

## A Case Report: Seckel Syndrome in A 5-Years Palestinian Girl

**Basal A Ahmed\***

*Specialist and Head of Pediatrics Department, Shaheed Mohammed Al - Durra Hospital, Palestine*

**\*Corresponding Author:** Basal A Ahmed, Specialist and Head of Pediatrics Department, Shaheed Mohammed Al - Durra Hospital, Palestine.

**Received:** April 29, 2019; **Published:** September 30, 2020

### Abstract

Seckel syndrome (SCKL) is an autosomal recessive (AR) disorder and the most common microcephalic osteodysplastic dwarfism. This syndrome is characterized by pre- and postnatal growth retardation, microcephaly with mental disabilities, and specific features of 'bird-headed like. (Prominent and beaked-like nose, receding forehead, large eyes, narrow face, receding mandible, and dental anomalies). In addition to. The syndrome is an extremely rare form of primordial proportionate dwarfism, the male to female sex ratio is equal, with more than 100 reported cases of SCKL in the medical literature since its original description in 1960, with an incidence of 1: 10,000 live born children.

A five-years-old Palestinian girl was presented to emergency room with typical characteristic symptoms of SCKL which include, short stature, growth failure, bird-headed like, microcephaly, mental disability with history of intrauterine growth retardation (IUGR (and associated with other malformation.

**Keywords:** *Seckel Syndrome; Microcephaly; Bird-headed; Mental Disability and Dwarfism*

### Introduction

Seckel syndrome also known as microcephalic primordial proportionate dwarfism, bird-headed dwarfism, Harper's syndrome, Virchow-Seckel dwarfism, and Bird-headed dwarf of Seckel [1,2]. SCKL is a heterogeneous an AR condition with incidence of 1:10,000 live born children [3-5], presenting at birth. The male to female sex ratio is 9:11 and both sexes are equally severely affected [6]. The syndrome is named after an American physician, Helmut Paul George Seckel [7]. This syndrome is characterized by IUGR and postnatal dwarfism, microcephaly, intellectual disability and characteristic orofacial features [8,9] and may be associated with other abnormalities noted are low-set ears with hypoplastic ear lobules, premature closure of cranial sutures, fifth finger clinodactyly, club foot, scoliosis, dislocation of radial heads, 11 pairs of ribs, cleft lip and palate, gastrointestinal malformations, cardiovascular, endocrine, hematopoietic and central nervous systems abnormalities [10-14].

### Case Report

A 5-year-old Palestinian girl was presented to our emergency room, EL Doura Pediatric Hospital with history of short stature, growth failure, intellectual disability, enuresis and encopresis. Tala is the 3<sup>rd</sup> girl in order of birth. Her parents have five girls. History of normal spontaneous vaginal delivery and uncomplicated pregnancy. Antenatal ultrasound showed IUGR and microcephaly during the second trimester. No similar cases in the family and family histories were unremarkable. Consanguinity was positive.

On physical examination at age of 5 years, her height, weight, and head circumference were 95 cm, 11 kg and 36 cm, respectively (all less than 3<sup>rd</sup> centile). She presented with delayed developmental milestones and severe growth retardation (Tala is short stature, and she was microcephalic). Her motor skills were age-appropriate but reduced muscle mass, her language skills were delayed, she can talk just few words either she is suffering from enuresis and encopresis. Tala has sessions of physiotherapy for Clubfoot. In general, she is a small, slender body habitus, she has typical facial appearance (Figure 1), a narrow face with a prominent beaked-like nose, receding sloped forehead, mandibular hypoplasia, high-arched palate, relatively large ears and large eyes, 4<sup>th</sup> finger clinodactyly, dry skin, erythematous and cold both hands and feet. A diagnosis of Seckel syndrome was made based on these clinical findings.



**Figure 1:** Frontal, Lateral views of the patient, show facial dysmorphisms with a 'bird-headed' appearance, prominent eyes, recessed forehead, a large beaked triangular nose, narrow face, micrognathia and dental anomalies.

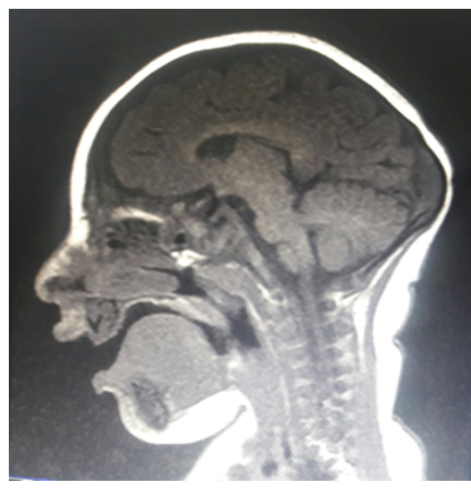
Complete blood count, renal and liver functions test, random blood sugar, serum electrolytes, cervical spine X-ray with skeletal survey, and urine analysis studies were all normal. The bone age was 3 years at a chronological age of 5 yr. Brain MRI reveals microcephaly due to early sagittal suture synostosis without structural abnormalities.

### Discussion

Seckel syndrome is clinically and genetically heterogeneous, AR disorder marked by prenatal proportionate short stature, severe microcephaly, intellectual disability, and characteristic facial features [1,15-17], without significant sex predilection, with a reported incidence of 1:10,000 live born children [3,5] and more than 100 cases have been published in the medical literature since its original description in 1960 [18]. SCKL is belonging to the group of osteodysplastic primordial dwarfism [19,20]. Recently molecular genetics have shown some aberration in a few chromosomes. It can be due to increased chromosomal instability or chromosomal breakage [21]. Chromosomal aberrations causing SCKL, with defective gene localized to chromosomes 2q33.3-34, 18p11.31-q11.2, and 3q22.1-q24 [2,22,23]. There are possibly ten genes linked to SCKL [24]. The parents of our case are first cousins, supporting an AR mode of inheritance. Developmental history in the present case revealed delayed of developmental milestones with history of IUGR and severe postnatal growth retardation. Postnatal growth deficiency (short stature with microcephaly) is on average seen in most cases, but 50% of cases showed association with decreased height [20,21]. Tala has intellectual disability, patients with SCKL exhibit moderate-to-severe mental retardation (intelligent quotient (IQ) < 50 in 50% of cases [15,21].

Craniofacial features of SCKL are striking with microcephaly secondary premature synostosis, “bird-headed profile” with prominent mid-face and beak-like protruded nose, receding forehead, large eyes, narrow face, and micrognathia, high arched palate, crowded teeth [2,9,25]. In the present case, the patient presented with characteristic craniofacial features of a “bird-headed profile.” She has severe microcephaly (below the third centile), receding forehead, low anterior hair line, narrow face, beaked prominent nose, relatively large eyes, relatively large ears, micrognathia, high arched palate and crowded teeth.

Other serious anomalies such as the central nervous system is affected in various degrees by SCKL have been reported in the literature [26-28]. Agenesis of corpus callosum, hypoplasia of the cerebellar vermis, cerebral cortex anomalies, cerebral cyst, pachygyria, open and closed lip schizencephaly, tonsillar herniation, semilobar holoprosencephaly and Chiari I malformation are all have been associated with SCKL [12,26,27,29,30] suggesting an underlying neuronal migration disorder. Craniosynostosis can be associated with SCKL in approximately 50% [9,30]. Brain MRI (Figure 2) for this patient was done, reveal abnormal skull deformity due to premature sagittal suture fusion (scaphocephaly), without structural deformity can be detected. Microcephaly and mental disability were noted.



**Figure 2:** Brain MRI reveal abnormal skull deformity due to premature sagittal suture fusion (scaphocephaly) without structural deformity.

Skeletal findings in SCKL may include hip dysplasia, clinodactyly of 5<sup>th</sup> finger [22], in our patient we found clinodactyly of 4<sup>th</sup> finger (Figure 3). Radiographic features such as microcephaly, steep skull base, asymmetric calvarium, delayed closure of sagittal suture, shortened humeri, bilateral dislocation of elbow, deep antgonial notch, short metacarpals, enlarged metaphysis, absence of secondary ossification centers, and hypoplasia of lower ilia and iliac angle have been reported [31-33]. Skull x-ray reveals microcephaly with steep skull base. Wrist x-ray shows delay bone age. Skeletal survey was normal.



**Figure 3:** Skin changes show erythema and clinodactyly.

Other serious anomalies such as neonatal cholestasis, endocrine (premature pubarche, hyperinsulinism, accompanying hypertriglyceridemia, dyslipidemia, and hyperandrogenism), cardiac (tetralogy of Fallot [TOF], atrial septal defect [ASD] and coarctation of aorta [CoA], cardiomegaly, and cardiac arrhythmias), vascular, gastrointestinal and 15 to 25% of patients have hematological abnormalities (aplastic anemia, pancytopenia, Fanconi anemia and acute myeloid leukemia) have also been reported [12,15,31-33].

Renal disorders such as renal tubular disorders, medullary hypoplasia, renal cysts, or renal hypoplasia are also seen [9,28]. Our patients were investigated for renal anomalies and no abnormalities were detected. Hypoplastic external genitalia, cryptorchidism and clitoromegaly also has been reported [21].

Skin involvement is another rare manifestation of SCKL [33], Brackeen, *et al.* have reported a patient with erythematous, scaly, lichenified plaques on her hands, knees, and feet with the diagnosis of atopic dermatitis and hypopigmented macules and papules on her chest, back, extremities, and sides of her face [34,35]. Our patient has coarse skin change, erythema with relatively coldness in both palms and feet associated with rough scaly skin (Figure 3), these features of atopic dermatitis and may be one of rare feature reported in SECKL till now.

Ophthalmological findings are retinal degeneration, astigmatism, myopia, telecanthus, antimongoloid slant and narrow palpebral fissures and large "bulging eyes" [36,37]. In this case, she has relatively large bulging eyes.

The differential diagnoses from other syndromes of growth deficiency with microcephaly, such as Dubowitz syndrome, fetal alcohol syndrome, Trisomy 18, De Lange syndrome, Bloom syndrome and Fanconi syndrome. Most of these syndromes show features such as microcephaly, facial asymmetry, micrognathia, and discrepancy of mid-facial region. However, Seckel syndrome show other features such as recessed forehead, large nose, 'bird-headed' appearance, and relatively small mandible, which are almost seen in our case reported [9,10,38].

### Management and prognosis

Management should be directed toward diagnosed as early as possible to avoid a possible associated complication such as death caused due to congenital heart disease (TOF, CoA), cardiac arrhythmias, renal disorders, pituitary insufficiency, hematological abnormalities (Fanconi anemia, leukemia), and early intervention, operative correction for craniosynostosis might be considered in children who develop cranial asymmetry [6,39,40]. Genetic counseling is recommended to prevent SCKL and its possible complications. The prognosis depends on the defects presented, but for the delay in growth and impaired mental development, is considered poor. Affected patients with Seckel syndrome do have a normal lifespan [6].

### Conclusion

Seckel syndrome is a clinically and genetically heterogeneous condition due to genes mutation that leads to chromosome instability with consequence of various characteristic features. Karyotype analysis and genetic counseling are essential for the definitive diagnosis. Early diagnosis and management are recommended to prevent the possible poor prognosis and possible associated complications.

### Bibliography

1. Harsha Vardhan B., *et al.* "Bird-headed dwarf of Seckel". *Journal of Indian Society of Pedodontics and Preventive Dentistry* 25 (2007): S8-9.
2. Napolitano R., *et al.* "Prenatal diagnosis of Seckel Syndrome on 3-dimensional sonography and magnetic resonance imaging". *Journal of Ultrasound in Medicine* 28 (2009): 369-374.
3. Kutlu R., *et al.* "Seckel Syndrome with Polyarteritis Nodosa". *Indian Pediatrics* 41.17 (2004): 1158-1161.

4. D'Angelo VA, *et al.* "Multiple intracranial aneurysms in a patient with Seckel syndrome". *Child's Nervous System* 14 (1998): 82-84.
5. Wynbrandt J and Ludman MD. "The encyclopedia of genetic disorders and birth defects". 3<sup>rd</sup> edition. NY: Infobase Publishing (2008): 344-346.
6. Seymen F, *et al.* "Seckel syndrome: report of a case". *Journal of Clinical Pediatric Dentistry* 26.3 (2002): 305-309.
7. Børghlum AD, *et al.* "A new locus for Seckel syndrome on chromosome". *European Journal of Human Genetics* 9.10 (2001): 753-757.
8. Harper RG, *et al.* "Bird-beaded dwarfs (Seckel's syndrome): A familial pattern of developmental, dental, skeletal, genital, and central nervous system anomalies". *Journal of Pediatrics* 70 (1967): 799-804.
9. Gorlin RJ, *et al.* "Syndromes of the Head and Neck". 4<sup>th</sup> edition. USA: Oxford University Press (2001): 387-390.
10. Ramachandran S, *et al.* "Bird-Headed Dwarfism (Seckel Syndrome) - A Rare Case Report TAF". *Preventive Medicine Bulletin* 12 (2013): 209-212.
11. Rappen U and von Brenndorff AI. "Cardiac symptoms in 2 patients with Seckel syndrome". *Monatsschrift Kinderheilkunde* 141 (1993): 584-586.
12. Shanske A, *et al.* "Central nervous system anomalies in Seckel syndrome: Report of a new family and review of the literature". *American Journal of Medical Genetics* 70 (1997): 155-158.
13. Espérou-Bourdeau H, *et al.* "Aplastic anemia associated with "bird-headed" dwarfism (Seckel syndrome). *Nouvelle Revue Francaise d'hematologie* 35 (1993): 99-100.
14. Adiyaman P, *et al.* "Seckel-like syndrome: A patient with precocious puberty associated with nonclassical congenital adrenal hyperplasia". *Journal of Pediatric Endocrinology and Metabolism* 17 (2004): 105-110.
15. Ramalingam K, *et al.* "Seckel syndrome: A report of a case". *Journal of Indian Society of Pedodontics and Preventive Dentistry* 30 (2012): 258-261.
16. Khetarpal P, *et al.* "Primordial dwarfism: overview of clinical and genetic aspects". *Molecular Genetics and Genomics* 291 (2016): 1-15.
17. Goodship J, *et al.* "Autozygosity mapping of a Seckel syndrome locus to chromosome 3q22.1-q24". *American Journal of Human Genetics* 67 (2000): 498-503.
18. Faivre L and Cormier-Daire V. "Seckel syndrome".
19. Mahesh N, *et al.* "Seckel syndrome: A case report of the rare syndrome". *Journal of Dr. NTR University of Health Sciences* 7 (2018): 223-227.
20. Faivre L and Daire VC. "Seckel syndrome. Orphanet Encyclopedia (2005).
21. Cherian MP. "Seckel cell syndromes or Seckel variants?" *Annals of Saudi Medicine* 24 (2004): 469-472.
22. Courtens W, *et al.* "Interstitial deletion 2q33.3-q34 in a boy with a phenotype resembling the Seckel syndrome". *American Journal of Medical Genetics* 71 (1997): 479-485.
23. Ichisima J, *et al.* "Verification and rectification of cell type-specific splicing of a Seckel syndrome-associated ATR mutation using iPSC cell model". *Journal of Human Genetics* 64.5 (2019): 445-458.

24. Sisodia R., *et al.* "Seckel syndrome: a rare case report". *Journal of Indian Society of Pedodontics and Preventive Dentistry* 32.2 (2014): 160-163.
25. Codd PJ., *et al.* "Seckel syndrome and moyamoya". *Journal of Neurosurgery Pediatrics* 3 (2009): 320-324.
26. Thapa R and Muhherjee K. "SCKL with asymptomatic tonsillar herniation and congenital mirror movements". *Journal of Child Neurology* 25 (2010): 231-233.
27. Kumar R., *et al.* "Semilobar holoprosencephaly in SCKL". *The Indian Journal of Pediatrics* 75 (2008): 519-520.
28. Can E., *et al.* "A case of SCKL with tetralogy of Fallot". *Genetic Counseling* 21 (2010): 49-45.
29. Hopkins T and Haines S. "Rapid development of Chiari I malformation in an infant with Seckel syndrome and craniosynostosis. Case report and review of the literature". *Journal of Neurosurgery* 98.5 (2003): 1113-1115.
30. Thompson E and Pembrey M. "Seckel syndrome: An over diagnosed syndrome". *Journal of Medical Genetics* 22 (1985): 192-201.
31. Borglum AD., *et al.* "A new locus for Seckel syndrome on chromosome". *European Journal of Human Genetics* 9 (2001): 753 - 757.
32. Doro Y. "Seckel syndrome in Hematology: Basic Principles and Practice E- Book: Basic Principles and Practice". The seventh edition. Editors Siberstein L, Heslop H, Weitz J, Anastasi J, Salama M and Abutalib S (2018): 350-394.
33. Bobabilla-Morales L., *et al.* "Chromosome instability induced in vitro with mitomycin C in five Seckel syndrome patients". *American Journal of Medical Genetics Part A* 123A.2 (2003): 148-152.
34. Brackeen A., *et al.* "Pigmentary changes and atopic dermatitis in a patient with SCKL". *Pediatric Dermatology* 24 (2007): 53-56.
35. Unal Y., *et al.* "Anesthetic management of a patient with SCKL and implanted pacemaker". *Paediatric Anaesthesia* 18 (2008): 676-677.
36. Guirgis M., *et al.* "Ocular manifestations of Seckel syndrome" 132.4 (2001): 596-597.
37. Aktas Z., *et al.* "Childhood glaucoma as an ophthalmic manifestation of SCKL". *Journal of Glaucoma* 22 (2013): e3-e4.
38. Ucar B., *et al.* "SCKL associated with atrioventricular canal defect: a case report". *Clinical Dysmorphology* 13 (2004): 53-55.
39. Majoor-Krakauer DF., *et al.* "Microcephaly, micrognathia, and bird-headed dwarfism: Prenatal diagnosis of a Seckel-like syndrome". *American Journal of Medical Genetics* 27 (1987): 183-188.
40. Goswami M and Aggarwal T. "Management of Seckel Syndrome: A Pediatric Case Report". *Journal of Dental Health, Oral Disorders and Therapy* 8.5 (2017): 00301.

**Volume 9 Issue 10 October 2020**

**©All rights reserved by Basal A Ahmed.**