chronic inflammatorycells.

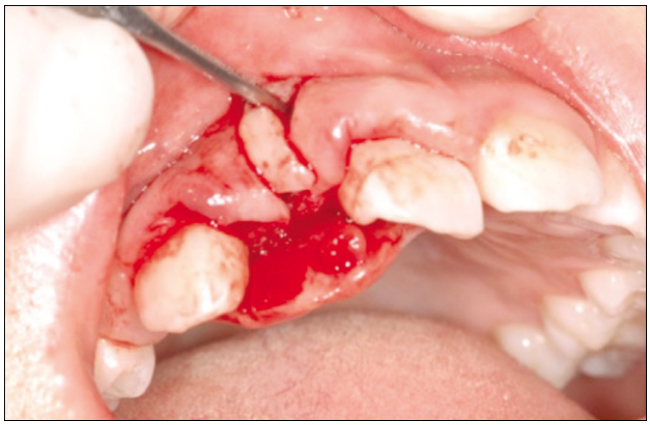

Fig. 2. Enlarged gingival lesion was removed using flap surgery.

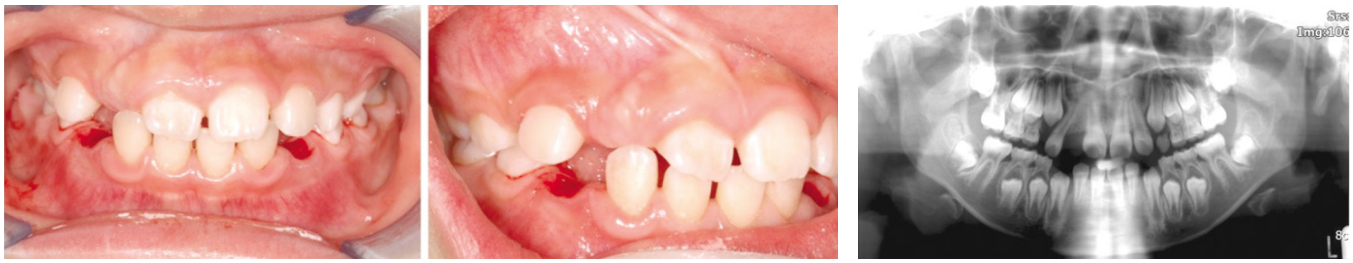

Fig. 1. Intraoral view and panoramic view at the age of 9 years. The maxillary right lateral incisor was ectopically erupted in maxillary right canine area.

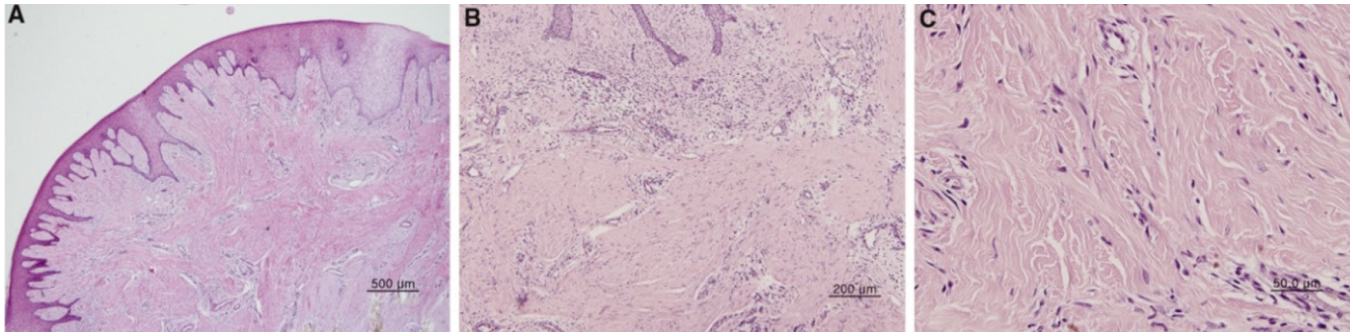

Fig. 3. Histopathologic examination. A: 40×, B: 100×, andC: 400×magnifications.

Immunohistochemicalstainings of CTGF (connective tissue growth factor), HSP-70 (heat shock protein-70), MMP1 (matrix metalloproteinase-1), PCNA (proliferating cell nuclear antigen), CMG2 (capillary morphogenetic protein-2), and TNF-α (Tumor necrosis factor-α) were analyzed by immunohistochemical (IHC) array method previously described[9] (Fig. 4). IHC array showed increased expression of CTGF, HSP-70, MMP-1, PCNA, CMG2, and TNF-α in keratinocytes, fibroblasts, endothelial cells, and macrophages of gingival fibromatosis

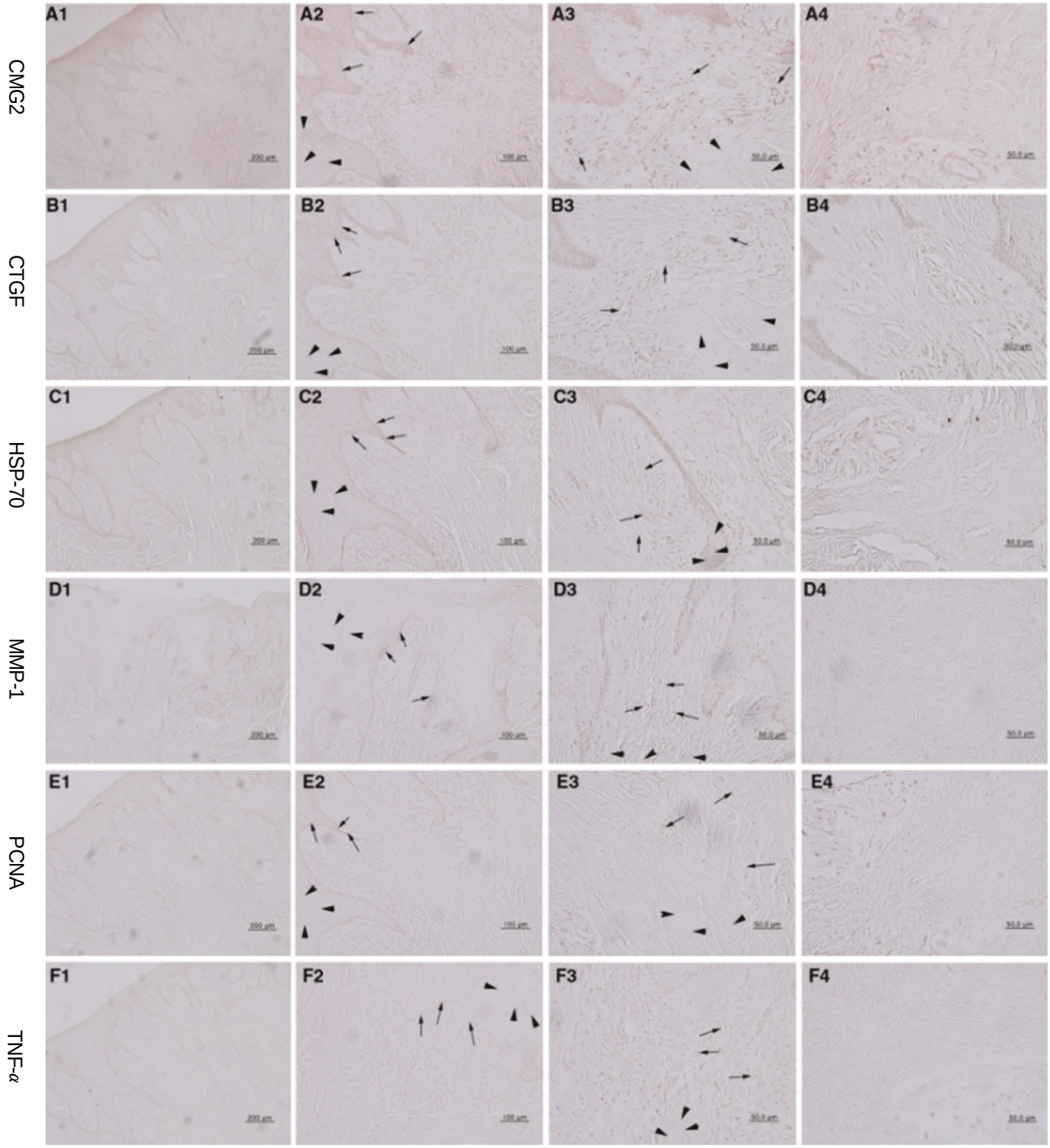

Fig. 4. Immunohistochemical(IHC) array method. The immunostains of CMG2, CTGF, HSP-70, MMP-1, PCNA, and TNF-α were done to illustrate the positive reactions in the gingival epithelium and fibrosed connective tissue of the fibromatosis lesion.(arrow: gingival epithelium, arrow head: connective tissue)

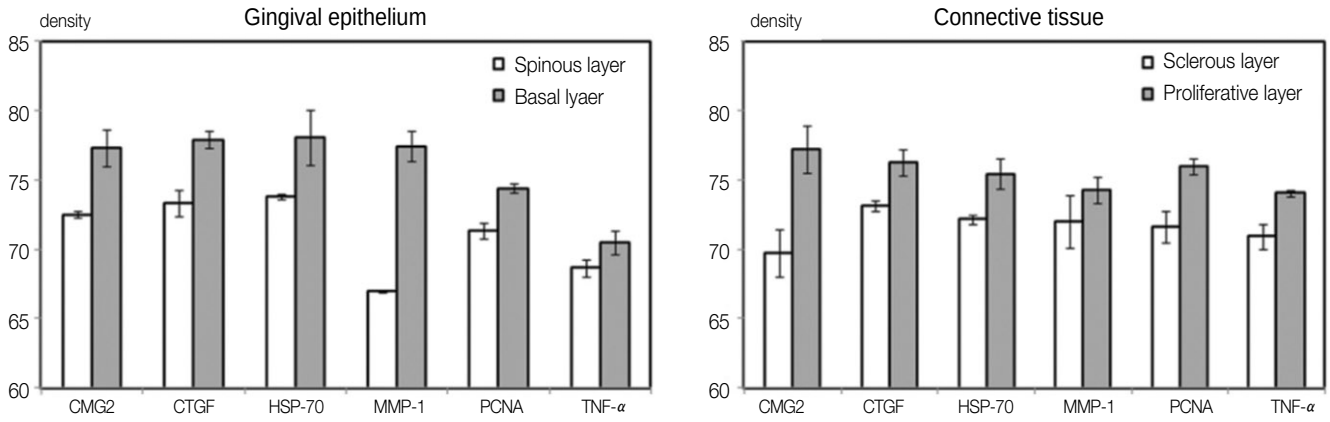

Fig. 5. The statical analysis of the IHC array examined in the study. The positive reaction of each immunostain was detected in the similar cell types and same pathological lesions.

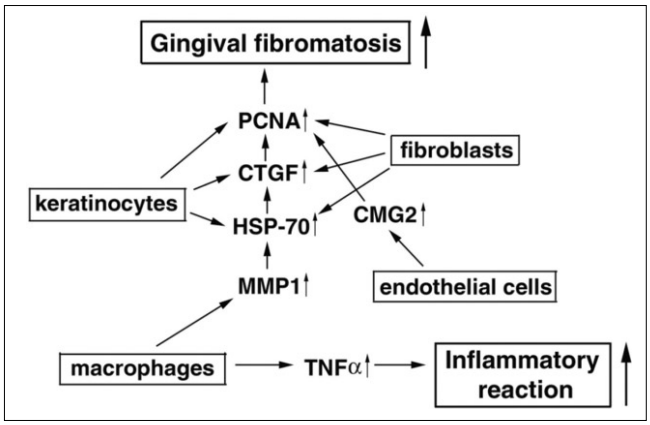

Fig. 6. Simplified genetic signaling pathways in the present case of gingival fibromatosis by immunohistochemical array method. The main cascade pathway of MMP1/HSP-70/CTGF/PCNA was involved with inflammatory reaction, de novo angiogenesis, and proliferation of keratinocytes and fibroblasts.

tissue (Fig. 5). Therefore, it was suggested that the gingival fibromatosis be caused by the concomitant overexpression of CTGF, HSP-70, MMP1, PCNA, CMG2, and TNF-α, resulted in fibroepithelial proliferation and inflammatory reaction (Fig. 6). In the simplified genetic signaling pathway based on the statistical analysis of IHC array the cascade pathways of MMP-1 / HSP-70 / CTGF / PCNA was activated by the inflammatory reaction and *de nove* angiogenesis, which was also mediated by TNF-α and CMG2, espectively. Resultantly the fibroblasts in the connective tissue as well as the keratinocytes in the gingival epithelium were simultaneously proliferated continuously.

Byhistopathologic and clinical findings, he was diagnosed as idiopathic gingival fibromatosis. After an uneventful follow-up period for 6 months, the orthodontic treatment started for the reposition of maxillary right lateral incisor. Becausethe recurrence of gingival fibromatosis cannot be predicted, the prophylactic periodontal examination should be recommended whenever the teeth were scaled and polishedat every orthodontic visit. Even after the orthodontic treatment, a kind of permanent fixed retention was applied to prevent any recurrence.

Ⅲ. Discussion

Idiopathic gingival fibromatosis is a rare condition characterized by a generalized enlargement of the gingiva. This condition is usually asymptomatic, thereby, considered as an isolated disorder[10]. The idiopathic gingival fibromatosis usually occurs in generalized symmetrical pattern but sometimes in localized unilateral pattern. The localized gingivalfibromatosis usually affects the maxillary molar and tuberosity area, particularly on the palatal surface. When there is severe involvement, teeth are almost completely covered and delayed eruption. And displacements of teeth can occur[11].The present was belong to the localized idiopathic gingival fibromatosisformed in the maxillary anterior area, which showed a unusual location for the idiopathic gingival fibromatosis.

The biochemical mechanism involved in gingival fibromatosisetiopathology is still remained to be elucidated.

However, the IHC array analysis applied on the present idiopathic gingival fibromatosis disclosed the potential genetic signaling pathways involving the MMP-1 / HSP-70 / CTGF / PCNA relevant to the chronic inflammatory reaction and de nove angiogenesis of the fibrous stroma. Periodontal pathogens stimulate release of TNF-α from gingival macrophages[12]. Various studies have demonstrated that TNF-α increases collagen accumulation and proliferation in intestinal myofibroblasts[13,14]. CTGF levels are related to thedegree of fibrosis, suggesting that common pathwaysexist between drug-induced and non-drug-induced gingivalfibrosis.A novel finding is that CTGF is expressedboth in the connective tissue stroma and in gingivalepithelial cells in vivo in fibrotic tissues, but not in normaltissues[15]. MMPs are a family of Zn-containing proteases that degradeECM proteins. The balance between ECM synthesis and itsdegradation by MMPs, regulatesECM remodelling. Its disturbance may lead to overgrowth[16,17]. PCNA is a 36-kDaacidic nonhistone nuclear protein that bears an importantfunction in DNA synthesis[18,19]. Its cell concentrationis directly correlated with the proliferative state of the cell,increasing through G1, peaking at the G1/S phase interface,decreasing through G2, and reaching low levels in Mphaseand interphase[19-21]. PCNA expression, therefore,is believed to be a good indicator of cell proliferation. And CMG2, which is mutated in juvenile hyaline fibromatosis,also involves gingival overgrowth[22]. These molecular factors recruited in this study may indicate the harmonious orchestration of the gingival fibromatosis to proliferate and accumulate the involved cells and stromal matrix.

Gingival fibromatosis is a disease that can be controlledwith varying degrees of success[23].Whengingival enlargement is minimal, debridement of thetooth surfaces and good oral hygiene may be sufficientto control the disorder. However, in severecases like this one, surgical excision may be necessary[24]. Many techniques have been used for the excisionof the enlarged gingival tissues, including: an externalor internal bevel gingivectomy[3,25]; anapically positioned flap[23]; elecrocautery[26]; anda carbon dioxide laser[5]. In the present case,an internal gingivectomy was attempted for minimizing postoperative pain and bleeding.

There is no consensus among authors regardingthe timing for surgery[3]. Some clinicians havesuggested that the best time to perform surgery iswhen all the permanent teeth have erupted[24].In the present case, the enlarged gingival tissueswere excised prior to the eruption of the permanentteeth because of the compromised aesthetics and inorder to facilitate eruption. Recurrence of the gingival enlargement is commonover varying periods[24,25], and is most oftenseen in children and adolescents rather than olderpatients[27]. However, whether and when it willoccur is not predictable[24]. Gregory[28] suggests aesthetic and psychological satisfaction of children is more important than a recurrence. The local and psychological benefits, even temporary, must not be underestimated and may outweigh the probability of recurrences[8]. In this case, surgical procedure and orthodontic treatment should not be delayed, because the boy has showed several significant problems, such as esthetic problem, malpositioning of teeth and obstructing the eruption of permanent teeth. The role of the pediatric and the periodontist dentist in monitoring gingival health and controlling gingival inflammation is very important.

Ⅳ. Summary

The present case showed the localized idiopathic gingival fibromatosisformed in the maxillary anterior area, which showed an unusual location for the idiopathic gingival fibromatosis. The enlarged gingival lesion was treated by surgical removal of gingival excess, and the orthodontic treatment was also performedfor the reposition of maxillary right lateral incisor. Bythe IHC array method, it was suggested that the gingival fibromatosis be caused by the concomitant overexpression of CTGF, HSP-70, MMP1, PCNA, CMG2, and TNF-α, and finally resulted in fibroepithelial proliferation and inflammatory reaction. After treatment, regular recalls are necessary to evaluate his oral hygiene, and the stability of the orthodontic and periodontal treatment.

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국문초록

특발성 치은 섬유종증에 의한 상악 측절치의 변위

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특발성 치은 섬유종증은 드물게 나타나는 질환으로 외과적 제거 후에도 쉽게 재발될 수 있다. 이 질환은 보통 전반적인 양상으로 양측성으로 나타나고, 때때로 국소적인 양상으로 편측성으로 나타나기도 하며, 국소적인 양상일 경우 보통 상악구치부나상악 결절 부위에 나타난다. 이 질환으로 인해 치아 변위, 부정 교합, 저작, 발음, 심미적인 문제 등이 발생할 수 있다.

5세 남아가 상악 우측 유측절치 부위의 치은 비대를 주소로 내원하였고, 9세경에 재내원 시 상악 우측 측절치의 심한 변위가 관찰되었다. 본 환아는 이 질환에 연관된 어떠한 의과적 병력 및 가족력이 없었으며, 임상적, 조직병리학적 검사 결과 특발성 치은 섬유종증으로 진단되었다.

교정적인 방법으로 변위된 치아를 재배열시키기 위해 상악 우측 중절치와변위된상악 우측 측절치 부위의 과증식된섬유성 조직을 외과적으로 제거하였다. 이 질환의 유전적 특성을 알기 위해 제거된 조직을 간단한 면역조직화학 배열법을 사용해 평가하였다. 평가 결과 병소 조직의 각질세포, 섬유모세포, 내피세포, 대식세포 내에 CTGF, HSP-70, MMP-1, PCNA, CMG2, TNF-α의 증가된 발현이 관찰되었다. 따라서 치은 섬유종증은 치은 조직의 섬유 상피성 증식과 염증 반응에 의한 CTGF, HSP-70, MMP-1, PCNA, CMG2, TNF-α의 수반하는 과발현에 의해 발생되었다.

주요어: 치은 증식, 특발성 치은 섬유종증, 치아 변위, 면역조직화학 배열법