Case Report
Silver-Russell Syndrome: A case Report of Three Years Old Yemeni Boy

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Abstract

Silver Russell Syndrome (SRS) is a rare condition. For diagnosis of SRS at least four of the following criteria should be present which are intrauterine growth retardation , postnatal growth retardation , preservation of occipitofrontal head circumference, classic facial phenotype (broad prominent forehead with small triangular face, small narrow chin and low set ears) and body asymmetry. There is no data about cases of SRS reported in Yemen. We present a three years old Yemeni boy with SRS. He is the first child of Yemeni consanguineous parent's average length. He is born following normal pregnancy. The boy fulfilled the criteria proposed by Price et al and Azzi et al for diagnosis of SRS but have no body asymmetry nor feeding difficulty. The patient was diagnosed as SRS on clinical ground. Chest X-rays, Echocardiography and hormonal analysis had no significant results. Genetic analysis had not done because it is not available at Yemen.

Key words: Silver Russell Syndrome, short stature, Boy, Al-Mukalla ,Yemen

Introduction:

Silver Russell Syndrome (SRS) constitutes a rare heterogeneous entity. It was first described by Silver in 1953[16] and then by Russell in the following year[14] . The incidence of SRS ranges from 1 in 30,000 to 100,000 live births and it occurs in all races. More than 500 cases have been reported with equal sex predilection and widely varied phenotypic features [5,6].

Diagnosis still remains clinical as no etiology or specific tests have been established [7]. SRS is characterized by short stature without catch - up growth, normal head size for age, a distinctive triangular face with prominent forehead, low set ears and clinodactyly of fifth fingers [8].

Over the years, many clinical signs have been added. However, no consensus definition has yet been established making a clinical diagnosis difficult [9,10]. Price et al [13], defined the diagnostic criteria for the classical phenotype. For the diagnosis of SRS at least four of the following criteria should be present: 1) Intrauterine Growth Retardation (IUGR) (birth weight ≥2 SD below the mean), 2) postnatal growth retardation (body length ≥2 SD below the mean), 3) preservation of occipitofrontal head circumference, 4) classic facial phenotype (broad prominent forehead with small triangular face, small narrow chin and low set ears) and 5) asymmetry (especially of the limbs). Characteristic clinical features are more easily identified in infants and younger children than in adults [12].

Recently in September 2016[17] 41 task force members from 16 countries, chosen for their publication record and expertise in SRS, collaborated to develop this consensus statement regarding diagnosis of SRS. This Consensus Statement has adopted a scoring system for diagnosis of SRS named Netchine–Harbison clinical scoring system (NH-CSS), which was proposed by Azzi and his colleagues in 2015[1] and it proved the NH-CSS more sensitive (98%) than other previous systems [4,11].According to the NH-CSS ,SRS can be diagnosed clinically when 4 of the 6 criteria are present, table 1.

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Table (1) Netchine–Harbison clinical scoring system for diagnosis of SRS [1]

Clinical criteria	Definition
SGA (birth weight and/or birth length)	≤−2 SDS for gestational age
Postnatal growth failure	Height at 24 ± 1 months ≤−2 SDS or height ≤−2 SDS below mid-parental target height
Relative macrocephaly at birth	Head circumference at birth ≥1.5 SDS above birth weight and/or length SDS
Protruding forehead*	Forehead projecting beyond the facial plane on a side view as a toddler (1–3 years)
Body asymmetry	LLD of ≥0.5 cm or arm asymmetry or LLD <0.5 cm with at least two other as ymmetrical body parts (one non-face)
Feeding difficulties and/or low BMI	BMI ≤−2 SDS at 24 months or current use of a feeding tube or cyproheptadine for appetite stimulation
- Clinical diagnosis is considered if a patient scores at least four of six from these criteria. Protruding forehead* is equivalent to 'prominent forehead. SGA =small for gestational age, SDS= Standard deviations score, LLD eg length discrepancy	

Case report:

Three years old boy from Al-Hamy city; Hadhramout Governarate, Republic of Yemen was seen at the author's clinic with symptoms of URTI, and on clinical examination revealed that he has had distinctive facial features and short stature. On history and physical examination, the following points were elicited: Family history: the patient is the first baby. The second baby died two days after delivery, his body weight was 1.6 kilogram (birth weight ≥2 SD below the mean), the cause of death is unclear. Father and mother are consanguineous, both are with average length. Prenatal and natal history: Delivery is vaginally and birth weight is 1.4kg (birth weight ≥2 SD below the mean) .No other abnormalities detected during prenatal, natal and post natal. Psychomotor milestones are grossly normal. Voice normal but with high pitched infantile tone. Review of systems is unremarkable.

On examination: patient is conscious, a febrile, active, no jaundice.

Body weight 8.5kg, height 71 cm (both ≥2 below SD below the mean), Head: is large with increased anteroposterior diameter, head circumference 64.5 cm (Dolichcephaly) broad prominent forehead. Face is small triangular with small narrow chin and low set ears. Chest: bronchovascular breathing. CVS: normal double rhythm,no murmurs. Abdomen: soft no organomegaly. Extremities: No body asymmetry, no deformities and other physical examination was irrelevant.

CNS: Intact with no developmental delay.Eyes: no apparent squint.

Genitalia: no micropenis, with descended testis.

The patient's relatives are advised to travel abroad to Egypt for further evaluation and investigation as a case of short stature and big head.

Figure (1) & (2)

Figure (1) and figure (2) shows short stature with the height of the patient in compare to hand of the plastic chair

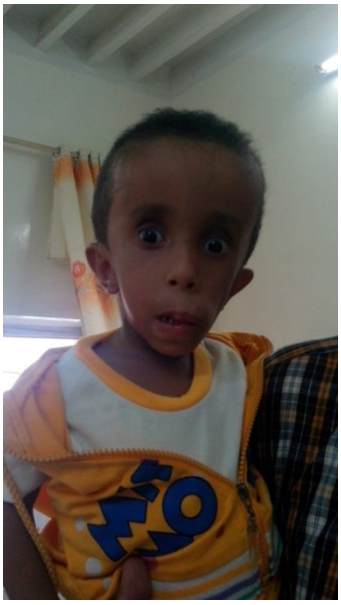

Figure (3) show the characteristics facial features of RSS including broad prominent forehead with small triangular face, small narrow chin, low set ears, with preservation of occipitofrontal head circumference

Blood investigation is done with complete blood count(CBC) reveals : hemoglobin (Hb): 10.5 gm\dl, mean corpuscular volume (MCV) and mean corpuscular hemoglobin concentration (MCHC) was low ,white blood cells(WBC) : 8800 cells\l, platelet count: 174000\l , Random blood sugar (RBS):72 mg\dl , blood urea 18 mg\dl,serum creatinine 0.4 mg\dl, serum calcium 10 mg\dl, alkaline phosphatase was 380 iu/ dl.

Plain x-ray of left wrist that showed delayed

bone age, and brain CT scan was normal, echocardiography done with no significant results.

Growth hormone (GH) did not reach to the peak of 10 nanogram after provocation test by insulin. thyroid function test was normal. Genetic study was not done

Treatment with recombinant human growth hormone (rhGH)

(Somatropine) was started at Egypt at age of 2years and 2 months and in a dose of 0-1- 0-2 U\kg s.c given at night for 6 days\week and advised to continue till reach normal height. The patient continue on treatment for about 6 months with gained of height about 7 cm(height before starting treatment is 64 cm) then the father stopped it because results was unsatisfactory and due to financial issues.

Consent: Written informed consent was obtained from the patient's family for publication of this case report and accompanying images. The parents of the boy have agreed to show the face of their child, but they did not agree to show other parts of the body to be exposed naked. A copy of the written consent is available for review by the Editor -in –Chief of this journal

Discussion:

SRS constitutes a rare entity. There is no statistical numbers reported in Yemen regarding this syndrome. The severity of clinical features of this condition ranges from mild to classical cases. The incidence in western countries ranges from 1 in 30,000 to 1 in 100,000 newborns, all sexes and races are affected.

The cause of SRS is unknown, most cases being sporadic. Some families with apparent autosomal dominant inheritance have been reported; while autosomal recessive and X-linked inheritance has also been suggested [13] It is most likely that one or more imprinted genes are implicated. Gicquel et al and Bliek et al [8,2] have found hypomethylaton of the H19 gene in patients with SRS .

In our reported case clinical diagnosis of SRS is established by finding 4 diagnostic criteria which is small for gestational age (Intrauterine Growth Retardation), postnatal growth retardation , preservation of occipitofrontal head circumference, classic facial phenotype (broad prominent forehead with small triangular face, small narrow chin and low set ears) which constitute 4 of 5 criteria according to Price et al [13], and 4 criteria of 6 according to Netchine–Harbison clinical scoring system[1] for diagnosis of SRS, both of them are enough for diagnosis. The confirmatory diagnosis of clinical SRS is by Cytogenetic and molecular genetic studies [15], but unfortunately genetic study are not available in Yemen to show the exact one or more imprinted genes whose implicated in this syndrome .

Our patient described has no skeletal anomalies and this does not interfere with the diagnosis. Also there is no genitourinary tract anomalies as well as gastrointestinal disorders such as gastroesophageal reflux disease or esophagitis, as there were not an intrinsic feature of this syndrome [17].

Although report by Blissett et al [3] supports the hypothesis that oral motor dysfunction (OMD) is the primary cause of both feeding problems and speech difficulties in some children with SRS, our patient has no feeding difficulties with normal speech [16].Although neurodevelopmental is of average intelligence reported cases of mental impairment is present[12].

In an attempt to verify the diagnosis, the characteristics of our patient are compared to 143 patients described by Wollmann [18] in Table (2)

Table (2) Frequency (%) of clinical characteristics in 143 children with Silver Russell Syndrome reported by Wollmann et al [18] and those of our patient.

Clinical characteristics	Frequency	Clinical characteristics of our patient
Birth weight <3rd percentile	94%	+
Short stature	99%	+
Asymmetry	51%	-
Relative macrocephaly	64%	+
Triangular face	79%	+
Down-slanting corners of mouth	46%	-
Irregular teeth	28%	-
Ear anomalies	53%	+
Clinodactyly V	68%	-
Brachydactyly V	48%	-
Syndactyly V	19%	-
Simian crease	25%	-
Café-au-lait spots	19%	-
Psychomotor retardation	37%	-
Muscular hypotrophy/-tonia	45%	-
Squeaky voice	22%	+
Early puberty	8%	n.a
Precocious puberty	5%	n.a
(+ present, – not present, n.a. not assessable)		

The management of SRS requires the cooperation of a team of specialists which include pediatric endocrinologist ,pediatric gastroenterologist ,pediatric dentists, orthodontists and orthognathic surgeons ,orthopaedics for the correction of asymmetry if present , and finally psychologist[12]. Treatment with recombinant human growth hormone (rhGH) therapy given via daily subcutaneous injections. will help the kid grow much more, but satisfactory results is beneficial if it is given early before 2 years [15].In our reported case treatment is delayed and growth hormone treatment begins at age of 2 years and 6 months. Growth hormone was tried in this patient for 6 months but without benefit and finally stopped.

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 with prominent forehead. The accuracy of clinical diagnosis is influenced by the clinician's skill in recognizing and noting the clinical features of a patient.

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متلازمة سيلفير- روسيل: تقرير لحالة طفل يمني عمرة 3 سنوات

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الملخص

متلازمة سيلفير– روسيل تعد متلازمة نادرة الحدوث. يوجد هناك خمسة علامات تشخيصية لهذة المتلازمة حسب برايس وزملائه أو ستة علامات حسب أزي وزملائه وهي حدوث تأخر في النمو الجنيني للطفل مع نقص في الوزن عند الولادة، تأخر في النمو بعد الولادة، الاحتفاظ بالنسبة الأمامية الخلفية لمحيط الرأس، وجود الصفات الكلاسيكية في الوجه(جبهة واسعة وبارزة مع وجود وجه صغير مثلث– ذقن صغير وضيق– وجود مستوى منخفض للأذنين) وأخيرا وجود عدم تساو في الاطراف وخصوصاً الأطراف السفلية، يضاف إلى ذلك صعوبات في الرضاعة والأكل. لكي نشخص المتلازمة فأنه يلزم وجود على الأقل أربع صفات من الخمسة أو الست علامات وهي متواجدة في الحالة المبلغة.لا توجد هناك معلومات عن حالات تم الإبلاغ عنها كمتلازمة سيلفير– روسيل في اليمن. نحن نبلغ عن حالة نادرة لطفل يمني عمره ثلاث سنوات تم تشخيصه كمتلازمة سيلفير– روسيل، وهو الطفل الأول لعائلة يمنية لأبوين أقارب و طولهم هو في المتوسط الطبيعي وقد ولد من حمل طبيعي، وقد انطبقت علية جميع المواصفات المطلوبة لتشخيص هذه المتلازمة ما عدا أنه لا وجود لعدم تساو في الاطراف وخصوصاً الأطراف السفلية ولا يوجد صعوبات في الرضاعة والأكل.

الكلمات المفتاحية: قصر القامة، متلازمة سيلفير– روسيل، طفل يمني