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### Abstract

Hutchinson–Gilford progeria syndrome (HGPS) is a rare autosomal recessive genetic disorder that occurs as a point mutation in the LMNA gene. It is a rare hereditary disorder, with approximately 100 cases reported in the medical literature. These patients and our case show features of aged appearance (pseudosenilism), loss of subcutaneous fat texture, growth retardation, sclerodermatous skin, ‘horse riding posture’, bird-face appearance, beaked nose, high pitched voice, protruding knees and elbows, underweight, short stature, malformation of the teeth, micrognathia, hypodontia, malocclusion, craniofacial disproportion, atherosclerosis and cardiovascular disorders. Unlike typical findings of HGPS, diffuse alopecia and prominent scalp veins were not observed in our case. Patients with HGPS have an average life span of 13 years, owing to myocardial infarction and congestive heart failure and our case also has atherosclerosis and heart failure. The study reported extra- and intraoral findings in a 24-year-old male patient with HGPS who came to our faculty with complaints about absence of teeth and psychological problems caused by absence of teeth and HGPS findings such as pseudosenilism, growth retardation and short stature. The data described necessary dental examinations and treatments for our patient and have reviewed the literature.

*Keywords: atherosclerosis, dental care, growth retardation, progeria, pseudosenilism, tooth loss*

### Introduction

The reported prevalence of Hutchinson–Gilford progeria syndrome (HGPS), that is childhood progeria,<sup>1</sup> is one in 8 million births. If unreported cases are considered, the estimated birth prevalence is one in 4 million births. HGPS is an autosomal recessive genetic disorder (sporadic cases have been reported).<sup>1-5</sup> It is a rare hereditary disorder, with approximately 100 cases reported in the medical literature.<sup>6</sup>

HGPS is caused by a mutation in the gene called LMNA. The LMNA gene encodes the Lamin A and Lamin C proteins which is the structural scaffolding and mechanisms of chromatin regulations that holds the nucleus of a cell together. Recently, point mutation in the LMNA gene has been found in patients with HGPS. The abnormal, truncated version of lamin A protein that called progerin causes Progeria. Progerin makes the nucleus unstable. That cellular instability leads to the process of premature aging and disease in Progeria.<sup>1,7-10</sup> This disorder is 1.2 times more common in male than in female.<sup>11</sup>

Subsequent study demonstrated the endogenous growth hormone resistance and malnutrition in children with HGPS.<sup>12</sup> Elevated levels of serum triglycerides, total cholesterol, low-density lipoprotein cholesterol, and reduced levels of high-density lipoprotein cholesterol have been reported.<sup>13,14</sup> Patients with HGPS also show an increase in hyaluronic acid levels and an increase in cholesterol and phospholipid values due to increased urine.<sup>13</sup> Children with HGPS appear normal at birth, and usually the syndrome is noticed first within 1–2 years.<sup>15</sup>

Pseudosenile appearance begins 1–2 years after birth, with the following characteristic findings: sclerodermatous wrinkled skin, alopecia, prominent scalp veins, hyperpigmentation, loss of subcutaneous fat tissue starting from birth, abduction limitation in joints due to periarticular fibrosis, ‘horse riding posture’, bird-face appearance, beaked nose, thin cyanotic lips, high pitched voice, protruding knees and elbows, underweight, growth retardation, short stature, delayed eruption and malformation of the teeth, micrognathia, hypodontia, malocclusion, tendency for dental caries, craniofacial disproportion, atherosclerosis and cardiovascular

disorders.<sup>1-4,8-10,16-18</sup> In these cases, tooth roots may be hypoplastic and cementum may not be present. Teeth may be lost in adolescence.<sup>2,19</sup> The diagnosis is based upon a thorough clinical evaluation, characteristic physical findings, a careful patient history and diagnostic genetic testing.<sup>20</sup>

Patients with HGPS have an average life span of 13 years, owing to myocardial infarction and congestive heart failure.<sup>21,22</sup> However, the case of a 45-year-old man with HGPS has been reported in the literature.<sup>22</sup> We report a case of HGPS for its rarity and age of patient that is longer than average life span of HGPS. The patient allowed his information and photos to be used for this manuscript provided that the eyes were covered with black strips.

**Case Report.** A 24-year-old man applied to our faculty with complaints about esthetic problems, discomfort eating due to early teeth loss and psychological problems caused by absence of teeth and HGPS findings such as pseudosenilism, growth retardation and short stature. According to information received from the patient's family, he spontaneously lost his teeth without decay few years after their eruption.

The diagnosis (HGPS) is based on the recognition of common clinical features, anamnesis and blood tests. DNA sequence analysis could not be performed because it is not easy to find and financial problems of the patient. Calcific atheromatous plaques were observed in the distal abdominal aorta at the abdominal CT scan. According to ECO results; advanced tricuspid valve insufficiency, right heart enlargement, mild-moderate mitral valve insufficiency, pericardial effusion was detected. The renal and hepatic function were found normal due to blood tests and USG. It was learned that the patient is suffering from respiratory distress only during speech and excessive effort. His mental skills showed no signs of retardation. He does not use any medicine and cardiologist offered the surgery for his heart diseases six years ago but, because of the high risk of losing his life while operation, he rejected the surgery.

Patient referred for genetic counseling to medical school for genetic tests but the test could not be made because of absence of required materials. Growth hormone level (0.97 ng/mL) was normal and total cholesterol level was slightly low (109 mg/dL). The normal blood level of cholesterol is 130 mg/dL. He is 149 cm and 42 kg. He did not have hearing loss or excessive sweating. His parents had a consanguineous marriage (maternal and paternal grandfathers are siblings). His two female and three male siblings had no similar clinical manifestations with HGPS, like pseudosenile appearance, horse riding posture, atherosclerosis and cardiovascular disorders, growth retardation, short stature, delayed eruption and

malformation of the teeth, micrognathia, hypodontia. Due to information that taken from his family, his pseudosenile appearance has begun when he was 2 years old.

Unlike typical findings of HGPS, diffuse alopecia and prominent scalp veins were not observed (Figure 1a). Clinically, our patient had growth retardation (Figure 5), aged appearance (Figure 1a), hyperpigmentation, bird-face appearance, beaked nose (Figure 1b), thin cyanotic lips, high pitched voice, micrognathia, oligodontia, premature milk and permanent tooth loss, horse riding posture (Figure 4), mid-facial hypoplasia, atrophic alveolar crest (Figure 2a-2b), mild camptodactyly (Figure 3a) (fingers were flexed even in the normal state), tufting at some fingertips (Figure 3b), dystrophic nails, hypoplastic clavicularae, limitation of mouth opening (Figure 6), protruding knees and elbows (Figure 7), underweight and short stature.



**Figure 1. (a) Anteroposterior and (b) Lateral Views**

As a result of the clinical and radiographic examination, the patient's dental problems were observed as follows: (a) Oligodontia (he has only teeth 13, 16, 17, 24, 25, 26, 27, 36, 37, 46, 47); (b) impacted lateral tooth (tooth 22); (c) nonoccluded inverted molar tooth (47); (d) hypoplastic roots; (e) micrognathia, (e) atrophic alveolar crest; (g) limitation of mouth opening, h) malocclusion.



(a)



(b)

Figure 2(a)-2(b). Intraoral View of the Case



(a)



(b)

Figure 3. Dorsal (a) and Ventral (b) Side Views of Hands



Figure 4. Horse Riding Posture and Whitening of Hair



Figure 5. Growth Retardation Compared to an Adult Individual



Figure 6. Limitation of Mouth Opening

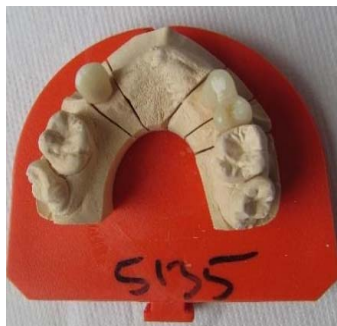


Figure 7. The Protruding View of Elbows

Scaling and prosthetic restorations (Figure 9) were performed. Oral hygiene training was provided to help the patient achieve oral dental health. Function, phonation and aesthetics were restored to the patient who completed the dental treatment (Figure 8). It was noted that in the control appointments the patient exhibited more confident behavior than before the dental treatment was initiated.



**Figure 8. The View After all Dental and Prosthetic Treatments**



(a)



(b)

**Figure 9. Completed fixed (a) and removable (b) prosthetic restorations of the patient**



**Figure 10. Oligodontia, Impacted Lateral Tooth, Nonoccluded Inverted Right Lower Molar Teeth and their Hypoplastic Roots in the Radiographic View**

## Discussion

The general and intraoral findings in our patient were consistent with HGPS based on a literature review. Unlike Cockayne syndrome, which causes an aged appearance, the absence of neurological and ocular problems and hearing loss in our patient strengthens the diagnosis of HGPS.<sup>23</sup> Furthermore, contrary to previous reports, the aged appearance in our patient was observed since infancy and there were no cataracts in the eyes, which differentiated the diagnosis from that of Werner's syndrome.<sup>24</sup>

The age at onset of a pseudosenile appearance and absence of hydrocephalus in our patient differentiated the diagnosis from that of Wiedemann Rautenstrauch syndrome (neonatal progeroid syndrome).<sup>25</sup> He spontaneously lost his teeth without decay a few years after their eruption and his panoramic radiographic image (Figure 10) suggested genetic disorders such as Papillon-Lefevre syndrome and Hypophosphatasia.

Papillon-Lefevre syndrome (PLS) is a rare autosomal recessive disorder characterized by palmar-plantar hyperkeratosis, early loss of primary and permanent teeth without decay because of severe destructive periodontitis, severe alveolar resorption, tooth mobility, abscesses.<sup>26</sup> Our patient had no hyperkeratosis and severe periodontitis so PLS is divided in the differential diagnosis.

Hypophosphatasia (HP) is a rare, inherited disorder characterized by defective mineralization of bone and teeth and deficient serum and bone alkaline phosphatase (ALP) activity. The most frequently documented dental manifestation is the premature loss of teeth as a result of hypoplasia or aplasia of cementum.<sup>27</sup> It was seen that hypoplastic roots of teeth in our case's radiography as a common finding with our patients and HP but because of his pseudosenile appearance, horse riding posture, atherosclerosis and cardiovascular disorders and normal serum alkaline phosphatase level, also HP were divided in the differential diagnosis.

Our patient showed physical and developmental growth disturbances. Subsequent study demonstrated the endogenous growth hormone resistance and malnutrition in children with HGPS.<sup>12</sup> Another study demonstrated that overnight growth hormone concentrations were within the normal range<sup>28</sup> and growth hormone level of the patient was also normal at 0.97 ng/mL. Elevated levels of serum total cholesterol have been reported in the literature<sup>14</sup> but whereas total cholesterol levels of our patient was found to be slightly lower than normal at 109 mg/dL (130 mg/dL is the normal level).

Patients with HGPS also show an increase in hyaluronic acid levels, cholesterol and phospholipid values due to



increased urine.<sup>13</sup> But the reverse situation, total cholesterol level of the patient was slightly low at 109 mg/dL (130 mg/dL is the normal blood level of cholesterol).

The external appearance of patients with HGPS is different, and, in addition to chewing, feeding, phonation and aesthetic problems, their antisocial tendency is increased. Similar clinical behaviour was observed in our patient. Therefore, we believe that dentists have an important role in ensuring active participation of the patient in social life by eliminating the functional, phonation and aesthetic problems of HGPS. Dental treatments are necessary for these individuals who believe themselves to be isolated from society.

Before dental treatments are performed, consultations regarding the patient's medical problems should take place. Sometimes antibiotic prophylaxis may be required.<sup>2</sup> In our patient, prophylactic applications were performed in accordance with the pre-dental procedures. Patients with HGPS should consider the use of low-dose aspirin or anticoagulant medication, mainly because of diseases such as heart failure and atherosclerosis.<sup>2</sup> In our patient, necessary dental treatments such as scaling and prosthetic restorations were performed. The patient and his family were educated to provide motivation for oral hygiene.

## Conclusions

We believe that psychological support in addition to dental and medical treatments would be a suitable approach to help increase the quality of life of the patient. Dental treatments with the fewest possible instruments and uncomplicated approaches are appropriate in cases with limited mouth opening. Dental prosthetic preparation, impression and cementation procedures were difficult in the patient with limited mouth opening. Our patient lost his teeth shortly after their eruption without decay; therefore, HP and PLS were included in the differential diagnosis. However, when all other clinical findings and blood test results were evaluated together, the diagnosis of HGPS was confirmed. Dental treatment durations which were kept short due to patient's limitation of mouth opening, respiratory problems, continuous hospitalization since young age were thought to be more effective for both physician and patient. We hope to raise physician awareness of such cases and that treatment would be beneficial for the patient who may achieve more active participation in social life by eliminating functional, phonation and aesthetic problems.

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## Conflict of Interest Statement

None declared

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