CASE REPORT

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Floating-Harbor Syndrome in a Korean Patient with Short Stature and Early Puberty: A Case Report

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What is already known on this topic?

Floating-Harbor syndrome (FHS) is a rare genetic disorder characterized by short stature, language deficits, and distinctive facial appearance, caused by mutations in the *SRCAP* gene. Due to its non-specific clinical symptoms, there is poor awareness of FHS, leading to difficult and delayed diagnoses. Only two FHS cases were previously reported in Korea, with facial dysmorphism and intellectual disabilities, but not all showing short stature or early puberty.

What this study adds?

This study adds new insights by reporting the first Korean case of FHS with both early puberty and short stature, highlighting the effectiveness of combined human recombinant growth hormone and gonadotropin-releasing hormone agonist therapy for such cases. It emphasizes the significance of genetic testing, particularly *SRCAP* gene mutation analysis, for accurate FHS diagnosis and contributes to a better understanding of FHS's clinical spectrum and management.

ABSTRACT

Floating-Harbor syndrome (FHS) is a rare autosomal dominant genetic disorder characterized by proportionately short stature, lack of expressive language, and distinctive facial features, including a large nose, long eyelashes, deeply set eyes, and a triangular face. We present a case of an 11-year-old Korean girl who was initially suspected of having Noonan-like syndrome but was later diagnosed with FHS. The patient exhibited short stature, developmental language delay, dysmorphic facial features, and early puberty. Targeted exome sequencing revealed a heterozygous mutation, c.7303C>T (p.Arg2435Ter), in the *SRCAP* gene, confirming a diagnosis of FHS. She responded well to human recombinant growth hormone and gonadotropin-releasing hormone agonist, effectively suppressing bone maturation and improving her height standard deviation score from -4.6 to -2.4.

Keywords: Floating-Harbor syndrome, growth hormone therapy, short stature

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Introduction

Floating-Harbor syndrome [FHS, (MIM 136140)] is a rare condition characterised by short stature, delayed osseous maturation, language deficits, and a distinctive facial appearance. Mutations in the *SRCAP* gene which codes for SNF2-related CREBBP activator protein cause truncation of the SRCAP protein, leading to FHS.

To date, approximately 100 cases have been reported in medical literature. Poor awareness of the condition and the non-specific clinical symptoms of FHS make its diagnosis difficult and delayed. Only two cases of FHS have been reported in Korea (1,2). Both patients had facial dysmorphism and intellectual disabilities, but one patient did not exhibit short stature (1) and the other did not experience early puberty (2). In this report, we describe the clinical features and molecular analysis of an 11 years and 5-month-old girl with an *SRCAP* mutation who presented with short stature, developmental language delay, dysmorphic facial features, and early puberty.

Case Report

The female patient was born at 38 weeks of gestation through normal vaginal delivery with a birth weight of 2840 g [-0.89, Korean standard deviation score (SDS)]. No perinatal complications were observed. Her mother had a height of 162.5 cm (0.29 SDS), and the father had a height of 174 cm (-0.08 SDS), resulting in a predicted adult height, calculated using mid-parental height, of 161.7 cm (0.13 SDS) (see Figure 1A). Moreover, there was a family history of short stature, as evidenced by the maternal grandmother's recorded height of 155 cm (-1.21 SDS) (see Figure 1B). The patient had no other significant family history. She exhibited persistent short stature from birth and so chromosomal analysis was performed at the age of 10 months. However, only an inversion p11-q13 in chromosome 9, which could be interpreted as a normal mutation, was identified. At the age of 16 months, Noonan syndrome was suspected at another hospital because of her short stature and large ears. Subsequently, genetic testing for Noonan syndrome was performed, and no abnormalities were found. Due to the initial suspicion of a Noonan-like syndrome, recombinant growth hormone (rhGH) therapy was started at 4 years of age. At that time, her height was 83.4 cm (-4.63 SDS), her weight was 9.4 kg (-5.19 SDS), and her insulin-like growth factor 1 (IGF-1) level was 55.3 ng/mL (reference range: 43.8-239.7). The patient's language development progressed slowly, and she commenced speech therapy at the age of five and was able to speak sentences at approximately six years of age. As the patient's growth was tracked, there was a consistent pattern of lagging bone age progression. However, at the age of 8 years and 7 months, the bone age assessment exhibited a significant acceleration, revealing a bone age of 7 years and 9 months, a markedly rapid increase compared to prior assessments. Furthermore, during a follow-up physical examination conducted six months later, at the age of 9 years and 3 months, bilateral breast development was observed, indicating significant progression. Remarkably, within just one year, the bone age had advanced by 2 years and 3 months. In response to these developments, starting at the age of 9 years and 10 months, a gonadotropin-releasing hormone (GnRH) agonist was administered in combination with the rhGH therapy to suppress bone maturation.

At the age of 11 years and 5 months, she was transferred to our hospital to continue treatment for her short stature and early puberty. Her height was 131.5 cm (-2.59 SDS), and her weight was 28.4 kg (-2.0 SDS) (Figure 1A). During physical examination, several distinctive features were noted that differed from those of her parents. These included large ears, a short neck, a long nose with a narrow nasal bridge and wide nostrils, mild cubitus valgus, and clinodactyly. Breast development was well suppressed, and bone age was determined to be 11 years, which was six months less than her chronological age. In addition, there were no anomalies detected in her blood biochemistry or thyroid function tests.

We conducted targeted exome sequencing (TES) to identify the genetic causes of her persistent short stature and facial dysmorphism. DNA samples were obtained from peripheral blood leukocytes using the Chemagic™ Magnetic Separation Module I method (PerkinElmer Chemagen, Baesweiler, Germany) with a DNA blood 200 mL kit. The G-Mendeliome panel (Celemics, Inc., Seoul, South Korea) was used for library preparation, and sequencing was performed using the DNBSEQ-G400 (MGI Tech Co., Ltd., Shenzhen, China), generating 2×100 bp paired-end reads. The sequence reads obtained were aligned to the reference sequence based on the public human genome build GRCh37/UCSC hg19 using BWA-mem (version 0.7.17). Duplicate reads were marked with biobambam2, and base quality recalibration and variant calling was performed using the Genome Analysis Toolkit (GATK, version 4.1.8). Annotation was performed using variant effect predictor (VEP101) and dbNSFP v4.1.

TES revealed a heterozygous variant, NM_006662.3: c.7303C>T, p (Arg2435Ter), in *SRCAP* (Figure 2). The pathogenicity of this mutation was assessed following the guidelines established by the American College of Genetics and Genomics. Based on the criteria PVS1, PM2, and PP5, this variant was classified as pathogenic. Furthermore, it was not detected in the Genome Aggregation Database (gnomAD). Consequently, we have determined that this is a pathogenic variant causing a non-sense mutation, leading to the conversion of the arginine residue into a stop codon.

These results confirmed the presence of the *SRCAP* mutation, which ultimately led to a diagnosis of FHS. Notably, no *SRCAP*

variants were identified in the patient's father, mother, or sister. The patient was maintained on a regimen of 45 mg/kg/day of rhGH, which had been consistently administered at another hospital. GnRH agonists were discontinued at the age of 12 years. The patient consulted a doctor for the assessment of hyperopia, strabismus, and conductive hearing loss, which may be present in FHS. However, the findings of this assessment were unremarkable. The echocardiogram showed favourable results, and renal ultrasound showed a difference in size between the two kidneys but no other abnormalities.

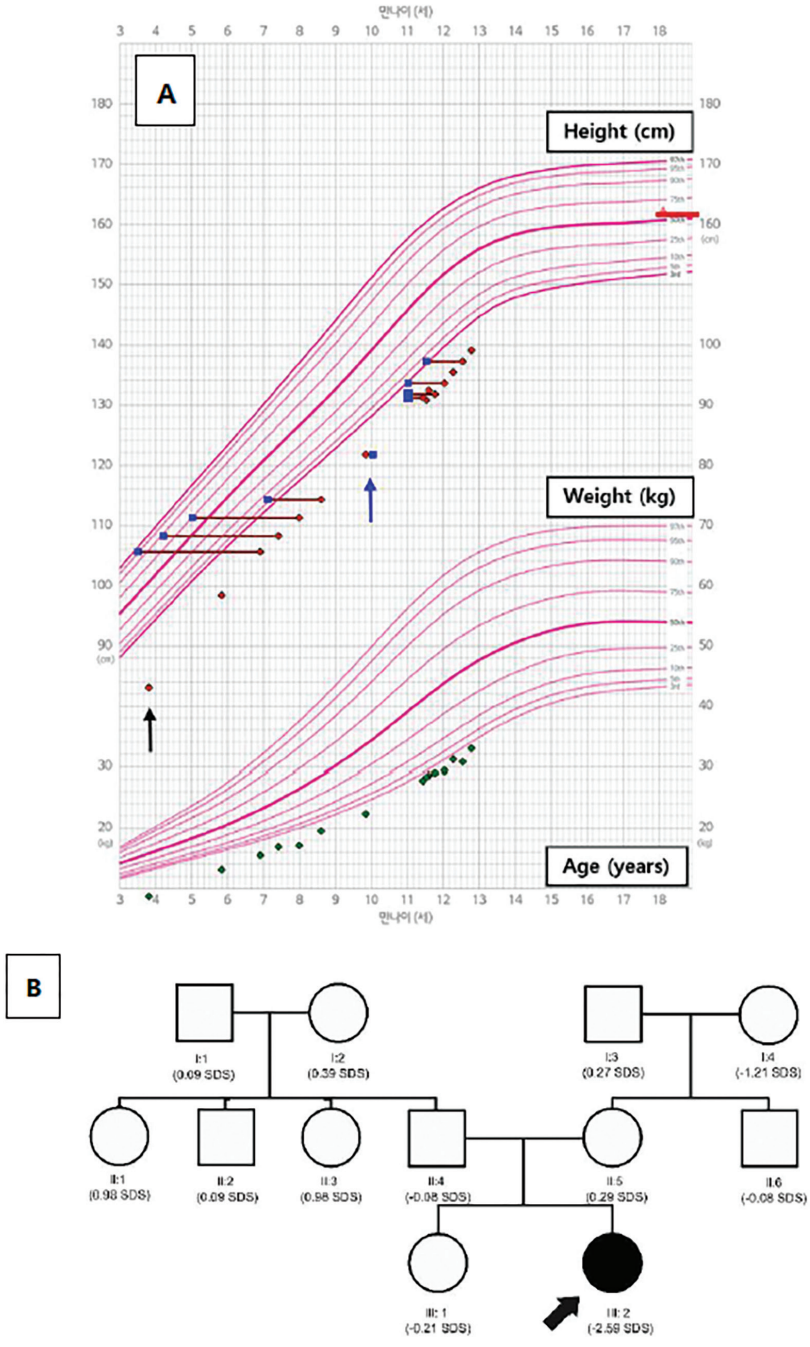

Figure 1. A) Reference growth chart for Korean females (3-18 years). Heights are marked with red dots, while weights are denoted by green dots. The blue dots represent the bone age. The mid-parental height trend is illustrated by a continuous red line. Significant milestones in the patient's medical treatment are highlighted: the commencement of recombinant human growth hormone therapy is marked by a black arrow, and the initiation of gonadotropin-releasing hormone agonist treatment is indicated by a blue arrow. **B)** Patient's family pedigree. The patient highlighted by a black arrow, and the height SDS corresponding to the age of each family member is also displayed
SDS: standard deviation score

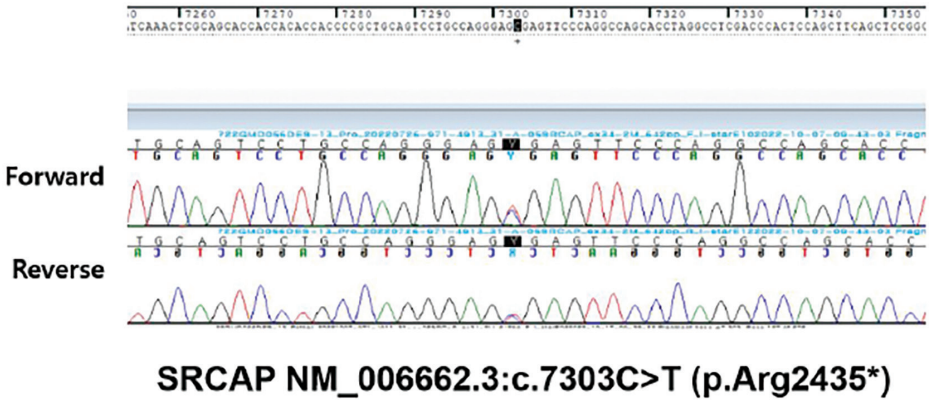

Figure 2. Results of Sanger sequencing of the *SRCAP* gene in the patient. NM_006662.3: c.7303C>T, p.(Arg2435Ter), heterozygote, non-sense

The patient is currently 13 years and 4 months old, with a height of 141.9 cm (-2.5 SDS) and a weight of 36.2 kg (-1.8 SDS). She is undergoing rhGH (60 mg/kg/day) therapy and receiving continuous speech therapy for delayed language development.

Discussion

In this report, we confirmed the presence of a heterozygous *SRCAP* variant using TES. The patient exhibited symptoms of short stature, developmental language delay, dysmorphic facial features, and early puberty.

FHS can present with symptoms resembling those seen in other genetic conditions. Noonan syndrome, 3M syndrome, Rubinstein-Taybi syndrome, and Silver-Russell syndrome must be differentiated from FHS. Noonan syndrome, which shares facial features and short stature with FHS, can be differentiated from FHS by a variety of physical abnormalities, including heart defects (3,4). Further, unlike in FHS, patients with 3M syndrome typically exhibit a large head and normal intelligence and speech development, with the possibility of hypogonadism in affected men (5). For Rubinstein-Taybi syndrome, patients often display a round face, severe intellectual decline, and normal bone age (6). In Silver-Russell syndrome, there are different features, such as an asymmetric body, café-au-lait spots, and blue sclera (7). As these conditions can present with symptoms resembling those of FHS, accurate diagnosis and genetic testing by a specialist are necessary.

Only two cases of FHS have been reported in Korea. Both patients had facial dysmorphism and intellectual disabilities, but one patient did not have short stature (1), and the other did not have early puberty (2). Therefore, our patient was the first in Korea to receive concurrent rhGH therapy and GnRH agonist therapy because of a short stature and early puberty.

The pathogenesis of short stature in FHS is not completely understood. It has been argued that GH deficiency, GH neurosecretory dysfunction, and IGF-1 signalling defects may be related to FHS, yet the evidence is limited due to the rarity of cases and lack of extensive scientific research (8). Contrasting with these uncertainties, another study has shown that the effects of rhGH therapy on FHS are modest at best, suggesting that the major molecular pathology of FHS is not caused by reduced GH secretion or activity (9). This highlights the necessity for additional research into the pathological mechanisms. In recent literature summarizing the experiences of 22 patients with FHS who received rhGH therapy, no side effects were reported. Notably, except for four individuals, there was a meaningful increase in height SDS compared to before treatment (8). In our case, the patient received rhGH therapy (45-60 mg/kg/day) for more than eight years. The final recorded height of the patient was 141.9 cm (SDS=-2.5), and no adverse effect of rhGH therapy was reported. In our patient, the growth rate improved. Given the rarity of FHS, there is limited information on the outcome of long-term treatment with rhGH. Further studies are necessary to clarify the longitudinal growth pattern and the real effectiveness and safety of rhGH therapy.

Recent studies have suggested a potential association between FHS and early puberty (9). However, the mechanisms underlying early puberty in FHS are again poorly understood. Several cases of precocious puberty in FHS patients have been reported, and some patients have undergone treatment with GnRH agonists (10,11,12). Treatment for early puberty in FHS resembles that for other forms of precocious puberty; however, its effectiveness requires further investigation. Our patient exhibited signs of puberty at the age of 9 years and 10 months. The rapid onset of puberty prompted the initiation of GnRH agonist therapy. This treatment successfully suppressed bone maturation. In FHS patients having symptoms of short stature and early puberty,

we speculate that GnRH agonist therapy could potentially delay bone maturation, thereby extending the duration of rhGH therapy.

At the initial diagnosis of FHS, the growth rate should be evaluated, and renal ultrasonography, blood pressure measurement, ophthalmic examination, hearing testing, dental examination, and genitourinary examination should be performed (8). For men, it is necessary to check for undescended testes. Orthopedic examination and evaluation of motor and language development are required for detecting hip dysplasia or other anomalies, as well as for genetic counselling.

Poor awareness of the condition and the non-specific clinical symptoms of FHS make its diagnosis difficult and often delayed. Patients with short stature, dysmorphic facial features, and developmental delays should undergo genetic investigation, including consideration of conditions such as FHS. In cases like ours, where FHS is accompanied by early puberty and short stature, rhGH therapy and GnRH agonist therapy may be beneficial.

Ethics

Informed Consent: Written informed consent was obtained from the patient's parents.

Footnotes

Authorship Contributions

Surgical and Medical Practices: Jooyoung Jeon, Il Tae Hwang, Concept: Jooyoung Jeon, Eu-seon Noh, Il Tae Hwang, Design: Jooyoung Jeon, Il Tae Hwang, Data Collection or Processing: Jooyoung Jeon, Il Tae Hwang, Analysis or Interpretation: Jooyoung Jeon, Literature Search: Jooyoung Jeon, Writing: Jooyoung Jeon, Eu-seon Noh, Il Tae Hwang.

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References

1. Choi EM, Lee DH, Kang SJ, Shim YJ, Kim HS, Kim JS, Jeong JI, Ha JS, Jang JH. The first Korean case with Floating-Harbor syndrome with a novel SRCAP mutation diagnosed by targeted exome sequencing. Korean J Pediatr. 2018;61:403-406. Epub 2018 Sep 16
2. Son HW, Lee JE, Oh SH, Keum C, Chung WY. Effects of long-term growth hormone therapy in a girl with Floating-Harbor syndrome. Ann Pediatr Endocrinol Metab. 2020;25:126-131. Epub 2020 Jun 30
3. Łaczmańska I, Kuliczkowska-Płaksej J, Stembalska A. Short stature in genetic syndromes: selected issues. Adv Clin Exp Med. 2018;27:409-414.
4. Zenker M, Edouard T, Blair JC, Cappa M. Noonan syndrome: improving recognition and diagnosis. Arch Dis Child. 2022;107:1073-1078. Epub 2022 Mar 4
5. Simsek-Kiper PO, Taskiran E, Kosukcu C, Arslan UE, Cormier-Daire V, Gonc N, Ozon A, Alikasifoglu A, Kandemir N, Utine GE, Alanay Y, Alikasifoglu M, Boduroglu K. Further expanding the mutational spectrum and investigation of genotype-phenotype correlation in 3M syndrome. Am J Med Genet A. 2019;179:1157-1172. Epub 2019 Apr 13
6. Milani D, Manzoni FM, Pezzani L, Ajmone P, Gervasini C, Menni F, Esposito S. Rubinstein-Taybi syndrome: clinical features, genetic basis, diagnosis, and management. Ital J Pediatr. 2015;41:4.
7. Inoue T, Nakamura A, Iwahashi-Odano M, Tanase-Nakao K, Matsubara K, Nishioka J, Maruo Y, Hasegawa Y, Suzumura H, Sato S, Kobayashi Y, Murakami N, Nakabayashi K, Yamazawa K, Fuke T, Narumi S, Oka A, Ogata T, Fukami M, Kagami M. Contribution of gene mutations to Silver-Russell syndrome phenotype: multigene sequencing analysis in 92 etiology-unknown patients. Clin Epigenetics. 2020;12:86.
8. Bo H, Jiang L, Zheng J, Sun J. Floating-Harbor syndrome treated with recombinant human growth hormone: a case report and literature review. Front Pediatr. 2021;9:747353.
9. Turkunova ME, Barbitoff YA, Serebryakova EA, Polev DE, Berseneva OS, Bashnina EB, Baranov VS, Glotov OS, Glotov AS. Molecular genetics and pathogenesis of the Floating Harbor syndrome: case report of long-term growth hormone treatment and a literature review. Front Genet. 2022;13:846101.
10. Stagi S, Galluzzi F, Bindi G, Lapi E, Cecchi C, Salti R, Chiarelli F. Precocious puberty in a girl with Floating-Harbor syndrome. J Pediatr Endocrinol Metab. 2007;20:1333-1337.
11. Homma TK, Freire BL, Honjo R, Dauber A, Funari MFA, Lerario AM, Albuquerque EVA, Vasques GA, Bertola DR, Kim CA, Malaquias AC, Jorge AAL. Growth and clinical characteristics of children with Floating-Harbor syndrome: analysis of current original data and a review of the literature. Horm Res Paediatr. 2019;92:115-123. Epub 2019 Nov 12
12. Galli-Tsinopoulou A, Kyrgios I, Emmanouilidou E, Maggana I, Kotanidou E, Kokka P, Stylianou C. Growth hormone deficiency: an unusual presentation of Floating Harbor syndrome. Hormones (Athens). 2011;10:236-240.