Russell–Silver syndrome associated with low conus medullaris

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ABSTRACT

Russell–Silver syndrome is a rare heterogeneous disorder mainly characterized by intrauterine and postnatal growth retardation, craniofacial disproportion, clinodactyly, variation in urogenital development, and skeletal asymmetry. It is rare to come across tethered cord-associated Russell–Silver syndrome. We report a rare case of Russell–Silver syndrome associated with low conus medullaris in a 2-year-old patient with demonstrative phenotype. Magnetic resonance imaging indicated a low conus medullaris at the inferior border of the L3 vertebral body. Urodynamic study revealed detrusor-sphincter dyssynergia and detrusor overactivity. A decision to follow-up the patient was made because of the suspicion of tethered cord syndrome. Even though tethered cord syndrome is not a common finding in Russell–Silver syndrome, it is important to consider tethered cord syndrome to avoid scoliosis and other long-term complications.

Key words: Clinodactyly, overactive detrusor, Russell–Silver syndrome, scoliosis, tethered cord syndrome

Introduction

Russell–Silver syndrome is a very rare genetic disorder. Russell and Silver described the disorder separately in 1953 and 1954, respectively. Russell described a syndrome of “intrauterine dwarfism” concomitant with craniofacial dysostosis, short arms, and other anomalies, while Silver described a syndrome of congenital hemihypertrophy, short stature, and elevated urinary gonadotrophins. The composite features were later identified with the combined term Russell–Silver syndrome.[1]

Russell–Silver syndrome is a genetically heterogeneous disorder, with a very wide variation in phenotype. It is also the first human disorder related with epigenetic mutation affecting two different chromosomes. Although the incidence of Russell–Silver syndrome is largely unknown, it is estimated to be 1 in 50,000–100,000 births.[1]

Price et al. described the major features of Russell–Silver syndrome: low birth weight (−2 standard deviation [SD]), poor postnatal growth ≤ −2 SD, and preservation of occipitofrontal circumference and asymmetry.[3]

Here, we present a rare case of Russell–Silver syndrome associated with low conus medullaris. Neurological findings are considered to be infrequent in Russell–Silver syndrome, However, Tubbs et al. reported a case of Russell–Silver syndrome with tethered cord.[1] This is believed to be the first and only reported case of Russell–Silver syndrome associated with tethered spinal cord until now.

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Case Report

We report a rare case of a 2-year-old male child, a product of nonconsanguineous marriage, who was clinically diagnosed as Russell–Silver syndrome associated with low conus medullaris. The patient presented with characteristic features of Russell–Silver syndrome, such as intrauterine growth retardation with subsequent marked postnatal growth impairment, body asymmetry, and triangular face. He was the third preterm infant, without a history of birth asphyxia. Because of preeclampsia, the mother underwent a cesarean delivery at 32 weeks of gestation. At birth, his weight was 1140 g, length was 34 cm, and had a head circumference of 28 cm. He has two more brothers with normal body habitus. There was no family history of dwarfism. Chromosome analysis could not be done because of financial reasons.

On physical examination, the patient was well appearing, but short and thin, with triangular facies, broad forehead, and low-set prominent ears. Asymmetry of the face with left eyelid ptosis, micrognathia, high-arched palate and downturned mouth corners, and hemihypertrophy on the right side, involving the lower limb and cryptorchidism, were also noted [Figure 1]. His height was 71 cm and weight was 6450 g, which were low as per his age, and his head circumference was 45 cm.

There were no cutaneous findings, such as café-au-lait macules or occult spinal dysraphism. No evidence of clonus or spasticity in his extremities was identified.

All the basic investigations were within the normal limit, including the level of the hormones. Magnetic resonance imaging (MRI) was obtained and it revealed a conus medullaris at the inferior border of the L3 vertebral body and L5-S1 posterior vertebral fusion defect [Figure 2]. No scoliosis was identified in our patient. However, urodynamic study showed overactive detrusor and detrusor-sphincter dysynergia which could indicate the presence of tethered cord syndrome. The patient was taken into follow-up with suspicion of tethered cord syndrome.

There was a delay in the early motor milestones owing to the decreased muscle bulk. According to Denver II developmental screening test, which was performed at the age of 14 months, language development was 14 months degree, fine motor development was 11.5 months degree, gross motor development was 10 months degree, and personal–social development was 13 months degree. No other clinicopathological findings were observed.

Additional informed consent was obtained from the patient’s legal guardian for whom identifying information is included in this article.

Discussion

Russell–Silver syndrome is a genetically heterogeneous disorder with each case having varying symptomatology. The degree of heterogeneity of the syndrome is emphasized by the large number of different potential genetic bases which have been put forward as causal.

Maternal uniparental disomy of chromosome 7 (mat-UPD(7)) was for many years the only recognized genetic abnormality in patients with Russell–Silver syndrome, accounting for approximately 10% of all cases. The phenotype of children with Russell–Silver syndrome and mUPD(7) is thought to differ from other Russell–Silver cases with less distinct facial characteristics, less micrognathia, and no downturned corners of the mouth reported. Nearly 50% of the patients have methylation defects on chromosome 11.[4,5] However, 40% of the patients have reported with no known genetic etiology.

Russell–Silver syndrome is characterized by severe intrauterine and postnatal growth retardation. It is also characterized by clinical features such as hemiatrophy, asymmetry, triangular face, high forehead, preserved head circumference, prominent low-set ears, small jaw, clinodactyly, camptodactyly, skeletal...
asymmetry, hypospadias, spinal deformity-scoliosis and/or kyphosis. Urogenital anomalies, growth hormone deficiency, congenital heart disease, and cleft palate or limb defects have also been reported.

There is no pathognomonic radiological feature for Russell–Silver syndrome, but delayed bone age, clinodactyly, phalangeal hypoplasia, ivory epiphyses, and second metacarpal pseudoepiphysis have been reported as suggestive features.

Neurological findings are considered to be infrequent in Russell–Silver syndrome. The case reported by Tubbs et al. describes the occurrence of Russell–Silver syndrome with tethered cord in a 20-year-old male. The patient also had a thoracic-progressing levscoliosis. In the MRI, conus medullaris was seen at the superior border of the L3 vertebral body with no fatty filum. One of the suggestions made by the authors was the possibility that an undiagnosed spinal cord tethering might be the culprit of some of the scoliosis cases that are associated with Russell–Silver syndrome.

Yamaguchi et al. performed a study that is considered to be the largest report in the English literature on spinal deformity in Russell–Silver syndrome. The study determined the prevalence of scoliosis and kyphosis in the general population of persons with Russell–Silver syndrome and it included 163 patients. The researchers considered that patients with Russell–Silver syndrome have a high prevalence of spinal deformity. Of the 163 respondents, 14% reported scoliosis, 3.1% reported kyphosis, and 3.8% reported both kyphosis and scoliosis, with an average age of diagnosis of 8 years.

Urologic abnormalities are frequently found in patients with Russell–Silver syndrome. Haslam et al. and Arai et al. reported abnormal excretory urograms, unilateral chronic pyelonephritis, unilateral ureteropelvic obstruction, severe vesicoureteral reflux, and horseshoe kidney. These clinical features occur frequently in VATER syndrome which has a known propensity for tethered cord syndrome. We did not diagnosed any structural anomaly of the urinary system in our patient, but urodynamic study showed overactive detrusor and detrusor-sphincter dyssynergia. Anticholinergic therapy was started.

With at least 40% of the cases with an unknown etiology, Russell–Silver syndrome has a range of phenotype from mild to severe, with heterogeneous genetic features and a heterogeneous group of conditions.

**Conclusion**

Russell–Silver syndrome has a very wide variety of phenotypes and clinical findings. Tethered cord syndrome is not a frequent component of Russell–Silver syndrome. There could be an association between tethered cord syndrome and scoliosis, which is seen in Russell–Silver syndrome, but there are not enough cases described in literature to prove this correlation. However, it is important to consider tethered cord syndrome in patients with Russell–Silver syndrome, to avoid scoliosis and other long-term complications.

**Declaration of patient consent**

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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**Conflicts of interest**

There are no conflicts of interest.

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