Case Report
Seckel Syndrome

Dr. Jaishree Vasudevan,* Dr. Karthik Surya R,** Dr. Thayumanavan S***

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Dr. Jaishree Vasudevan obtained her M.B.,B.S degree from the prestigious Devi Ahilya Vishwa Vidyalaya Indore in 1993 and her M.D degree in Paediatrics in 1996 from Pandit Ravi Shankar Shukla University , Raipur. She worked in Indraprastha Apollo hospital, Delhi following post-graduation and relocated to Chennai in 2000. She joined the present institution as Assistant Professor , Paediatrics in 2006 and is presently working as Associate Professor. Her special interests are genetics and nutrition in Paediatrics.

*Associate professor, **Senior Resident, ***Professor & HOD, Dept. of Paediatrics

Abstract

Though short stature is not uncommon in pediatric practice, there are only a few conditions where the growth retardation is very severe. One of them is Seckel syndrome, which is a cause for primordial dwarfism, and is extremely rare. The reported incidence is 1 in 10000[1] live births. We report a case of Seckel syndrome in a 14 month old child.

Key-words: Seckel Syndrome, Short stature, Dwarfism

Case report

14 months old male baby born of 3rd degree consanguinous marriage presented with dyspnea and tachypnea of 2 days duration, with past history of recurrent upper respiratory tract infection. The patient was a preterm baby with intrauterine growth retardation and was delivered at 32 weeks gestation age with a birth weight of 750 grams. He was admitted in NICU for the first 15 days of life and USG cranium showed features of hypoxic ischemic encephalopathy.

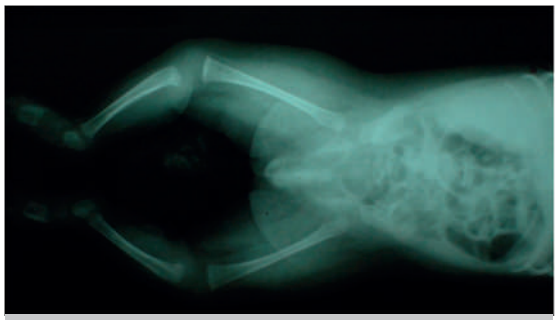

Figure 1 X ray both knees, showing delayed skeletal maturation

Figure 2 Clinical photograph

At present the child's chronological age is fourteen months. He weighs 2.4kg, length is 49.5cms and his head circumference is 34.5 cm. All these parameters fall below the 5th percentile. He has a flat occiput and sparse scalp hair. His anterior fontanelle is closed. He has an antimongoloid slant, low set small ears, prominent eyes, beaked nose, micrognathia, 5th finger clinodactyly and left undescended testis with mild hypotonia.

He has achieved head control and rolls over and creeps. He is active, babbles and recognizes immediate care givers. He is anemic with hemoglobin of 9.4gm%. He is euthyroid. X-rays of his skull and both hands showed findings of clinodactyly, delayed skeletal maturation and relative microcephaly with normal sutures. Chromosomal studies revealed a normal karyotype. These findings and his phenotype are consistent with Seckel syndrome.

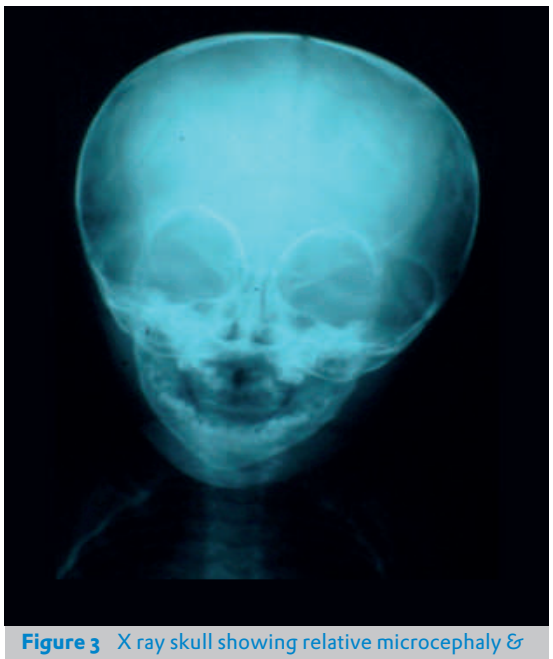

Figure 3 X ray skull showing relative microcephaly & normal sutures

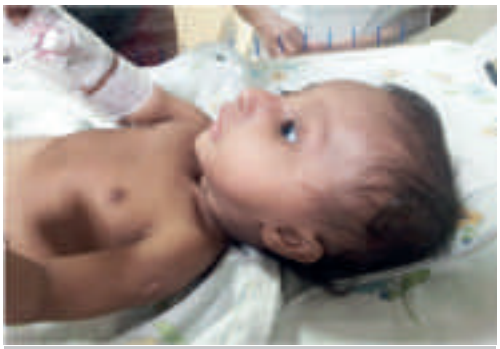

Figure 4 Clinical photograph – prominent nose, micrognathia (bird headed dwarfism)

Discussion

Seckel syndrome is a genetic disorder characterized by microcephaly and mental retardation with unique facial features with large eyes, beak like nose, narrow face and receding lower jaw[2]. Mental retardation is not as marked as might be expected in view of the very small brain[3]. The signs and symptoms of Seckel syndrome may be similar to those of another condition called microcephalic osteodysplastic primordial dwarfism type 2. Microcephalic osteodysplastic primordial dwarfism (MOPD) is characterized by intrauterine and postnatal growth retardation, short limbs (brachymelia), and microcephaly. However MOPD2 is associated with abnormalities of the bones which can be identified by performing X-rays during the first years of life. The humeri and femora are broad, shortened, and bowed in MOPD 2.

Seckel syndrome is a heterogeneous, autosomal recessive disorder that has been subclassified into types 1 through 4 depending on linkage to different chromosomal regions (3q22, 18p11, 14q, 21q22.3). The clinical characteristics of patients with Seckel syndrome type 4 (chromosome 21q22.3-qter; OMIM 611860) are similar to those of patients with other subtypes. Griffith et al[5], utilizing a genome wide association procedure in 2 consanguineous families with Seckel syndrome members, also localized the disorder to chromosome 21q22.3 and identified homozygous inactivating (nonsense, single base pair deletion or insertion) mutations in pericentrin 2 (PCNT2) in affected patients.

The centrosome is a cytoplasmic organelle that prepares the mitotic spindle for chromosome segregation and also regulates progression of the cell cycle through mitosis. Pericentrin 2 (PCNT2) is a centrosomal protein that is essential for the integrity of the mitotic spindle as it links the microtubules of the mitotic spindle apparatus to the centrosomal core. PCNT2 is also involved in the process of normal cell division at the G2-M checkpoint. Thus, loss of PCNT2 likely results in cell death because of defects in both chromosome segregation and mitosis. Rauch et al[6] and Griffith et al[5] have described clinical syndromes associated with biallelic loss-of-function mutations in the gene encoding PCNT2—also termed kendrin (PCNT2 - chromosome 21q22.3-qter - OMIM 605925).

The reason that loss-of-function mutations in PCNT2 result in 2 clinically similar (microcephaly, facial features, growth retardation) but distinct (proportionate versus non-symmetrical short stature, reasonably normal mentation versus developmental delay) disorders of MOPD II or Seckel syndrome is uncertain. It has been suggested that in MOPD II, the PCNT2 mutations may adversely affect function of the centrosome, while in Seckel syndrome the mutations may impair mitotic progression. Life span in primordial dwarfism is around 30 years8 of age, but survival up to 75 years has been reported[2].

Diagnostic criteria: [7]

Association of

- Proportionate dwarfism of prenatal onset
- Characteristic dysmorphic features including severe microcephaly and bird headed like appearance.
- Mental retardation
- Autosomal recessive inheritance.

Diagnosis:[7]

In most cases diagnosis depends on clinical findings. Increased chromosomal breakage has been reported but not in all patients. X-ray features include retarded bone age, dysplasia of the hip and dislocation of the head of the radius.

Antenatal Diagnosis:[7]

Recurrence of the disease can be suspected by observation of intrauterine growth retardation with microcephaly in the second trimester of pregnancy when a first child was born with Seckel syndrome. Linkage studies are difficult to use even in consanguineous families because of the heterogeneity of the disease. Early antenatal diagnosis can be performed for a couple who have had a first child with Seckel syndrome if the familial mutations have been identified.

Complications:[7]

Pancytopenia and acute leukemia have been reported in a few children with Seckel syndrome.

References

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LDL-C – BAD BOY AT ANY LEVEL?

We all know that a high level of bad cholesterol (LDL-C) is not good for the heart. Keeping this bad boy in check is the therapeutic and dietary goal of every cardiologist. Does it mean that it is good to have a persistently low level of LDL-C? If we are to go by the results of a study presented at the 61st Annual Scientific Session of the American College of Cardiology that is not the case. In that study, Dr. Paul Michael Lavigne and his co-workers from Tufts Medical Center in Boston found that persistently low level of LDL-C (unrelated to intake of cholesterol lowering drugs) increases the risk of cancer. This matched case control study was carried out on 201 cancer patients and 400 cancer free controls. Both groups were also matched by age, gender, tobacco use, blood pressure, body mass index, diabetes, and other factors. They found consistently low levels of LDL-C in cancer patients. Of course, it does not mean that low LDL-C level invariably leads to cancer. For the present, persons with high LDL-C should continue to follow cholesterol lowering guidelines.

http://www.nlm.nih.gov/medlineplus/news/fullstory_123357.html

- Dr. K. Ramesh Rao

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