Clinical spectrum of Silver - Russell syndrome

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Abstract

Silver - Russell syndrome is a clinically and genetically heterogenous condition characterized by severe intrauterine and postnatal growth retardation, craniofacial disproportion and normal intelligence downward curvature of the corner of the mouth, syndactyly and webbed fingers. Diagnosis of Silver - Russell syndrome remains clinical; no definite etiology or specific tests have been established. In the recent years, it has been shown that more than 38% of patients have hypomethylation in the imprinting control region 1 of 11p15 and one-tenth of patients carry a maternal uniparental disomy of chromosome seven. The pathophysiological mechanisms resulting in the Silver - Russell phenotype remain unknown despite the recent progress in deciphering the molecular defects associated with this condition. This case report describes the clinical features of Silver - Russell syndrome in a father and daughter.

Keywords: Postnatal growth retardation, Silver - Russell syndrome, short stature

Introduction

Russell - Silver syndrome is a pattern of malformation first described by Silver et al.,[1] in 1953 and then by Russell[2] in 1954. Silver et al.,[1] reported two unrelated children with congenital hemihypertrophy, low birth weight, short stature and raised gonadotrophins. Russell described five unrelated children with extreme intrauterine growth retardation and characteristic facial features. These children were short for age and two cases had body asymmetry. The characteristic features described by him were triangular shaped face with a broad forehead, pointed and small chin together with wide, thin shark – like mouth. Although each author emphasized rather different features, the composite features have been identified as Silver - Russell syndrome.[3] Attempts to separate Silver syndrome from Russell syndrome, depending on whether asymmetry is present or absent have not generally been accepted.

Case Report

A 12-year-old female patient presented with global developmental delay and facial dysmorphism. Her chief complaint was irregularly arranged teeth. On examination, her height was 125 cm (<3rd %) and having the following features: Hypertelorism, triangular face, low set ears, scanty eyebrows, depressed nasal bridge, frontal bossing, poor vision of the right eye, crowding of upper and lower dental arches [Figures 1 and 2]. She was found to have an ear tag on the right ear and a pit on the left ear [Figure 3]. However, she did not have any hearing difficulties. She had clinodactyly of the fingers and disproportionate toes [Figure 3]. She had trouble in running at school.

Her facial features were leptoprosopic facial form having a facial index of 173.4 with the increase in lower facial third, convex profile, posterior divergence, hyperactive mentalis and shallow mentolabial sulcus. She had incompetent lips with interlabial gap of 10 mm. On intra oral examination, she had high arch palate and lower midline shifted to the left by 3 mm. The maxillary and mandibular dentition crowding was 8 mm and 4 mm respectively. She had Class I molar
relationship on the right side and end - on the relationship on
the left side. Canine relationship was Class II on both sides.
She had an overjet of 3 mm and openbite of 6 mm. She was
found to have crossbite in relation to the left posterior region.
Cephalometric analysis indicated increased cranial base angle,
decreased anterior and posterior cranial base length. Maxilla
was retropositioned relative to cranium. Mandibular skeletal
base was retrognathic to cranium. In short, she had Class II
skeletal base, vertical growth pattern and deficient chin.

The father of this patient also had similar features [Figure 1].
The father was short. His ears were low set and had pits in
both right and left ears. He also had hypertelorism, scanty
eyebrows and hair on head absent, slanting eyes and poor
sweating and heat intolerance. Mother and sibling of the
patient were normal. Routine chromosome analysis of
daughter and father indicated normal karyotypes.

Hematological investigations of the 12-year-old patient where
carried out. Hematological values were within normal limits.
Based on the history, clinical examination and investigation
findings, a diagnosis of Silver - Russell syndrome was
made. Differential diagnoses considered were Fetal Alcohol
syndrome, Bloom syndrome and Robinow syndrome.

Patient was advised regarding growth hormone therapy and
orthodontic correction of malocclusion. The orthodontic
treatment plan was to have a period of rapid maxillary
expansion followed by fixed orthodontic therapy. The phase
of rapid maxillary expansion is completed [Figure 4].

Discussion

The incidence of Silver - Russell syndrome range from 1
in 3,000 to 100,000 live births and it occurs in all racial
groups. More than 500 cases have been reported with equal
predilection to male and female.[7] Russell hypothesized an
intrauterine challenge or stress at 6 and 7 weeks of gestation
although Gorlin et al., suggested either an end-organ
unresponsiveness to growth hormone or a bistructural
abnormality in growth hormone molecule. Marks et al.,[8]
in 1977 has quoted studies which suggested that there is a
spontaneous single gene and autosomal dominant mutation.
None of these hypotheses has been confirmed.[9] The etiology
is yet to be fully understood.

Individuals with Silver - Russell syndrome are short in stature.
Intrauterine growth retardation results in reduction in total
body cell mass and after birth, growth proceeds normally
with the child always-remaining small in comparison with
their peers. Insufficient growth hormone secretion has
been suggested as a contributory factor in some studies.[9]
Children with this syndrome have also been reported to have
craniofacial disproportion, low birth weight, asymmetry,
clinodactyly of the fifth finger, webbed fingers, normal
intelligence, low set ears, term gestation and downward
curvature of the corners of the mouth. Patient who reported
to our department also had normal intelligence, short stature,
craniofacial disproportion, webbed fingers and low set ears.
The other features often reported in the literature are frontal
bossing, syndactyly of feet and disproportionately short
arms. The above-mentioned features were also present in our
patient. Visual disturbance was reported as a rare finding by
Perkins and Hoang-Xuan[4] and Sreedevi et al.[10] Poor vision
of the right eye was reported in our patient.

Bartholdi et al.,[11] studied the methylation pattern at the
H 19 – insulin-like growth factor 2 locus in 201 patients
with suspected Russell - Silver syndrome. Methylation
defects were found to be restricted to patients who fulfilled
the diagnostic criteria for Russell - Silver syndrome. They
detected epimutations in an affected father and his likewise
affected daughter. The father of our patient also had very
similar features. The father was short in stature and having
normal intelligence. He had low set ears with ear pits. He had
scanty hair on head, scanty eyebrow, hypertelorism, slanting
eyes, poor sweating and heat intolerance.

The five core clinical diagnostic criteria of Silver - Russell
syndrome are:

![Figure 1: Triangular face with low set ears and hypertelorism of the 12-year-old girl and her father](image-url)
Due to clinical and genetic heterogeneities of this syndrome, patients who have four out of the above mentioned five features, could be diagnosed with Silver - Russell syndrome.\[12\]

**Conclusion**

Silver - Russell syndrome is said to be probably under diagnosed due to the broad range of features. The main features are severe intrauterine and postnatal growth retardation, relative macrocephaly and a characteristic small triangular face. The disease is associated with additional dysmorphic features such as fifth finger clinodactyly and webbed fingers. The accuracy of clinical diagnosis is influenced by the clinician’s skill in recognizing and noting the clinical features of a patient. Early diagnosis facilitates timely administration of general and orthodontic treatment options. This will facilitate healthy and good psychological development in a child with this condition.

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