CASE REPORT

Antenatal Diagnosis of Seckel Syndrome

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Introduction

Seckel syndrome, first described in 1960 is characterized by proportionate dwarfism of prenatal onset, microcephaly, and typical “bird-headed” profile (concurrent occurrence of beaked nose, receding forehead, prominent eyes, and micrognathia). It involves deoxyribonucleic acid (DNA) damage repair genes which cause chromosomal instability.

Case Report

Evaluation of the fetus in a 29-year-old primigravida showed severe intrauterine growth restriction with complex brain malformation with fetal dysmorphism. The family and past obstetric history is unremarkable, with non-consanguineous marriage.

Her previous scans included one at 12 weeks for nuchal translucency, and another an anomaly scan at 19 weeks, which both were unremarkable. In late second trimester, clinician had suspicion of growth restriction, and the sonographic examination demonstrated a complex brain malformation with severe intrauterine growth restriction (Table 1). Three-dimensional ultrasound (Fig. 1) showed facial dysmorphism—beaked nose with hypotelorism with mild proptosis with micrognathia.

The concurrent occurrence of complex brain anomalies with “bird headed” facial features with severe growth restriction led to a probable diagnosis of Seckel syndrome. The couple was counseled regarding the progressive nature and poor prognosis of the syndrome. Eventually, the patient had premature rupture of membranes and had preterm labor; she delivered a preterm male baby who died within 12 h of delivery.

Fetal chromosomal analysis was performed, and 25 metaphyses were studied. Mitomycin C stress test (50 ng/ml of mitomycin C for 48 h) was also performed to look for chromosomal breakage and radial formations, but the results were within normal limits. At birth, the baby weighed 886 g, length was 36 cm, and head's circumference was 20 cm, which were below third centile for the gestational age.

Postnatal examination (Fig. 2) and magnetic resonance imaging (MRI) examination (Fig. 3) of the baby corroborated antenatally identified facial features and brain abnormalities and confirmed the diagnosis of Seckel syndrome.

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Table 1 Ultrasound scans performed at regular intervals and their findings showing progressive growth restriction with complex brain anomalies and facial dysmorphism

Date	POG–LMP	POG–USG	Findings
08/11/2010	7 weeks 5 days	7 weeks 3 days	Unremarkable
10/12/2010	12 weeks 2 days	12 weeks 1 day	Unremarkable
25/01/2011	18 weeks 6 days	18 weeks 4 days	Unremarkable
18/04/2011	30 weeks 5 days	BPD—23 weeks 4 days AC—27 weeks 1 day FL—30 weeks 2 days	Microcephaly, attenuated lateral ventricles with interhemispheric cyst
19/04/2011	30 weeks 6 days	BPD—22 weeks 6 days HC—22 weeks 6 days AC—26 weeks 1 day FL—29 weeks 1 day	Microcephaly, brachycephaly, agyria, agenesis of corpus callosum, midline cranial fluid collection? schizencephalic cyst Dysmorphic facial features, hypotelorism with mild proptosis with micrognathia

POG period of gestation, *LMP* last menstrual period, *USG* ultrasonography, *BPD* biparietal diameter, *HC* head circumference, *AC* abdominal circumference, *FL* femur length

Fig. 1 Three-dimensional surface rendering of fetal profile showing large, prominent eyes, a beaked nose, and micrognathia with a receding chin **Fig. 3** Sagittal view of the fetal brain MRI showing large arachnoid cyst with absence of corpus callosum with gross cerebral atrophy **Fig. 2** Postnatal picture showing severe microcephaly and micrognathia typical for the description “bird-headed” dwarfism

Discussion

Antenatal ultrasonographic findings of severe intrauterine growth restriction with microcephaly, micrognathia, and facial dysmorphology with brain anomalies (agenesis of corpus callosum, large arachnoid cyst, absence of ventricular system) were confirmed through postnatal examination as Seckel syndrome.

Postmortem MRI delineated late absence of ventricular system suggestive of progressive and severe brain atrophy.

Classical Seckel syndrome with characteristic findings may be identified antenatally but milder cases known as Seckel variants are difficult to diagnose. As in the case of the “bird-headed” dwarfism, severe brain atrophy manifesting as the absence of ventricular system is late

Table 2 Different studies describing prenatal and postnatal findings in Seckel Syndrome

	Mielke et al. [1]	de Elejalde and Elejalde [2]	Majoor-Krakauer et al. [3]	Featherstone et al. [4]	Napolitano et al. [5]	Present study
GA at diagnosis, weeks	32	21	27	30	31	30
Family history	?	?	+	–	–	–
Sonographic findings/ associated anomalies	?	+	+	+	+	+
FGR	?	+	+	+	+	+
Microcephaly	?	+	+	+	+	+
Hypotelorism	?	–	+	+	+	+
Beaked nose	?	+	–	+	+	+
Micrognathia	?	+	–	+	+	+
Downslanting palpebral fissures	+	?	–	?	?	?
CNS anomalies	?	?	?	+ (encephalocele) ^a	+ (arachnoid cyst, corpus callosum distortion) ^a	+ (agenesis of corpus callosum, arachnoid cyst, absence of ventricular system) ^a
Additional postnatal findings	?	?	–	Low-set ears, clinodactyly, hypertonia, hyperreflexia	High arched palate, low-set ears, 5th finger clinodactyly, flexion contractures of knees	High arched palate, low-set ears

CNS central nervous system, GA gestational age, FGR fetal growth restriction

^a Detected or confirmed on MRI

appearing and progressive; it is not unusual to miss them at an early gestational age. However, with the advent of 3D ultrasonography, facial dysmorphism can be diagnosed earlier.

It is autosomal recessive in mode of inheritance with 25 % risk of recurrence. As the underlying genetic defect has not been elucidated and the chromosomal instability is not universal, antenatal diagnosis and recurrence could be suspected by observation of intrauterine growth restriction with microcephaly in a family with history of Seckel syndrome.

This is the sixth report describing perinatal diagnosis of Seckel syndrome, and third which has attempted to make an antenatal diagnosis of Seckel syndrome (Table 2).

Conclusion

In the event of severe intrauterine growth restriction with complex brain malformations detected prenatally, 3D ultrasonography is of the utmost importance to pick up

facial dysmorphism if any and is very helpful in identifying characteristic facial features of the underlying genetic syndrome. Postmortem examination helps in establishing the diagnosis and risk assessment for recurrence in future pregnancy.

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