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Chronic Renal Failure in Russell-Silver Syndrome

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= **Abstract** =

The Russell-Silver syndrome (RSS) is a disease characterized by intrauterine growth retardation with preserved head circumference, facial dysmorphism and short stature. Reported renal and urinary manifestations of RSS include horseshoe kidney, renal tubular acidosis, hydronephrosis, ureteropelvic obstruction and vesicoureteral reflux. Here we report a case of end-stage renal disease associated with RSS, which, to the best of our knowledge, has not been reported yet.
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Key Words : Russell-Silver syndrome, End-stage renal disease

Introduction

The Russell-Silver syndrome (RSS) is a disease characterized by intrauterine growth retardation with preserved head circumference, facial dysmorphism and short stature. It was first described by Silver in 1953 and then by Russell in 1954 [1, 2]. Price et al. [3] defined the diagnostic criteria for the classical phenotype of RSS as 1) birth weight below or equal to -2 SD from the mean, 2) poor postnatal growth, below or equal to -2 SD from the mean at diagnosis, 3) preservation of occipitofrontal head circumference, 4) typical facial phenotype, and 5) skeletal asymmetry. The incidence of this disorder is from 1 in 3,000 to 1 in 100,000 live births. Several genetic causes have been proposed to explain this syndrome; Abu-Amero et al. [4] reported that 10% of RSS patients have maternal uniparental disomy (mUPD) of chromosome 7 and up to 50% have methylation defects in the imprinted domain on chromosome 11p15. The phenotype of growth retardation has been explained by abnormalities in the pulsatile action of growth hormone [5].

In addition to the above-mentioned classical findings, diverse manifestations have been reported in association with RSS, such as feeding difficulty, learning disability and limb abnormalies. Renal and urinary manifestations of RSS include horseshoe kidney, renal tubular acidosis, hydronephrosis, ureteropelvic obstruction and vesicoureteral reflux. Here we add another renal manifestation of RSS; chronic renal failure (CRF).

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Case

A 14-year old boy visited the clinic because of proteinuria incidentally found at school screening

test. The patient was born at full term with birth weight 1.37 kg (<3rd percentile), height 32 cm (<3rd percentiles), and head circumference 21 cm (<3rd percentiles). His Apgar scores at birth were low of 4 at both 5 min and 10 min. Search for the etiology of intrauterine growth retardation including brain ultrasonography, echocardiography, chromosome analysis (46, XY), and congenital infection screening did not show abnormal findings. He had poor feeding and poor weight gain since birth.

At 23 months of age he visited our hospital because of growth retardation and developmental delay. His height was 68.2 cm (<3rd percentiles), weight was 6.5 kg (<3rd percentiles) and the head circumference was 45.5 cm (3-10th percentiles). He had triangular-shaped face, facial asymmetry, a broad forehead and small pointed chin. He also had low body mass index (BMI 14.3 kg/m^2), clinodactyly of little finger and undescended right testis. His language development was delayed. Laboratory studies of urinalysis, complete blood count and chemistry were within normal limits. The bone age was 6 month, which was significantly delayed. Growth hormone level without stimulation was within normal range of 5.37 ng/mL. Since his clinical findings met the diagnostic criteria of Price [3], he was diagnosed as RSS and followed for five years before lost to follow up.

At his re-visit in 14 years old due to proteinuria, he denied any significant medical history of medication, hypertention, hypoxic damage, or trauma. He was not ill looking and did not have edema. His height was 96.4 cm (<3rd percentiles), weight was 9.5 kg (<3rd percentiles) and his blood pressure was 125/69 mmHg (95-99th/50-90th percentile) (Fig. 1). Laboratory studies showed increased blood urea nitrogen (30 mg/dL) and serum creatinine (2.5 mg/dL), normal serum albumin (4.3 mg/dL), increased urine albumin and protein/creatinine ratio (3+ and 4.51). On kidney ultrasonography, both kidneys were small (right kidney 6.8 cm and left kidney 6.7 cm, normal range 7.1-88.7 cm) and parenchymal echogenicity was increased (Fig. 2). There were no hydronephrosis and abnormal findings on urethra and bladder. Voiding cystourethrography (VCUG) demonstrated no abnormal finding. Because of the advanced renal insufficiency, kidney biopsy was not done. Under the impression of chronic renal failure of unknown etiology, he was treated conservatively with ACE inhibitor, allopurinol, and sodium bicarbonate. His

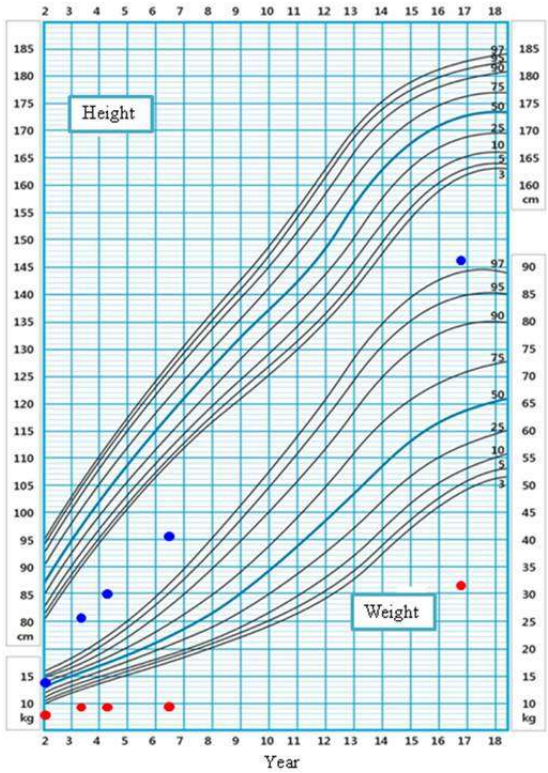

Fig. 1. Growth curve of the patient.

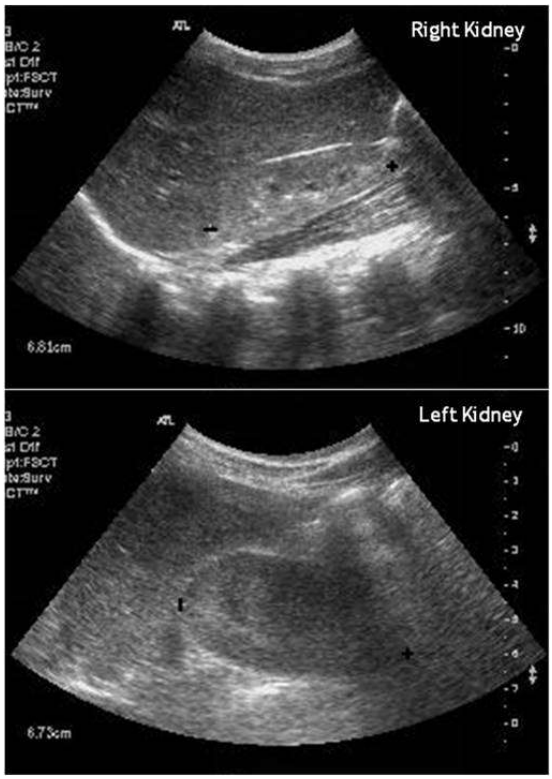

Fig. 2. Ultrasonography showed both kidneys of decreased size, increased parenchymal echogenicity but no hydronephrosis and no abnormal findings on urethra or bladder.

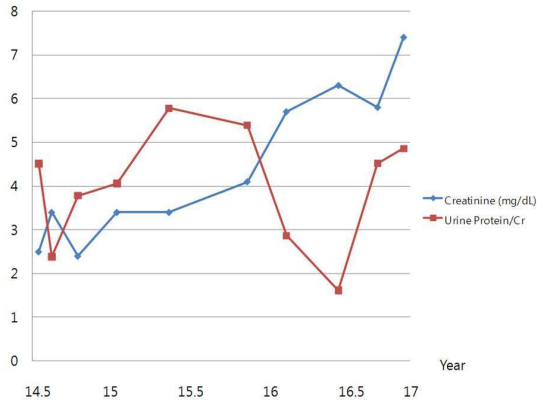

Fig. 3. Serum creatinine and random urine protein/creatinine of the patient.

renal insufficiency progressed steadily to the end stage renal disease requiring a replacement therapy in 3 years.

Discussion

Chronic renal failure is sometimes found in children as an incidental finding. The renal problems that may present as CRF in childhood are glomerulonephropathies, hereditary nephropathies, renal hypo-/dysplasia, urinary tract malformations and vascular nephropathies [6]. Many hereditary syndromes have been reported to cause CRF in children, which include Prune belly syndrome, primary oxalosis, infantile polycystic kidney disease, congenital nephrotic syndrome, juvenile nephrophthisis, Alport syndrome and infantile cystinosis [7]. Here, by reporting a case of CRF with RSS, we add RSS as one of those syndromes.

As demonstrated in our case of this report, the main features of RSS are severe intrauterine and postnatal growth retardation with preserved head circumference and facial dysmorphism. Our patients also had failure to thrive, delayed bone age, developmental delay, and a very low BMI as typical findings of RSS. The mechanism of growth retardation is yet to be revealed, but considered to be associated with abnormalities in the pulsatile action of growth hormone. Thus recombinant growth hormone has recently been applied for RSS [5]; however, our patient did not have a chance to be treated with growth hormone due to the follow-up loss. Among the limb anomalies of RSS such as clinodactyly of the little finger, syndactyly, camptodactyly, absence of fingers, a cleft hand and a hypoplastic thumb [8], our patient had clinodactyly of little finger.

Regarding the reported kidney problems of RSS, our patient had none of horseshoe kidney,

renal tubular acidosis, malacoplakia of the bladder, chronic pyelonephritis, hydronephrosis, or ureteropelvic obstruction and reflux [9-13]. Instead, CRF and contraction of the kidneys developed in our our patient; to the best of our knowledge, there has been no report on RSS patients with end-stage renal disease (ESRD) requiring renal replacement therapy, since Pubmed search using the terms of 'Russell Silver Syndrome' and 'renal failure' at the time of the preparation of this manuscript found no items. Unfortunately we do not have the information on the kidney condition when he was young and the onset of renal problem, such as proteinuria or renal insufficiency. Since it was too late to get any further information via kidney biopsy, we do not have the pathologic diagnosis of this patient either. On the other hand, VCUG revealed no reflux and there was no hydronephrosis. Thus, we speculate that the defective somatic growth also affected the growth of the kidneys. Or, the genetic defect of RSS, which is yet to be found, may also have affected the kidney and some pathology has progressed.

Here we report a reported case of ESRD associated with RSS. This case suggests us that the possibility of progression to CRF should be considered in caring RSS patients. Early detection of such a case in RSS patients and close follow-up would improve our understanding the pathogenesis of CRF.

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요 약

Russell-Silver 증후군에서의 만성 신부전

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안요한 · 이세은 · 강희경 · 하일수 · 정해일 · 최 용

Russell-Silver 증후군은 자궁내 성장 지연, 특징적인 얼굴 기형, 저신장을 특징으로 하는 질환이다. Russell-Silver 증후군에서 동반되는 신질환은 말굽신장, 신세뇨관 산증, 물콩팥증, 요관 깔때기막힘, 방광 요관 역류 등이 있다. 저자들은 Russell-Silver 증후군 환자에서 말기 신부전이 발생한 예를 경험하였으며 문헌 고찰에서 유사한 증례를 찾을 수 없었기에 보고하는 바이다.

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