

Silver: Russell Syndrome with Cryptorchidism

Sir,

An 8-year-old boy was admitted for evaluation of bilateral undescended testes and short stature. The boy is a product of non-consanguineous marriage and was delivered at term with birth weight of 1.5 kg. The parents noticed a mild facial asymmetry since birth and poorly developed scrotum with absent testicles. After evaluation, the parents were informed that the testicles would descend in the next few months. His motor and mental milestones were normal and he has average scholastic performance. The parents noticed that the child was shorter than peers. Parents denied birth trauma or any similar illness in other family members. Examination revealed severe short stature (100 cm, <3rd centile), height SDS-5, upper/lower segment ratio – 0.9, head circumference – 51 cm and underweight (10 kg, <3rd centile). He had triangular facies [Figure 1a], hemiatrophy, microdontia with caries [Figure 1b], sparse subcutaneous tissue, clinodactyly [Figure 1c] and bilateral cryptorchidism [Figure 1d]. The rest of the systemic examination was normal. He was diagnosed as a case of Silver-Russell syndrome (SRS). It is a heterogenous syndrome characterized by severe intrauterine growth retardation, relative macrocephaly, triangular face, clinodactyly, and skeletal asymmetry.^[1] Our patient had all the classical features of the syndrome resulting in the clinical diagnosis of SRS.

Cryptorchidism is reported in only 15% of patients with SRS.^[2] Further investigations revealed normal hematological, biochemical, and thyroid functions. His bone age was 6 years and had normal stimulated growth hormone (15 ng/ml) and testosterone (0.68 ng/ml) values. Ultrasonography revealed right testis in the inguinal area and non-visualization of left testis. A diagnostic laparoscopy found atrophic left testis in the abdominal cavity and the same was removed with correction of the right testis location. The parents were counselled regarding the need of growth hormone therapy.

SRS is associated with the genetic imprinting errors on centers situated on chromosomes 7 and 11p15. Maternal uniparental disomy of chromosome 7 is seen in about 10% of cases and hypomethylation of IGF2/H19 locus on 11p15 is seen in 60% of cases.^[3] There exists a strong correlation between the clinical phenotype and the extent of hypomethylation. Extremely hypomethylated patients present with congenital aplasia of the uterus and vagina in females and cryptorchidism or testicular agenesis in males.^[4] Our patient had bilateral cryptorchidism suggesting a severe methylation defect in 11p15 locus. The severe growth retardation in SRS is due to lower IGF-II, growth hormone GH deficiency, disordered GH axis and H19 hypomethylation. The growth retardation in our patient could be due to lack of downstream signaling molecules of growth hormone. Our



Figure 1: Clinical photograph

patient had normal stimulated growth hormone (15 ng/mL) level and hence the defect could be due to low IGF II and H19 hypomethylation. The exact cause of short stature could not be ascertained due to lack of facilities in our laboratory.

**Babul Reddy H, Neelaveni K¹,
Hari Kumar KVS²**

Consultant Endocrinologist, ESI Hospital, Sanath Nagar, Hyderabad, ¹Departments of Endocrinology, Osmania General Hospital, Hyderabad, ²Command Hospital, Lucknow, Uttar Pradesh, India
E-mail: hariendo@rediffmail.com

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DOI:
10.4103/2141-9248.121226