**A rare case of Silver–Russell syndrome associated with growth hormone deficiency and urogenital abnormalities**

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**ABSTRACT**

**Introduction:** Silver–Russell syndrome (SRS) is a very rare genetic disorder. This is usually characterized by asymmetry in the size of the two halves or other parts of the body. **Background:** We are presenting a case of SRS with growth hormone (GH) deficiency and urogenital abnormalities. **Case Report:** A 15-year-old boy a product of non-consanguineous marriage brought with a history of short stature and poor development of secondary sexual characters. There were no adverse perinatal events, but weighed 1500 g (<3rd centile) at birth. He had delayed developmental milestones. He has had a poor appetite and feeding difficulties since childhood. On physical examination, he had a broad forehead, triangular facies, and low-set prominent ears. Asymmetry of the face, upper and lower extremities was noted, with hemihypertrophy on the right side. His height was 119 cm (<3rd centile) and weight was 18 kg which were low (<3rd centile) as per his age. He was biochemically euthyroid and GH stimulation testing with clonidine (0.15 mg/m²) showed low GH levels at 30’, 60’, and 90’ were 1.7, 1.6, and 1.1 ng/ml, respectively. On micturatingcystourethrogram, grade V complex was noted on the right side. Dimercaptosuccinic acid (DMSA) showed normal functioning kidneys. He was started on recombinant GH with a height velocity of 10 cm/year. **Conclusion:** Urogenital abnormalities are rare but well described anomalies associated with SRS, and all cases have to be screened for them. GH deficiency is not uncommon in SRS, and GH treatment proves to be beneficial.

**Key words:** Silver-Russell syndrome, growth hormone deficiency, urogenital anomalies

**INTRODUCTION**

Silver and Russell were the first to describe a syndrome of intrauterine dwarfism recognizable at birth with craniofacial dysostosis, hemihypertrophy, disproportionately short arms, and other anomalies.[1,2] Although each of the two authors described rather different findings, the composite features were later identified with the combined term Silver–Russell syndrome (SRS). It is characterized by short stature, frontal bossing, small triangular facies, sparse subcutaneous tissue, shortened and incurved 5th fingers, and in many cases, asymmetry. The diagnosis is based on distinct prenatal growth restriction and the presence of typical dysmorphic features, including short stature and limb asymmetry.[3] Here, we are presenting a case of SRS with growth hormone (GH) deficiency and urogenital abnormalities.

**CASE REPORT**

A 15-year-old boy product of non-consanguineous marriage presented with a history of short stature and poor developmental of secondary sexual characters. He was the second pre-term infant, without history of birth asphyxia. At birth, his weight was less than 1500 g (<3rd centile) and length was 43 cm (<3rd centile). He had delayed developmental milestones. He has had a poor appetite and feeding difficulties since childhood. He had one more brother with normal body habitus.
On physical examination, he was well-appearing, thin, and short with normal head circumference, with a broad forehead, triangular facies, and low-set prominent ears. Asymmetry of the face, upper and lower extremities was noted, with hemihypertrophy on the right-side [Figure 1]. His height was 119 cm (<3rd centile) and weight was 18 kg which were low (<3rd centile) as per his age. No cafe-au-lait macules were noted.

All basic investigations were within the normal limit. On provocative GH stimulation with clonidine (0.15 mg/m²) showed low GH levels at 30, 60, and 90′ were 1.7, 1.6, and 1.1 ng/ml, respectively. On micturatingcystourethrogram, grade V complex (vesicoureteric reflex) was noted on right side reflecting abnormalities in urethral valves [Figure 2]. DMSA showed normal functioning kidneys. Chromosome analysis could not be done because of financial reasons. Intelligence and psychomotor development were normal as per his socioeconomic status.

**DISCUSSION**

SRS is also called asymmetry dwarf-dysgenesis syndrome.[4] SRS was first described by Silver and colleagues in 1953 and later by Russell in 1954. Clinically and genetically SRS is a heterogeneous disorder, and the underlying defect is unknown. Chromosome abnormalities have been found to be associated with the disease; among them chromosomes 7 and 17 are frequently involved. In 7% of sporadic cases, maternal uniparental disomy of chromosome 7 has been detected. Recent findings suggested that imprinting defects in the region of 11p15 also play a role in SRS.[5]

Over, the past several years, more than 400 patients with mild to classic phenotypes have been described. The estimated incidence of SRS ranged from 1 in 3000 to 1 in 100,000 but there was no such epidemiological data available in India. Male and female children are equally affected.

The clinical features of SRS involve poor growth, low birth weight, short height, asymmetry between two sides of the body, and genital anomalies. In our case, the involved diagnostic features were intrauterine growth restriction, a triangular-shaped face, asymmetry of the face, upper and lower extremities with hemihypertrophy on the right side. Haslam et al.[6] reported renal abnormalities (abnormal excretory urograms, unilateral chronic pyelonephritis, unilateral ureteropelvic obstruction, severe vesicoureteral reflux, and unilateral pyelonephritis). The prevalence of these abnormalities in SRS necessitates a complete urogenital evaluation, including appropriate radiologic examinations.

Pathophysiologically, growth failure is a primary abnormality. Patients typically present with intrauterine growth retardation, difficulty in feeding, failure to thrive, or postnatal growth retardation. Adequate catch up growth often does not occur, and GH insufficiency may be present and subnormal responses to provocative GH stimulation have been reported in a significant number of children with SRS.[7] GH therapy is often considered for a child with SRS who has not manifested adequate catch-up growth at the age of 2 years. The use of GH was approved by the US Food and Drug Administration in 2001 in children born small for gestational age who have not yet manifested adequate catch-up growth at the age of 2 years.

In conclusion, urogenital abnormalities are rare but well described anomalies associated with SRS and all cases have
to be screened for them. GH deficiency is not uncommon in SRS, and GH treatment proves to be beneficial.

REFERENCES


