

## CRANIOFACIAL MORPHOLOGY AND DENTAL FINDINGS OF SECKEL SYNDROME: CASE REPORTS OF TWO SIBLINGS

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### Abstract

Seckel Syndrome (SS) is a rare form of primordial autosomal recessive dwarfism involving multiple malformations. The major characteristic features of SS are intrauterine and postnatal growth deficiency, severe microcephaly, craniofacial dysmorphism which includes characteristic 'Bird-headed' appearance, prominent nose, sloped forehead, receding jaw, low-set ears with hypoplastic lobules and large eyes with down-slanting palpebral fissures. Characteristic skeletal anomalies include premature closure of the cranial sutures and fifth finger clinodactyly. In addition to the characteristic craniofacial dysmorphism and skeletal defects, abnormalities have been described in the cardiovascular, hematopoietic, endocrine and central nervous systems.

Dental abnormalities include enamel hypoplasia, hypodontia, microdontia, taurodontic root morphology and a high-arched palate. Retarded bone age and moderate to severe mental retardation (I.Q. < 50 in 50% of cases) are observed in patients with Seckel Syndrome.

The purpose of this paper is to describe craniofacial morphology and dentition in two siblings with Seckel Syndrome and to present the dental treatments provided for these patients.

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### Introduction

Seckel Syndrome (SS) is a rare form of primordial autosomal recessive dwarfism, with an incidence of 1:10000 live-born children without any sex predominance. Etiology of the syndrome, which involves multiple malformations, remains unclear and both sexes are equally affected<sup>1</sup>.

SS is probably autosomal recessive and chromosome breakage has been suggested to explain the multiple clinical phenotypes. The severity of microcephaly could explain the different life expectancies for these patients. Death occurs during childhood in most of the cases, but some live much longer<sup>2</sup>.

The major characteristic features of SS

are intrauterine and postnatal growth deficiency, severe microcephaly, craniofacial dysmorphism, which includes characteristic 'Bird-headed' appearance, prominent nose, sloped forehead, receding jaw, low-set ears with hypoplastic lobules and large eyes with down-slanting palpebral fissures. Characteristic skeletal anomalies include premature closure of the cranial sutures and fifth finger clinodactyly<sup>3</sup>.

In addition to the characteristic craniofacial dysmorphism and skeletal defects, abnormalities have been described in the cardiovascular, hematopoietic, endocrine and central nervous systems. Retarded bone age and moderate to severe mental retardation (I.Q. < 50 in 50% of cases) are observed in patients with SS. In one half of cases, head circumference is more retarded than height, while for the remainder it is as retarded as height.

Other systemic manifestations associated with SS include Fanconi anemia, leukemia, chronic nephritis, dysgenesis of cerebral cortex and corpus collosum, as well as a vast spectrum of skeletal defects<sup>1</sup>.

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The purpose of this paper is to describe the craniofacial morphology and dentition in two siblings with SS and to present the dental treatments provided for these patients.

## Case Reports

### Case 1

Nine-year-old boy with the diagnosis of SS (Fig. 1) was referred to our pediatric dentistry clinic for the treatment of his aching primary molar tooth. Each of two siblings signed an informed consent form before clinical and radiographical examinations.



**Figure 1.** Two siblings with Seckel Syndrome: 9-year-old boy and 6-year old girl with 93 cm and 72 cm height, respectively (Both less than 3rd centile).

He was born to healthy, consanguineous (first cousins) parents. The first pregnancy of mother resulted in a spontaneous abortion and the second pregnancy produced a healthy male who was 12-year-old at the time of the conduction of the present study. Our patient with SS is the third child of the family. The pregnancy and family histories were unremarkable. He was born normally at term with low birth weight (1740 gr). His postnatal growth was very poor, in spite of proper feeding.

The past medical history of the patient revealed a dislocation of hip, which was treated when the patient was 5-month-old. The parents noticed growth deficiency when he was 1-year-old at first. After the birth of his sister who has similar physical appearance and severe growth deficiency, the parents referred to Pediatric Department of Faculty of Medicine and two siblings were diagnosed as SS.

On the physical examination, a typical 'bird-like' facial appearance (a prominent nose, a sloped and small forehead, midfacial hypoplasia and a receding jaw), low-set ears, is very stunted, but proportional stature with severe microcephaly were observed (Fig. 2). Unilateral cryptorchidism was also noted.



**Figure 2.** Frontal view of case 1.

At 4.5 years of age, the patient's weight, height and head circumference were 6900 gr, 75 cm and 41 cm, respectively and at 9 years of age, his weight, height and head circumference were 10 kg, 93 cm and 41.2 cm, respectively (all less than 3<sup>rd</sup> centile).

The bone age was 4 year 9 months when his chronological age was 9 years old (Fig. 3).



**Figure 3.** Hand-wrist radiograph of the boy patient showing 4 years 9 month old skeletal maturation.

He was observed to have borderline mental retardation (I.Q.= 55) and psychomotor development showed retarded milestones (walking at age 2, talking at age 3). The parents reported that he quickly forgot the things he

learned and continued going to a special care school.

The patient had a history of frequent respiratory infections and his routine blood counts revealed high levels of white blood cells. Possible adhesion defects and focal infections have been investigated, but no pathology was found. The cardiovascular, abdominal and neurological examinations were normal.

Hypercellular bone marrow, extensive necrosis and 2-3% blasts were observed at aspiration biopsy of the bone marrow. These findings revealed that the patient was at the risk of Chronic Myeloid Leukemia (CML) and routine controls of the patient were planned.

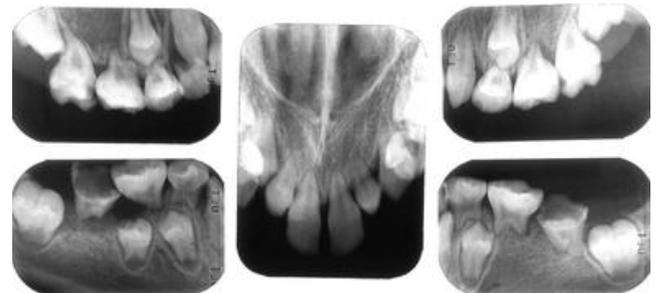
The patient was examined at the Department of Endocrinology and growth hormone therapy was thought to be ineffective or even harmful for this patient, because of his syndrome and the findings of aspiration biopsy of the bone marrow.

On the intraoral examination, micrognathia, microdontia, anterior open-bite, increased overjet, diastemas between permanent incisors, teeth with triangular crown form, mobility and enamel hypoplasia, high-arched and narrow palate were observed (Fig. 4).



**Figure 4** Intraoral view of the boy patient showing microdontia, anterior open bite, triangular crown form, diastemas between the teeth and enamel hypoplasia.

Radiographic examination revealed that the right mandibular second permanent premolar and both maxillary second permanent premolars were congenitally missing and teeth were with short roots and have abnormal root morphology (Fig. 5). However, normal dental age was observed.



**Figure 5.** Periapical radiographs of the boy patient showing three congenitally missing second permanent premolars except the mandibular left one and teeth with short roots and abnormal root morphology.

Steiner's cephalometric analysis was performed and skeletal Class II mal-relationship and extreme posterior rotation of mandible were observed. GoGn- SN angle was 53 (Standard values:  $30.5 \pm 4.5$ ). The morphology of sella turcica was compared with normal perpendicularly oriented anterior sella turcica wall morphology. Oblique anterior wall morphology was observed in both patients (Fig. 6).



**Figure 6.** Skeletal Class II malocclusion, extreme posterior rotation of mandible and oblique anterior wall morphology were observed at Steiner's cephalometric analysis of the boy patient.

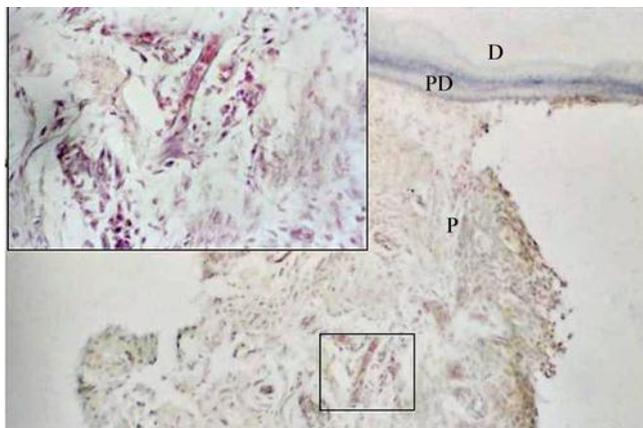
Dental treatment of the patient consisted of filling the carious primary and permanent molar teeth and stainless steel crowns were placed on permanent first molar teeth with excessive loss of tooth structure, in order to protect the vertical dimension of occlusion (Fig. 7). Fissure sealants were placed on primary first molar teeth. Oral hygiene instructions and dietary advice were given. Because he was born and has been

continuously residing in Isparta city, a high fluoride area of Turkey, there was no indication of professional fluoride application for this patient.



**Figure 7.** Panoramic radiograph of the boy patient after the dental treatments were performed.

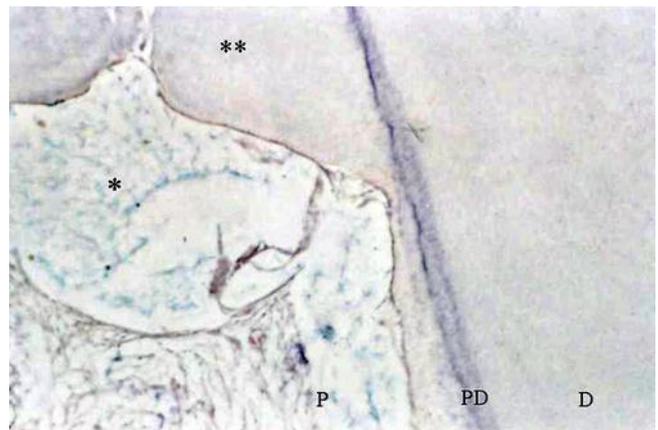
The physiologically exfoliated first and second primary molar teeth were used for histopathological investigation. In decalcified sections, there was no significant pathology of histological structures of dentinal, predentinal and pulpal tissues (Fig. 8a).



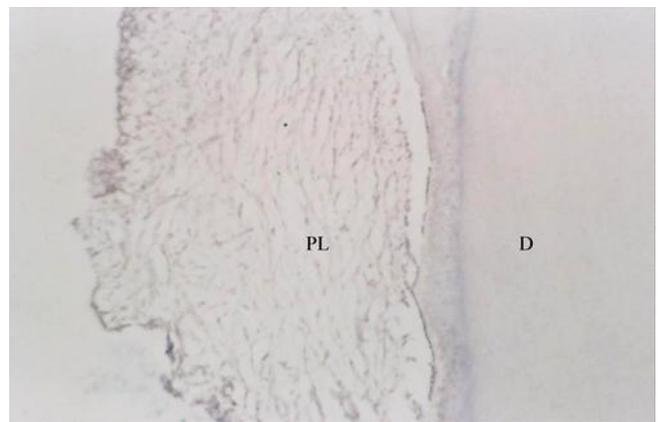
**Figure 8** Histopathological photographs of the first and second primary molar teeth of the boy patient which were taken from the sections stained with hematoxylin eosin. (a) X10 and X40 magnification. (P: Pulp, PD: Predentin, D: Dentin, PL: Periodontal Ligament, \*:Space, \*\*:Osteodentin)

An osteodentin structure was observed as a different structure from pulp and dentin structures along the pulp-dentin border (Fig. 8b).

There was no increase in the number of the white blood cells at vascular and interstitial regions, however osteoclast-like large nucleated giant cells were observed at periodontal ligament (Fig. 8c).



(b) X10 magnification.



(c) X10 magnification.

## Case 2

Six-year-old girl (Fig. 1) was the fourth child of the family. She was born normally at term at the end of uneventful pregnancy period with low birth weight (1600 gr). At 1 year of age, she was treated at hospital with the diagnosis of pneumonia.

Physical examination findings were similar to the case 1. There was severe growth deficiency, the characteristic Seckel face, including a prominent nose, a sloped and small forehead, midfacial hypoplasia and a receding jaw and bilateral clinodactyly of the fifth finger. She was hyperactive, playful and had a pleasant appearance.

Her routine blood counts revealed high levels of white blood cells and low levels of hemoglobin. Frequent respiratory infections were also noted for this patient.

At 1 year of age, the patient's weight, height and head circumference were 3600 gr, 53 cm and 38 cm, respectively and at 6 years of age, his weight, height and head circumference

were 7200 gr, 72 cm and 38.5 cm, respectively (all less than 3<sup>rd</sup> centile).

The bone age was 1 year 4 months when her chronological age was 6-years-old (Fig. 9).



**Figure 9.** Hand-wrist radiograph of the girl patient showing 1 year 4 month old skeletal maturation.

She was observed to have borderline mental retardation (I.Q.= 50) and her psychomotor development was similar to case 1 (walking at age 2, talking at age 3).

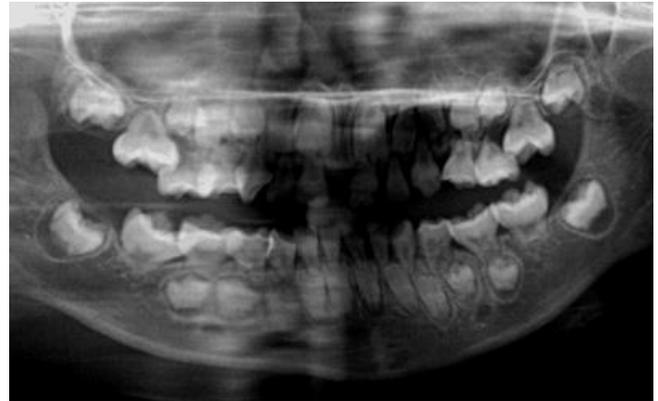
Results of the aspiration biopsy of the bone marrow were also similar to case 1. For this reason, growth hormone or another medical therapy was not performed for these patients with SS and routine controls of the patients were planned.

On intraoral examination, micrognathia, microdontia, teeth with triangular crown form and mobility, a high-arched and narrow palate were observed (Fig. 10). There was no carious tooth in her mouth.



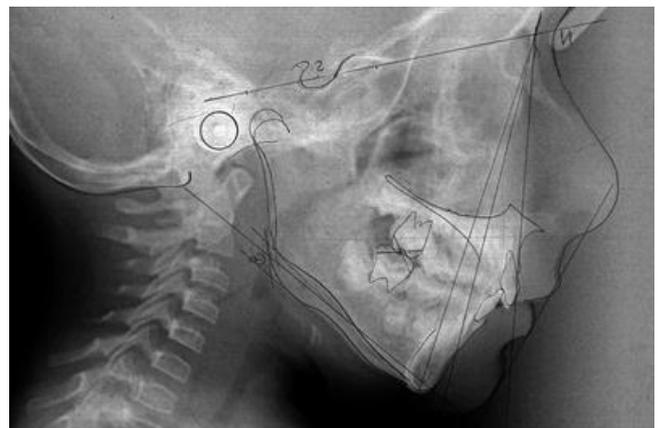
**Figure 10.** Intraoral view of the girl patient showing microdontia and triangular crown form.

Radiographic examination revealed that there was no congenitally missing tooth and teeth were with short roots and have abnormal root morphology. There was ectopic eruption of first permanent teeth (Fig. 11). Normal dental age was also noted.



**Figure 11.** Panoramic radiograph of the girl patient showing ectopic eruption of the first permanent molars and teeth with short roots and abnormal root morphology.

Skeletal Class II mal-relationship and extreme posterior rotation of mandible were observed at Steiner's cephalometric analysis. GoGn- SN angle was 50 (Standard values: 30.5±4.5) (Fig. 12).



**Figure 12.** Findings of the Steiner's cephalometric analysis for the girl patient were the same of the findings for the boy patient.

The distal surfaces of the primary second molar teeth were trimmed and ectopic permanent first molar teeth were planned to erupt in their normal position. Fissure sealants were placed on all primary molar teeth. Oral hygiene instructions and dietary advice were given.

## Discussion

Mental deficiency is present in half of the cases with levels of IQ below 50. Moderate mental deficiency has been observed in some cases<sup>2,4</sup>. Our patients were observed to have borderline mental retardation. Although these patients tend to have a sociable personality, they can be easily distracted.

Various orofacial anomalies have been reported for SS. Dental abnormalities include enamel hypoplasia<sup>3,4</sup>, hypodontia<sup>4</sup>, microdontia<sup>2,4</sup>, taurodontic root morphology<sup>4,5</sup>. Several cases have demonstrated a high-arched palate<sup>2,4</sup> and cleft palate has also been reported<sup>5</sup>. Cleft palate was not observed at the present cases. There was no congenitally missing tooth on the radiographic examination of the case 2, but it was observed that all of her permanent first molar teeth were in ectopic position. Ectopic eruption has been reported in two cases of SS previously<sup>5</sup>.

Normal dental age was observed at the present cases as it was reported in the majority of the previous case reports. Besides this, cases with delayed dental age were also reported in the literature<sup>5</sup>.

Hematopoietic disorders have been reported in approximately 15% of patients with SS<sup>6</sup>. Acute myeloid leukaemia<sup>7</sup> and pancytopenia were described<sup>2,8</sup>. The authors suggested that the patients with SS may be at high risk of developing acute myeloid leukemia. However, risk of chronic myeloid leukemia was noted following the aspiration biopsies of the bone marrow of both patients and the relevant specialists planned routine controls of the patients.

The importance of serial ultrasound scans during pregnancy is revealed once more by the present case reports. Because our patients were not followed by serial ultrasound scans, severe intrauterine growth retardation (IUGR), microcephaly and prominent facial features could not be diagnosed at prenatal period. Parents may be informed that the majority of cases of severe IUGR and microcephaly are detectable by serial ultrasound scans from 16-20 weeks of pregnancy<sup>9</sup>. In near future, linkage studies may identify the underlying pathogenesis which is responsible for the features of the SS.

Early intervention, including preventive dental care has great importance. Congenitally

missing teeth and mal-relations can be diagnosed in early period and preventive dental care can be managed for these patients.

## Conclusions

Because of the history of frequent infection and high levels of white blood cells in the present cases, dental infections can enhance these conditions. In addition, preventive treatments can avoid unnecessary pain. It is essential that the patients with SS should be followed regularly in order to reduce the risk of subsequent dental diseases.

## Declaration of Interest

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