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Case Report

Clinical Diagnosis of Silver-Russel Syndrome Using Netchine-Harbison Criteria in a Resource-limited Setting

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ABSTRACT

Silver-Russell Syndrome (SRS) is a rare genetic congenital growth disorder characterized by intrauterine growth restriction, postnatal growth failure, hemihypertrophy and craniofacial dysmorphism. Recognized by the Genetic and Rare Diseases Information Center, the syndrome presents considerable diagnostic challenges in resource-limited settings where genetic testing is often inaccessible. This case report presents a 4-month-old female infant with marked asymmetry in limb growth, particularly hemihypertrophy on the left side of the body and notable facial dysmorphism. A clinical diagnosis of Silver-Russell Syndrome was established based on detailed clinical evaluation and the Netchine-Harbison Clinical Scoring System (NH-CSS). All the six diagnostic criteria were fulfilled, including the two mandatory ones – small for gestational age status (SGA) and postnatal growth failure. Multidisciplinary care, involving pediatricians, geneticists, endocrinologists, and nutritionists, was recommended to ensure optimal growth and development. This case highlights the importance of clinical tools like NH-CSS and the value of early diagnosis in managing SRS.

Keywords: Growth Retardation; Hemihypertrophy; Netchine-Harbison Score; Russell-Silver Dwarfism; Silver-Russell Syndrome

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INTRODUCTION

Silver-Russell Syndrome (SRS) is a rare and heterogeneous congenital disorder first described in 1953. It is primarily characterized by a distinctive set of clinical features, including intrauterine growth retardation (IUGR), craniofacial dysmorphia—most notably macrocephaly—and limb asymmetry such as hemihypertrophy.[1,2] Other hallmark features include a triangular face, clinodactyly, short stature, and frontal bossing. The estimated prevalence is approximately 1 in 100,000 live births [1,3,4]. Etiologically, SRS is associated with either maternal uniparental disomy of chromosome 7 (mUPD7) in about 7–10% of cases or hypomethylation at the 11p15.5 imprinting control region 1 (ICR1) in approximately 35–50% of cases. The syndrome presents significant diagnostic and therapeutic challenges due to its clinical and genetic heterogeneity. The syndrome may stem from disruptions in specific genetic or epigenetic pathways or represent a spectrum of clinically related phenotypes. Affected children often face delayed milestones, speech and language difficulties, and learning disabilities, necessitating early diagnosis and a multidisciplinary approach.[5] A thorough understanding of SRS's etiology and clinical manifestations is essential for effective management and improved patient outcomes.

CASE REPORT

A 4-month-old female infant from Maharashtra, born to consanguineous parents of low socioeconomic status, was brought to the outpatient department with complaints of facial dysmorphism, hemihypertrophy of the left side of the body,

feeding difficulties and poor weight gain. The patient had a birth weight of 1300 grams, suggestive of low birth weight and a history of perinatal asphyxia requiring NICU admission. There was no family history of similar presentations. On examination, pronounced asymmetry was observed in limb lengths, and circumferences were noted. The left upper limb measured 22 cm compared to 20 cm on the right, and the left lower limb measured 26 cm versus 22 cm on the right. Mid-arm circumference was 10.5 cm on the left and 9.5 cm on the right, mid-thigh circumference measured 15 cm and 14 cm, respectively. The left foot and left labia majora were noticeably hypertrophied compared to the right side. Anthropometric measurements recorded were: length 54 cm, head circumference 37 cm, and chest circumference 32 cm. Facial dysmorphism was evident, though specific features such as a triangular face, frontal bossing, or downturned mouth were not explicitly described. The differential diagnosis initially considered Beckwith-Wiedemann Syndrome due to hemihypertrophy. However, the presence of IUGR and asymmetry supported the clinical suspicion of Russell-Silver Syndrome (RSS).

The chronological clinical events and assessments for the patient, including initial presentation, anthropometric evaluation, and application of the Netchine-Harbison Clinical Scoring System (NH-CSS) is shown in table 1.

Table 1: Showing the timeline of Clinical Events and Observations in the Present Case

Date	Age	Clinical event/observation
05/05/2025	4 month	Presented with left side hemihypertrophy, facial dysmorphism, feeding difficulties and poor weight gain
05/05/2025	4 month	anthropometric measurements recorded
07/05/2025	4 month	Evaluated using the Netchine Harbison Clinical Scoring System (NH-CSS)

Note: This table summarizes the clinical timeline for the presented case of Silver-Russell Syndrome, highlighting key events in diagnosis and assessment. Source: Original table created by the authors based on clinical observations.

Figure 1 shows an infant with visible hemihypertrophy affecting the left upper and lower limbs, a characteristic feature of Silver-Russell Syndrome (SRS). ***Source:*** *Original clinical image from the present case, used with informed parental consent.*

Figure 1: Hemihyperthrophy of left foot

The image (fig. 1) shows an infant with visible hemihypertrophy affecting the lower limbs, a characteristic feature of Silver-Russell Syndrome (SRS). ***Source:*** *Original clinical image from the present case, used with informed parental consent.*

DISCUSSION

This 4-month-old female infant presents with a constellation of clinical features suggestive of Russell-Silver Syndrome (RSS), a rare congenital disorder characterized primarily by intrauterine growth retardation, postnatal growth failure, body asymmetry (fig. 1), and feeding difficulties. The diagnostic evaluation in this case was guided by the Netchine-Harbison Clinical Scoring System (NH-CSS), which is currently one of the most reliable clinical tools for identifying RSS, especially in resource-limited settings where genetic testing may not be readily available. According to NH-CSS, the diagnosis of RSS is supported if four out of six specific clinical criteria are met, including the mandatory presence of either small-for-gestational-age (SGA) status or postnatal growth failure.

Table 2: Showing Netchine-Harbison Clinical Scoring System (NH-CSS) Criteria and Definitions

Criterion	Definition
SGA	Birth weight/length ≤ -2 SD
Postnatal growth failure	Height ≤ -2 SD at 24±1 months or below mid-parental height
Relative macrocephaly	HC ≥1.5 SD above weight/length at birth
Protruding forehead	Forehead protrusion in toddler age
Body asymmetry	≥0.5 cm limb length discrepancy or asymmetry in ≥2 body parts
Feeding difficulties/low BMI	BMI ≤ -2 SD at 24 months or use of feeding support

This table outlines the six diagnostic criteria defined by the Netchine-Harbison Clinical Scoring System (NH-CSS), used in the clinical diagnosis of Silver-Russell Syndrome.[6] Criteria met in the mentioned patient is tabulated in table 3. This table demonstrates how the presented case fulfilled all six NH-CSS diagnostic criteria for Silver-Russell Syndrome, including the two mandatory components (SGA and postnatal growth failure)

Table 3: Application of Netchine-Harbison Clinical Scoring System (NH-CSS) Criteria in the Present Case

NH-CSS Criterion	Findings in This Case
Small for Gestational Age (SGA)	Birth weight of 1300 grams—below -2 standard deviations (SD) for gestational age
Postnatal Growth Failure	At 4 months, the infant's weight was 3.2 kg and length was 54 cm—both below -2 SD
Body Asymmetry	Notable limb-length discrepancy and left-sided soft tissue hypertrophy
Feeding Difficulties	Ongoing feeding issues contributing to poor weight gain
Relative Macrocephaly	Head circumference (37 cm) was disproportionate to the infant's weight and length
Protruding Forehead	Present as frontal bossing, a characteristic craniofacial feature of SRS

The patient was born with a significantly low birth weight of 1300 grams, placing her well below the -2 standard deviation mark for term neonates, thus fulfilling the criterion for SGA. Furthermore, at 4 months of age, her weight is only 3.2 kg, indicative of severe postnatal growth failure. These two mandatory criteria are both clearly satisfied. The patient also demonstrates notable body asymmetry, with left upper and lower limb lengths exceeding their right-sided counterparts by 2 cm and 4 cm respectively. In addition, mid-arm and mid-thigh circumferences are increased on the left side. This marked hemihypertrophy is a well-recognized feature of RSS and fulfils the body asymmetry criterion. Feeding difficulties are another prominent feature in this case, further supporting the diagnosis. The child has documented feeding issues, a common problem in RSS, contributing to poor weight gain and requiring early nutritional interventions.

Although the patient was initially described as having a dysmorphic face, further clinical examination confirmed the presence of frontal bossing, a key feature used to assess the "protruding forehead" criterion in the Netchine-Harbison Clinical Scoring System (NH-CSS) (Figure 4). Additionally, her head circumference of 37 cm is disproportionately large relative to her weight (3.2 kg) and length (54 cm), supporting the presence of relative macrocephaly at birth, another NH-CSS criterion. With these findings, the patient meets all six NH-CSS criteria, including both of the essential ones, further strengthening the clinical diagnosis of RSS.

Early diagnosis of Russell-Silver Syndrome is vital for initiating timely management. Children with RSS are at increased risk of hypoglycemia, developmental delays, and psychosocial challenges related to short stature and visible asymmetry. Nutritional support, feeding interventions, and in some cases, growth hormone therapy are crucial components of early care. Periodic monitoring for metabolic complications and orthopedic evaluations for limb discrepancies is also necessary. In our patient, the early identification using NH-CSS not only confirms the clinical suspicion of RSS but also sets the stage for multidisciplinary interventions to optimize her growth, development, and quality of life.

CONCLUSION

This case illustrates the importance of early recognition of the signs of Silver-Russell Syndrome (SRS), particularly in resource-limited settings where genetic testing is unavailable. Application of the Netchine-Harbison Clinical Scoring System allowed to make a strong clinical diagnosis, enabling timely and appropriate interventions, including support for feeding, growth, and managing limb differences. Multidisciplinary care and continuous monitoring are key to improving outcomes in affected children. This case highlights the value of careful examination in identifying and managing rare conditions like SRS.

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