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Dental and Skeletal Characteristics and Behavioral Aspects of the Patient with Floating-Harbor Syndrome Compared with Twin Sister

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Abstract

Floating-Harbor syndrome (FHS) is a rare genetic disorder. This report introduced in a patient with FHS. Distinctive facial characteristics, severe skeletal class 3 malocclusion with underdeveloped maxilla and protruded mandible, congenital missing teeth, microdontia and ectopic positions of maxillary teeth were presented in the patient. In his twin sister, mild skeletal class 3 malocclusion with protruded mandible was observed but congenital missing teeth and microdontia were not observed. High-arched palate, narrow V-shaped maxillary arch compared to wide and ovoid mandibular arch and inverse relationship between the maxillary and mandibular intermolar width resulted in posterior crossbite were confirmed by model analysis of the patient. These were not observed in the twins. Behaviorally, poor cooperation during dental treatment because of mental retardation was observed in the patient.

Key words : Floating-Harbor syndrome, Dental and skeletal characteristics, Behavioral aspects, Twins

Ⅰ. Introduction

Floating–Harbor syndrome (FHS) is a rare autosomal dominant genetic disorder[1]. FHS is caused by heterozygous mutations in exons 33 and 34 of the Snf2-related CREBBP activator protein (SRCAP) gene on chromosome 16p11.2[2-4]. SRCAP gene mutations are de novo truncating mutations and SRCAP protein activates the CREBBP gene that is involved in the regulation of cell growth and division[5]. The frame-shift mutation in exon 34 which is the last exon of SRCAP produces a C-terminal-truncated SRCAP protein that has lost its functional domain. These result in leading to a dominant negative effect[6]. These are mostly sporadic cases, occasionally with parent-to-child transmission[7].

The general features of FHS are characterized by the triad of proportionate short stature with delayed bone age, characteristic facial appearance and delayed speech development[7-11]. Other features, such as mild mental retardation, low birth weight, posteriorly rotated ears with low implantation, short neck and clinodactyly of the fifth finger have also been reported related to FHS[12,13].

Dental and skeletal features of abnormalities, such as malocclusion[13,14], supernumerary incisor[15], hypoplastic maxilla[16], small jaw[13], agenesis of the mandibular incisors[17], micrognathism[18] and teeth malformation have been reported[13].

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This case report aimed to present the dental and skeletal characteristics and behavioral aspects of a patient with FHS compared with those of his twin sister without any underlying diseases.

Ⅱ. Case Report

The protocol was approved by the Institutional Review Board of Kyungpook National University Dental Hospital (IRB No. KNUDH-2021-07-06-00).

A 8-year-old patient with rare FHS in Korea came to Kyungpook National University Dental Hospital with his twin sister for a dental consultation. There was no prior history of FHS in his family. Clinical examination, cephalometric radiographs, panoramic radiographs, model analysis and behavioral aspects were assessed in both twins.

Distinctive facial characteristics of FHS including triangular face, low-set ears, deeply set eyes, broad bulbous nose and short philtrum were observed in the patient (Fig. 1A, 1B). Skeletal class 3 malocclusion with severe retruded and underdeveloped maxilla and mildly protruded mandible was also observed (Fig. 1C, 1D).

Generalized delayed dental age, especially on the maxilla was observed in panoramic radiograph of the patient. Ectopic positions of the maxillary right canine, maxillary right first premolar and maxillary left second premolar, microdontia on the mandibular central incisors and congenital missing on the maxillary left canine were also observed (Fig. 1E). Posterior crossbite, high-arched palate and narrow V-shaped maxillary arch compared with wide and ovoid mandibular arch were revealed by analysis of a dental cast model and photographs of the patient. In addition, intermolar width of mandible was

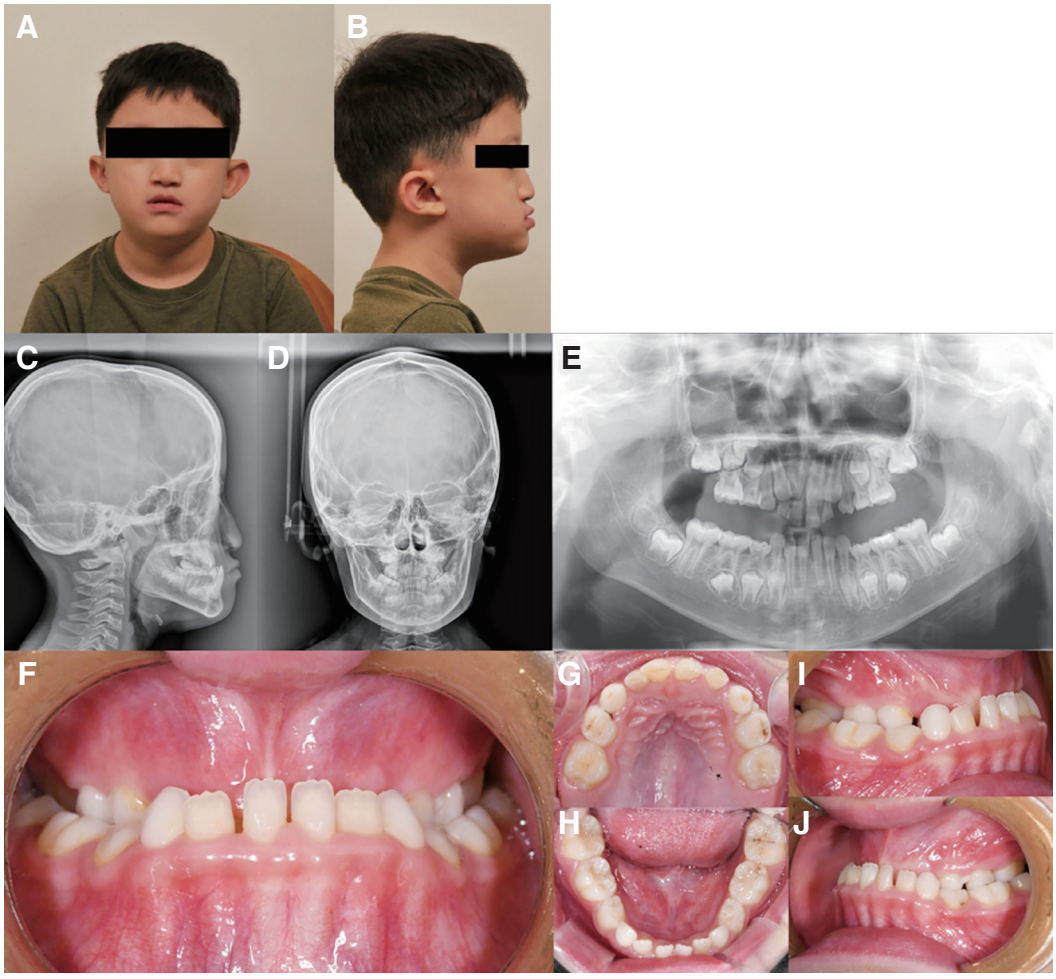

Fig. 1. Patient with Floating-Harbor syndrome. (A) Frontal-extraoral view. (B) Lateral-extraoral view. (C) Lateral cephalometric view. (D) Frontal cephalometric view. (E) Panoramic view. (F-J) Intraoral views.

wider than that of the maxilla in the patient. Maxillary arch perimeter of the patient was shorter than that of his sister, but a slight difference was observed in the mandibular arch perimeter between the twins. Overextruded and lingually inclined mandibular anterior teeth, deep overbite and decreased lower facial height were also observed in the patient (Fig. 1F-J, 3A, 3B, Table 1).

Behaviorally, mild mental retardation was presented in the patient. Compared with his sister, he was required to visit more times for his dental treatment because of his poor cooperation.

The characteristic facial appearances of FHS in eyes, ears and nose were not observed in his fraternal twin sister, without any underlying disease (Fig. 2A, 2B).

Table 1. Comparison of the arch width and arch perimeter between the patient with Floating–Harbor syndrome and the twin sister (mm)

			Patient with FHS	Twin sister
Arch width	Maxilla	ICW	28.5	30.5
		IMW	31.0	37.0
	Mandible	ICW	21.0	24.0
		IMW	37.0	35.0
Arch perimeter	Maxilla		72.06	76.72
	Mandible		66.52	67.52

FHS: Floating-Harbor syndrome, ICW: intercanine width, IMW: intermolar width

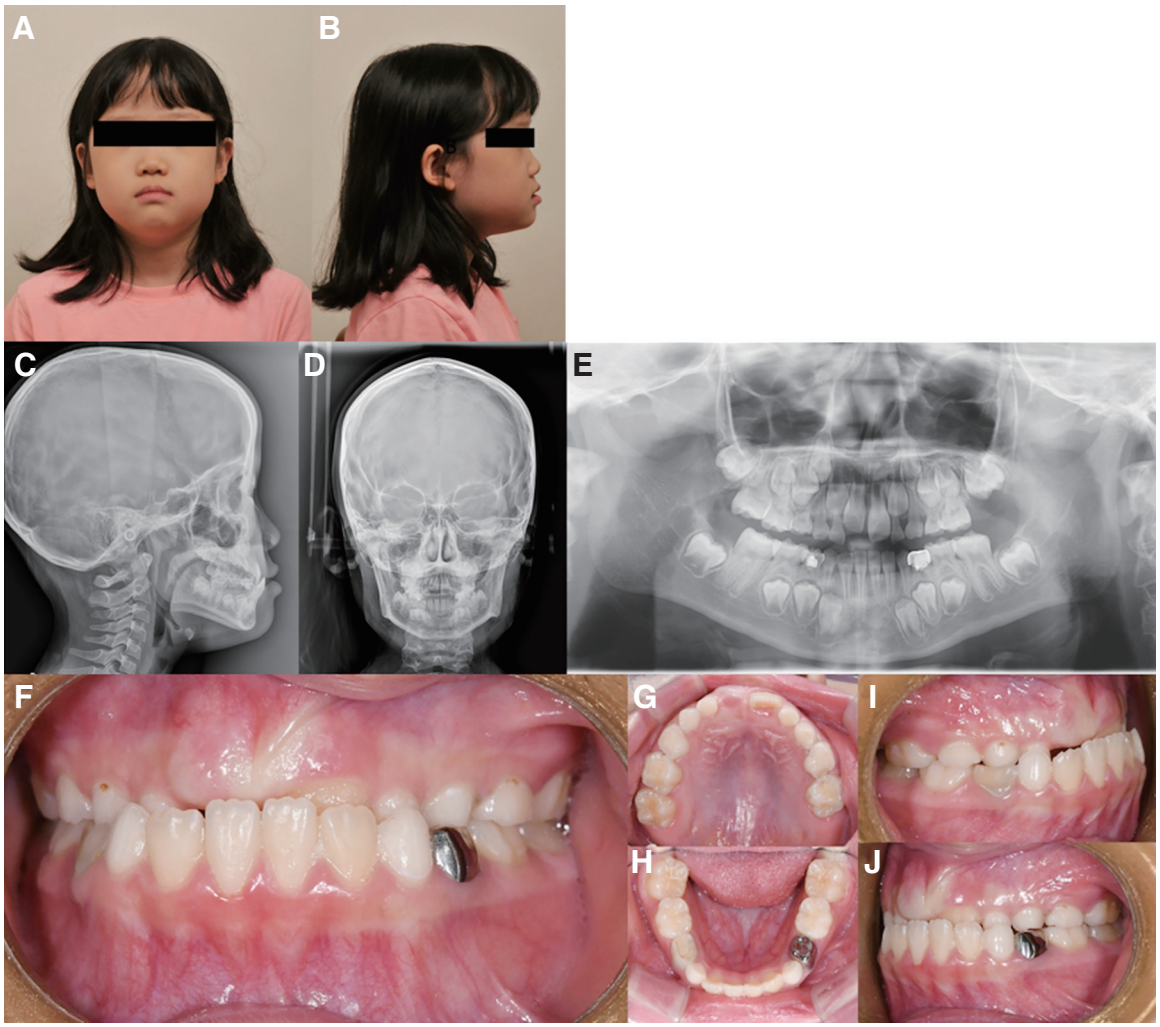

Fig. 2. Twin sister without any underlying disease. (A) Frontal-extraoral view. (B) Lateral-extraoral view. (C) Lateral cephalometric view. (D) Frontal cephalometric view. (E) Panoramic view. (F-J) Intraoral views.

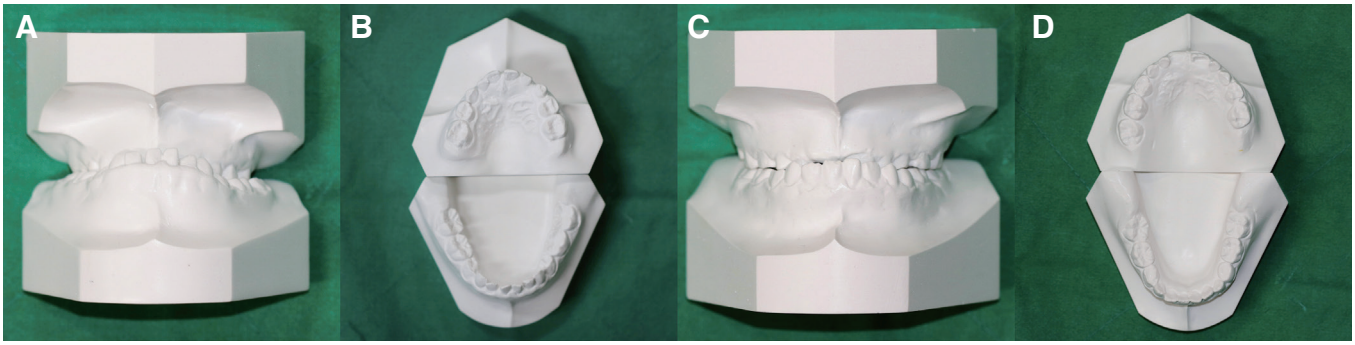

Fig. 3. Comparison of dental cast model. (A, B) Patient with Floating-Harbor syndrome. (C, D) Twin sister.

Mild skeletal class 3 malocclusion with relatively normal maxilla, protruded mandible and normal skeletal relationship was observed (Fig. 2C, 2D).

Normal tooth morphology and dental age, except for delayed development in the maxillary left first and second molars were observed in panoramic radiograph of the sister(Fig. 2E).

Anterior crossbite without posterior crossbite and ovoid or U-shaped maxillary and mandibular arch were revealed by analysis of the sister's dental cast model and photographs (Fig. 2F-J, 3C, 3D). Normal ranged maxillary and mandibular intermolar width and arch perimeter were also observed.

Cooperative behavior during dental treatment was shown in the sister.

Ⅲ. Discussion

FHS is a rare genetic disorder with SRCAP mutation and the prevalence of FHS is unknown. Approximately 50 cases of FHS have been reported[19].

In the presented case, the patient was diagnosed with FHS with a novel SRCAP mutation (c.7732dupT, p.Ser2578Phefs*6) by targeted exome sequencing used for determining causative variants[19,20], which was not found in his parents or the twin sister[19].

Triangular face, wide nose tip, short philtrum, deep eyes and low-set ears were included as the general morphologic features of FHS[1,7-11]. These were also observed in the patient with FHS, but not in his sister. These morphologic characteristics were to be helpful for the diagnosis of FHS. Small head circumstance, cryptorchidism, strabismus, hearing loss, wide thumbs and low birth weight had been reported in studies concerning FHS, but these were not observed in our patient[1,10,11,19,21]. In addition, congenital heart defects, urogenital anomalies, seizures, gastroesophageal reflux and recurrent otitis media were not observed in the patient[1,7,10,19].

Although the final diagnosis was confirmed by chromosomal analysis, establishing common features only appeared in patients with FHS might be helpful for the clinical diagnosis of FHS. The comparisons of clinical characteristics between the patient with FHS and his twin sister were thought to provide important characteristics for diagnosing FHS.

To examine the characteristics of FHS, especially in the orodental area, the radiographs, photographs and dental cast model of twins were analyzed. Severe skeletal class 3 malocclusion with posterior crossbite was shown in the patient, while mild skeletal class 3 malocclusion without posterior crossbite was shown in his twin sister. Mildly overdeveloped mandible was observed in both twins, but severely retruded and underdeveloped maxilla was observed only in the patient with FHS.

Dentoskeletal features of FHS had been characterized by a delayed osseous maturation, hypoplastic maxilla, high-arched palate and small jaw[4,16,22,23]. It was thought that hypergrowth of the mandible was affected by genetic factors. In the family histroy of both twins, anterior crossbite with hypergrowth of the mandible was affected by maternal side. The underdeveloped maxilla shown only in the patient was probably influenced by FHS. The relationship between the maxilla and mandible due to mouth breathing and the lower position of the tongue might be exacerbated by the narrowed upper pharyngeal airway caused by adenoid hypertrophy.

Comparing the tooth development and eruption between the twins, ectopically positioned teeth, congenital missing

teeth, and generalized delayed dental age, especially in the maxilla were observed in the patient, which were not shown in the twin sister. The maxillary arch perimeter and intermolar width of the patient were much shorter than those of his sister, but slight differences in the mandibular arch perimeter and intermolar width were observed between the twins. These might be caused by space deficiency due to the hypoplastic maxilla as well as genetic control. Overextruded and lingually inclined mandibular anterior teeth were also observed in the patient. This was thought to be an adaptation of the mandibular teeth to compensate for the skeletal discrepancy between the maxilla and mandible. Microdontia of mandibular central incisors was observed in the patient but not in his sister. Tooth size and morphology are known to be influenced by genetics[24]. These were likely to be similar in both twins but the above difference in tooth size might be an effect of FHS.

Behaviorally, very positive cooperation during dental treatment was presented in the twin sister. Poor cooperation was presented in the patient and more dental visits were required compared to twin sister. Children's cooperation can vary depending on their temperament. But, mild mental retardation which could be affected to his behavioral aspects was shown in the patient. Similar to the patient, poor cooperation during dental treatment is reported in many other patients with FHS because of mild mental retardation[12,13].

By comparing the characteristics of the patient with FHS and his twin sister, we tried to provide the features that could be helpful for the clinical diagnosis of FHS. Further studies are required to explain and evaluate the standardized dental and skeletal characteristics and behavioral aspects of FHS.

IV. Conclusion

Although FHS is a rare genetic disorder, various characteristics have been reported. By comparing the patient with FHS with his twin sister without any underlying disease, we might suggest a useful guideline for the assessment of important findings for FHS diagnosis.

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국문초록

Floating-Harbor 증후군 환자와 쌍둥이 여동생의 치성 및 골격성 특성과 행동 양상 비교

임종화 · 김기민 · 이제식 · 남순현 · 김현정

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Floating Harbor 증후군 (FHS)은 드문 유전질환이다. 본 증례는 FHS를 가진 환아에 대해 소개하였다. 환아는 독특한 얼굴 형태, 저성장된 상악과 전돌된 하악을 동반한 심한 골격적 3급 부정교합, 결손치, 왜소치, 상악 치아의 이소맹출을 보였다. 쌍둥이 여동생은 하악 전돌을 동반한 경미한 골격성 3급 부정교합은 보였으나 결손치와 왜소치는 보이지 않았다. 높은 구개궁, 넓은 난형의 하악궁에 비해 좁은 V형의 상악궁, 역의 관계의 상하악 구치간 폭경으로 인한 구치부 반대교합이 환자의 모델 분석을 통해 확인되었다. 이러한 특성은 쌍둥이에서는 나타나지 않았다. 행동면에서 환아는 경미한 정신지체로 인해 치과 치료 중 낮은 협조도를 보였다.