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# Case of Seckel Syndrome in a 9-month-old Girl

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**Abstract**

**INTRODUCTION:** Seckel syndrome is a rare case. It belongs to an autosomal recessive disorder. It commonly leads to osteodysplastic, microcephaly, and dwarfism, which are proportional to prenatal onset. Microcephaly, bird-headed-like appearance, and mental retardation are common dysmorphic in the future. This case report present a patient with Seckel syndrome and this case will be discussed comprehensively.

**CASE REPORT:** A patient 9-month-old girl came to the hospital with a chief complaint of growth disturbance. Her growth was not the same as her peer. She was stunted and failed to thrive. Microcephaly and a dysmorphic face (bird-headed) appeared with a broad face, prominent forehead, large eyes, prominent curved nose, and micrognathia were found in physical examination. Her organ was in normal condition. According to the radiology examination, the bone age was appropriate for the age of a newborn (<3 months). Patient had global developmental delay. Based on clinical manifestation patient can be witnessed with Seckel syndrome, to confirm the diagnosis chromosomal test is needed. There is no specific treatment. Management for the patient was growth and developmental intervention.

**CONCLUSION:** Seckel syndrome is a rare disease. The diagnosis was challenging and sometimes could miss diagnosed with another syndrome. In this case, the diagnosis was made by clinical presentation and laboratory examination. There was no specific treatment. We assess the patient with Seckel syndrome. A gene or chromosome examination is needed. Meanwhile, the examination was limited and need a high cost. Educating the family about the patient's condition has been done.

## Introduction

Seckel syndrome is a rare case. It belongs to an autosomal recessive disorder. The syndrome commonly leads to short stature, prenatal and postnatal growth disorders, with features of certain facial characteristics (micrognathia, ear malformations, and bird-like face), microcephaly, defects in bone, premature closure of the head sutures, and mental retardation. This syndrome is caused by genetic defects in the chromosomes 3q22.1-q24 (SCKL1), 18p11.31-q11.2 (SCKL2), and 14q23 (SCKL3). By this condition, several anomalies are commonly present such as a specific type of dwarfism with mental retardation, low birth weight, and many others. One form of Seckel syndrome is caused by a mutation in the gene coding for ATR located on chromosome 3q22.1-q24, where this gene has an important role in the response to repair damaged DNA. The incidence of Seckel syndrome in Indonesia is currently unknown because it is a very rare syndrome. This syndrome was first reported by Seckel in 1960, and until now the prevalence is not known with certainty, it is estimated that there is one incidence of Seckel syndrome per 10,000 births in the world, with only about 100 cases that have been reported since the syndrome was first discovered [1], [2].

Craniofacial feature includes moderate mental retardation, severe microcephaly, receding forehead, large eyes, and micrognathia, lending prominence to the midface and beaked curved nose. Limb anomalies include clinodactyly of the fifth finger, abnormal finger flexion creases, dislocation of the radial head, and hip dysplasia. This case is commonly diagnosed by clinical findings. In some cases, increased chromosomal breakage has been reported, but cannot be used as a tool for the diagnosis [1], [2].

The rarity of this syndrome, the lack of diagnostic tests, the variety of phenotypic abnormalities, and the abnormalities on different chromosomes make it difficult to prevent and manage Seckel syndrome [1]. The growth and development problems of Seckel syndrome were not equal to normal. Monitoring nutrition, monitoring puberty development, and short stature, so that if there are deviations in growth and development, early intervention can be done. Management of Seckel syndrome in practice is still limited to overcoming existing complaints.

## Case Report

A 9-month-old girl was referred to the pediatric department with the chief complaint of the growth was not suitable for children of their age. Her body weight was 2.7 kg, length was 48 cm. Her head circumference was small and shaped like a bird with a nose that has a curve, micrognathia, and ear malformations (Figure 1). The patient could sit upright without being supported and only shifted the buttocks. The patient did not want to crawl. The patient could reach the cube holding it in each hand, and pick up small objects such as nuts, raisins, or pieces of biscuits. The patient could eat cake by herself and hold milk bottle with some help because her hands were relatively small. When a toy was put out of reach, the patient stretched out her arm trying to get it. The patient was not able to pronounce "papa" or "mama" or imitate certain sounds and when approached from behind by their parents, the patient looked back. The patient routinely brought to a child development clinic to monitor his growth and development. There were no abnormalities in the heart, eyes, hearing, or hormonal. Since birth, the patient was rarely sick, only post-immunization fever. There is no history of another congenital disease in the first and second-degree relative in her mother and father's family. Meanwhile, the great-grandfather of the patient from her father family is stunted (Figure 2).

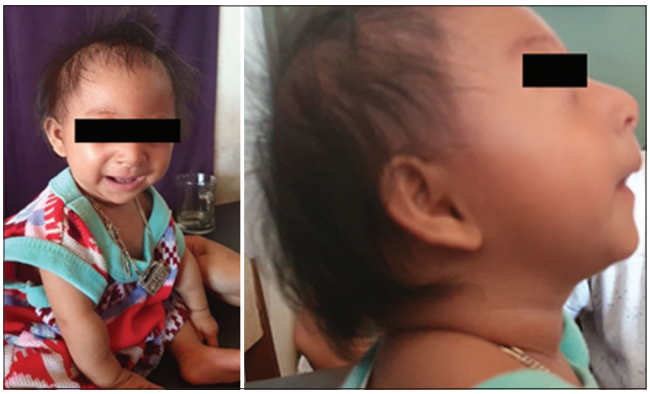

*Figure 1: Facial characteristics (micrognathia, ear malformations, and bird-like face)*

There were no problems during pregnancy, no history of abortion, and routinely checked up with an obstetrician once a month. Her mother ate rice with side dishes (vegetables and chicken/egg/fish) 3 times a day, did not drink special formula milk for pregnant women, but regularly consumed vitamins. Her mother did not suffer from hypertension, diabetes mellitus, heart disease, or asthma. There were no abnormalities in ultrasound examination at the 2$^{nd}$ and 4$^{th}$ month of pregnancy, but at the 7$^{th}$ month of pregnancy, in ultrasound examination, the baby was small and did not match the gestational age with an estimated fetal weight of 700 g and 1150 g at the 8$^{th}$ month of pregnancy. The patient was born prematurely by cesarean delivery due to fetal distress with a weight of 1150 g, length of 35 cm, and head circumference of 25 cm then admitted to NICU for 3 days and in the Level II neonate ward for 9 days with an incubator. The patient was breastfed until 3 months old, formula milk until now, milk porridge from 6 months old until now, filtered pulp from 8 months old until now, and no food allergies.

On evaluation, patient was alert, with a regular and good quality heart rate of 114 beats per minute, respiratory rate of 25 breaths per minute, temperature 36.8°C, and oxygen saturation of 98%. The patient had microcephaly, was bird-headed, and had a prominent curved nose, no down slating fissure eyelid, no deviation conjugate, and no low set ear. There were no gallop or murmur sounds during heart auscultation and normal breath sound. No organ or

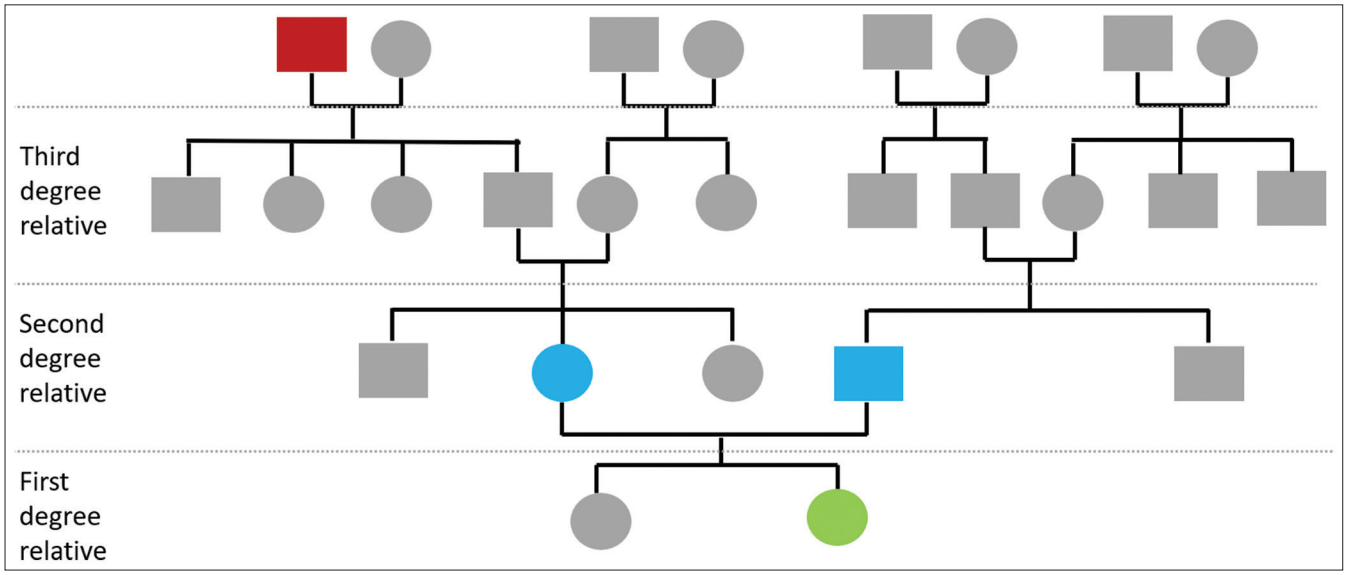


*Figure 2: The family tree of the patient in the first and second degree-relative. The blue color is the patient's parents, green color is the patient. The red color is the great-grandfather of the patient from her father's family is stunted. This picture declared no history of congenital disease or any syndrome in the family history*

masses could be palpated in the abdomen. The remaining neurological examination was normal.

Her body weight was 2.7 kg and length was 48 cm, which is in the z score <−3 standard deviation (severely underweight) in weight for age and the z score <−3 standard deviation (severely stunted) in height for age according to the World Health Organization growth chart and her genetic height potential was 151–168 cm. Her head circumference was 31 cm, which is in the z score <−3 standard deviation (microcephaly). Her nutritional status was well-nourished in the z score in −1 Standard deviation. Her length was 48 cm with an upper segment of 29 cm and a lower segment was 19 cm with an upper/lower ratio was 1.52 (proportional).

The mother stimulates the child's development at all times according to child's age and readiness. The hearing test is within normal limits. On the Denver II, screening was suspect. A cognitive adaptive test/clinical linguistic and auditory milestone scale examination was children with possible mental retardation. Mullen's examination was very low.

The laboratory examination results showed complete blood count, liver, and renal function were within normal limit. The parameter of renal function was BUN at about 20; creatinine serum at about 0.13; and GFR about152 ml/min/1.73 $m^2$. The blood glucose of this patient was 100 mg/dL. Urinalysis was in the normal limit, erythrocyte 8/hpf, and leukocyte 2/hpf. Anti-Rubella IgM non-reactive and Thyroid function tests (TSH and T4) were within normal limit. Insulin-like growth factor-1 head examination was within the normal limit. Evaluation of Otoacoustic Emission Examination was within normal limits. Echocardiography was done for this patient. According to this examination, the cardiac is normal with ventricular ejection fraction (EF teich 65.7%). Bone age examination showed bone architecture and alignment were normal, with no bone fractures and joint dislocations, and no osteolytic or osteoblastic processes. The joint surface and joint space were normal. A bone survey revealed that the bone pattern was appropriate for newborns (28 days) (Figure 3).

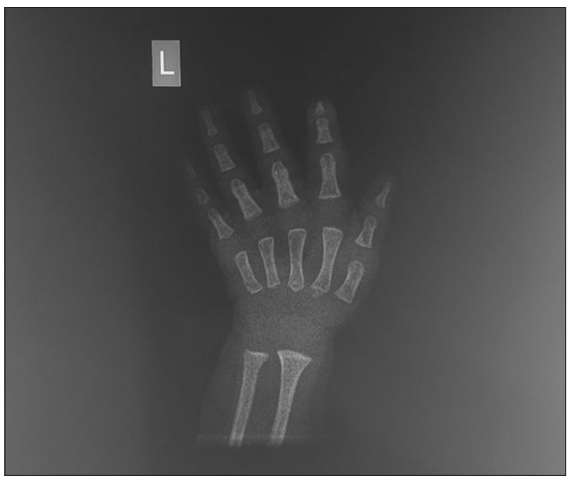


*Figure 3: The bone age is aligned with the age of the newborn*

According to the clinical manifestation and laboratory findings, patient was diagnosed with Seckel syndrome. Genetic confirmation was not common examination in diagnosing Seckel syndrome due to the high cost and unavailable reagent. Thus, we could not determine the subdivision of Seckel syndrome. According to the clinical manifestation and laboratory finding, it is closely related to Seckel syndrome. Treatments are supportive for development and of nutrition to meet the needs of macro and micronutrients. There were no specific treatments.

## Discussion

Minimalizing this syndrome is difficult due to unclear etiology. The previous research has found several loci that are related to the disorder. First, it is known due to defects on chromosome 3q22.1-q24, ataxia-telangiectasia, and Rad3-related protein (ATR) gene for Seckel syndrome 1 (SCKL 1), 18p11.31-q11.2 for SCKL 2, and 14q23 for SCKL 3. It becomes the predominant locus for Seckel syndrome. Besides the heterogeneity of chromosome disorder, the test also requires quite a high amount of time and cost thus this defect is rarely checked. Nowadays, the ATR signaling pathway becomes the most pathway event though ATR genes are not only defects [3].

The characteristic of Seckel syndrome is intellectual disabilities, microcephaly, premature closure of cranial sutures that inhibit brain development, the retardation of intrauterine, postnatal development, and mental retardation. Other physical appearance anomalies are dwarfism appearance, a dysmorphic face called "bird-headed," a prominent beaked nose, large eyes, the antimongoloid slant of palpebral fissures, dysplastic ears, and micrognathia. In addition to delayed bone age, 11 pairs of ribs, strabismus, dysplastic ears, cryptorchidism, clitoromegaly, hirsutism, crowded teeth with malocclusion, agenesis of the corpus callosum, pachygyria, microphthalmia, optic nerve hypoplasia, high-arched palate, enamel hypoplasia, and hypodontia or oligodontia could happen with this disorder [4], [5], [6]. Cardiovascular, hematopoietic, endocrine, and central nervous systems disorders are sometimes found in this syndrome [7], [8], [9].

In Seckel syndrome, several endocrinological disorders can be found, such as decreased production of growth hormone, precocious puberty, stunted growth, and hypoplasia of the adrenal glands. Children with Seckel syndrome can find several problems in the heart and blood vessels, including persistent ductus arteriosus, atrial septal defect, and ventricular septal defects, and aneurysms can also be found in intracranial blood vessels. Several disorders can be found in Seckel syndrome, including agenesis of the

corpus callosum, arachnoid cysts, hypoplasia of the cerebellar vermis, pachygyria, and ventricular dilatation of the brain. Mental retardation occurs in all cases of children with Seckel syndrome, this is due to the small size of the head circumference, which has occurred since the second trimester of pregnancy; therefore, brain growth is inhibited. In some cases, an IQ was found below 50, whereas usually Seckel syndrome sufferers have mild-to-moderate retardation without any delay in motor development, but it can be severe if there are malformations in the brain. In most cases, children are usually very active and friendly to people, but the attention of children with Seckel syndrome is very easy to get distracted. In most cases, the working-up diagnosis of Seckel syndrome has been made by the clinical manifestation, even though the definitive diagnosis is made from gene analyses such as SCKL 1,2 or 3. Availability of the tools and cost become the common problem. Additional examinations needed are an X-ray to check the bone age, frequent hip dysplasia, and dislocation of the head of the radius [9], [10].

Sometimes Seckel syndrome is difficult to distinguish from other disorders because of the similarity of symptoms, such as growth disturbance with microcephaly which is also seen in Dubowitz syndrome, fetal alcohol syndrome, trisomy 18 syndrome, de Lange syndrome, Bloom syndrome, and Fanconi syndrome. Another syndrome that may resemble Seckel syndrome is Cockayne syndrome because it has symptoms such as dwarfism, retinal atrophy, deafness, delayed milestones, and sensitivity to radiation. In addition, progeria also needs to be considered considering its symptoms are similar to Seckel syndromes, such as characterized by retarded physical development, abnormal facies, skeletal abnormalities, and early onset of scleroderma. In distinguishing Hallermann-Streiff from Seckel syndrome, it is necessary to pay attention to the following seven signs, such as (1) dyscephalia and birds face, (2) dental abnormalities, (3) proportional short stature, (4) hypotrichosis, (5) skin atrophy, especially in the nose, (6) microphthalmos. bilateral, and (7) congenital cataracts. Meanwhile, to distinguish it from Dyggve-Melchior-Clausen (DMC) syndrome, it is necessary to pay attention to the presence of microcephaly, short trunk dwarfism, mental retardation, and rough face. Investigations such as radiographs show generalized platyspondyly with double hump end plates, irregularly ossified femoral head, hypoplastic odontoids, and lace-like appearance of the iliac crests. These radiological features are highly pathognomonic of the DMC syndrome. The presence of phenotypic heterogeneity appears to be an obstacle in determining this disorder. This is the reason behind the error or overdiagnosis of the syndrome. Patients with Seckel syndrome can live long lives with mental retardation and physical limitations. Patients with Seckel syndrome can live up to 75 years old. Meanwhile, limited evidence related to life survival rate is still limited [11], [12], [13], [14], [15]. Death in Seckel syndrome is mostly caused by cardiovascular, hematological (acute myeloblastic leukemia), endocrinology, musculoskeletal, and other central nervous system diseases [2].

In this case, the patient was diagnosed with Seckel syndrome because of clinical symptoms and supportive radiological examinations. As for the clinical symptoms that appear to be clinically proportional to dwarfism from the prenatal onset, specific dysmorphic facial features include the presence of severe microcephaly and a bird's-head appearance, and mental retardation. No organ system disorders were involved, nor was specific therapy given. After that, we conduct education about the disease and further complications that may arise.

The growth hormone treatment was indicated for patients that had a history of intrauterine growth and or retardation without sufficient height that can catch it up at 2–4 years. The mean of growth or weight, in this case, was short of gestation age or SGA. This treatment could effectively increase the height of the patient. Their result showed that the children were healthy and had a normal response to GH provocative test. Growth hormone treatment for a long time showed results in an enhancement of final height, and body mass index standard deviation scores (BMI SDS) ranged from −3.0 to −3.9 [16].

## Conclusion

Seckel syndrome is a rare disease. The diagnosis was challenging and sometimes could miss diagnosed with another syndrome. In this case, the diagnosis of Seckel syndrome was made by clinical presentation and laboratory examination. A gene or chromosome examination is needed. Meanwhile, the examination was limited and need a high cost. No specific treatment was given in this case. Commonly, the treatment of this case is supportive and focused on the other abnormalities in each patient. Providing physiotherapy to maintain their mobility, and balance, reduce bony deformities, and improve independence is needed. Family counseling has been done in this case.

## References

1. Cherian MP. Seckel-Like Syndrome or Seckel Variants?. Ann Saudi Med. 2004;24(6):469-72.
2. Faivre L, Cormier-Daire V. Seckel syndrome. Orphanet encyclopedia; 2005 [cited 2020 December 18th]. Available from: URL: orpha.net/data/patho/GB/ uk-Seckel(05).pdf.
3. Tatar A, Ocak Z, Doneray H, Isik E, Yesilyurt A, Ozkan B, Oztas S. Seckel Syndrome with Spontaneous Chromosomal Instability. Turkish Journal of Medical Sciences. 2008;38(1):77–81.

4. Kalay E, Yigit G, Aslan Y, et al. CEP152 is a genome maintenance protein disrupted in Seckel syndrome. Nature Genetics. 2011;43:23–6. https://doi.org/ 10.1038/ng.725.
5. Martin CA, Ahmad I, Klingseisen A, et al. Mutations in PLK4, encoding a master regulator of centriole biogenesis, cause microcephaly, growth failure and retinopathy. Nature Genetics. 2014;46:1283–92. https:// doi.org/10.1038/ng.3122.
6. Shaheen R, Al Tala S, Almoisheer A, Alkuraya FS. Mutation in PLK4, encoding a master regulator of centriole formation, defines a novel locus for primordial dwarfism. J Med Genet. 2014;51:814–6. https://doi.org/10.1136/jmedgenet-2014-102790.
7. Verloes A, Drunat S, Gressens P, Passemard S. Primary Autosomal Recessive Microcephalies and Seckel Syndrome Spectrum Disorders. GeneReviews. Initial 2009;1993-2022.
8. De Coster PJ, VerbeecK RM, Holthaus V, Martens LC, Vral A. Seckel syndrome associated with oligodontia, microdontia, enamel hypoplasia, delayed eruption, and dentin dysmineralization: A new variant? J Oral Pathol Med. 2006;35:639-41.
9. Chanan-Khan A, Holkova B, Perle MA, Reich E, Wu CD, Inghirami G, et al. T-cell clonality and myelodysplasia without chromosomal fragility in a patient with features of Seckel syndrome. Haematologica 2003;88:ECR14.
10. Goswami M, and Anggrawal T. Management of seckel syndrome: a pediatric case report. Journal of Dental Health Oral Disorder and Therapy. 2017;8(5):610-12.
11. Sisodia R, Raj RK, Goel V. Seckel syndrome: a rare case report. J Indian Soc Pedod Prev Dent 2014; 32(2):160-3. https://doi.org/10.4103/0970-4388.130983.
12. Krishna K. Cockayne's syndrome. Indian J Dermatol Venereol Leprol. 1995;61:310-1.
13. Sowmiya R, Prabhavathy D, Jayakumar S. Progeria in siblings: A rare case report. Indian J Dermatol. 2011;56:581-2.
14. Thomas J, Ragavi BS, Raneesha P, Ahmed NA, Cynthia S, Manoharan D, et al. Hallermann-streiff syndrome. Indian J Dermato. 2013;58:383-4.
15. Elalaoui SC, Mariam T, Ilham R, Yassamine D, Abdelaziz S. A recurrent mutation in Moroccan patients with DyggveMelchior-Clausensyndrome: Report of a new case and review. Indian J Hum Genet. 2011;17:97-9.
16. Niels HB, Ole DW, Carsten H, Thomas B, Allan F, Jan F. Growth hormone treatment, final height, insulin-like growth factors, ghrelin, and adiponectin in four siblings with Seckel syndrome. Journal of Endocrinology and Metabolic. 2011;995-1000.