Roberts Syndrome, Normal Cell Division, and Normal Intelligence

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Roberts-SC phocomelia syndrome (RS) is an autosomal recessive disorder of symmetric limb defects, craniofacial abnormalities, prenatal and postnatal growth retardation, and mental retardation. Patients with RS have been reported to have premature separation of heterochromatin of many chromosomes and abnormalities in the cell-division cycle. No case has been reported who had normal intelligence and normal cell division with typical clinical features of the RS. We report a case of a six-year-old male with clinical and radiologic findings of typical RS with normal cell division and normal intelligence.

Although he showed growth retardation, his intelligence was normal. Van Den Berg and Francke later reported that 79 out of 100 cases of Roberts syndrome had premature cell separation (PCS). We think that this case may demonstrate severe expression of the Roberts syndrome even though PCS is not exhibited. The limb involvement of this case was symmetrical, and he showed phocomelia of upper limbs, equinus valgus deformity of ankle, aplasia of fibula, and shortness of fifth toes while his hands and feet were normal with 5 rays each. Craniofacial abnormalities of this case were typical; he showed scaphocephaly, mild hypertelorism, mandibular hypoplasia, dysplastic helix of ear, narrowing of external auditory canal, and cleft palate with wide gap.

This report supports the theory that normal intelligence can make social-personal adjustment possible even if all of the stigmata of Roberts syndrome is present.

Key Words: Cleft palate, ectromelia, craniofacial abnormality

Roberts-SC phocomelia syndrome (RS) is an autosomal recessive disorder of symmetric limb defects, craniofacial abnormalities, prenatal and postnatal growth retardation, and mental retardation. The disorder carries the name of John B. Roberts, who presented a male infant with bilateral cleft lip and tetraphocomelia. Another name of this condition often found in literature is “the (SC) pseudothalidomide syndrome”, because of the resemblance to malformations seen in the thalidomide embryopathy.

Patients with RS have been reported to have premature separation of heterochromatin of many chromosomes and abnormalities in the cell-division cycle. Seventy-nine percent of individuals with the Roberts syndrome show premature centromere separation (PCS) in chromosomal study. They are clinically indistinguishable from the 21% who do not have PCS. In Roberts syndrome, mental retardation is a common, but inconstant abnormality. It has been reported that Roberts syndrome could present a number of craniofacial anomalies of variable severity: craniosynostosis, macrocephaly, ocular hypertelorism, prominent eyes, cleft lip and palate, microgenia, hypoplasia of nose, dysplastic ear etc. Also, hematologic manifestations in the RS has been presented such as leukemoid reactions, intermittent thrombocytopenia, marked eosinophilia. Postmortem autopsy revealed horseshoe kidney, absence of gall bladder, and congenital heart anomalies in some reports.

There have been some reports on the heterogeneous clinical features of Roberts syndrome and variable phenotypes. However, no case has been reported who had normal intelligence and normal cell division with typical clinical features of the RS. We report a case of a 6-year-old male whose clinical and
radiologic findings present typical features of RS but who shows normal cell division and normal intelligence.

**Case Report**

A 6-year-old male presented at our department for the operation of cleft palate from the Social Care Center for children with disabilities without parents. We could not get any information about his antenatal care, delivery history, nor his parents. He was evaluated for Roberts syndrome before palatoplasty. A precise history-taking and physical examination was done and routine hematology and chemistry, chromosome assay, skull series, simple radiographs of limbs, abdominal CT, brain MRI, were also performed.

His intelligence was normal. He weighed 14.3kg (below 3 percentile) with a height of 98.5cm (below 3 percentile). His growth has been retarded and his developmental age was between 18 and 24 months. Bilateral phocomelia and equinus valgus deformity of ankle were evident in all limbs (Fig 1, left). The short leg brace with valgus strap was applied for equinus valgus deformity of ankle, which improved his gait problem (Fig 1, right). Corneal opacities were not noted. Mild hypertelorism was evident in orbital and nasal areas (Fig 2, left). Mandibular hypoplasia was evident on cephalometry. A dysplastic helix of ear and narrowing of external auditory canal were noted (Fig 2, middle). His head circumference was 49.0 cm (above 25 percentile). His head anteroposterior diameter and biparietal diameter were 18.0 cm and 14.5 cm respectively. Scaphocephaly was evident on clinical measurements and photographs (Fig 2, right).

A cleft of soft palate and two thirds of hard palate with wide gap were noted (Fig 3, left). Palatoplasty using 2-flap and vomer flap was performed under general endotracheal anesthesia (Fig 3, right). Bilateral phocomelia and thumb anomalies were evident on upper limbs (Fig 4, above left and below left). Deficiency of fibula, shortness of fifth metatarsal bone were evident on lower limbs (Fig 4, above right).
right and below right). The hands and feet were normal with 5 rays each (Fig 4, below left and right). Brain parenchyma was normal on a brain MRI. Horseshoe kidney or renal hypoplasia, agenesis of gall bladder, genital anomalies were not evident on abdominopelvic CT. His WBC count, differential blood count, and platelet count were normal.

On postoperative day 10 he was sent back to the Social Care Center for children with disabilities without parents. Speech therapy was started.

Fig 2  Craniofacial anomalies. (Left) a mild hypertelorism is noted in orbital and nasal areas. (Middle) mandibular hypoplasia is seen. A dysplastic helix of ear and narrowing of external auditory canal are seen. (Right) Scaphocephaly. AP diameter is 18.0cm, BPD is 14.5cm.

Fig 3  Cleft palate. (Left) Preoperative state: cleft of soft palate and two thirds of hard palate with wide gap is seen. The vomer is also seen. (Right) Postoperative appearance after palatoplasty using 2-flap and vomer flap.
Fig 4  Bilateral phocomelia and fibular deficiency. (Above left) Bilateral phocomelia and thumb anomalies are evident on upper limbs. (Above right) Bilateral equinus valgus deformity of ankles are evident on lower limbs. (Below left) The radius and ulna are absent on radiography. (Below right) A deficiency of fibula and shortness of 5th metatarsal bone are seen on radiography.
DISCUSSION

Roberts syndrome is a rare autosomal recessive disorder, involving growth and mental retardation, craniofacial abnormalities, and limb reduction defects. In Roberts syndrome, mental retardation is a common, but inconsistent abnormality. Although this case showed growth retardation, his intelligence was normal.

Premature centromere separation (PCS) consists of "puffing" or "repulsion" of the constitutive heterochromatin and is most clearly and frequently seen in chromosomes 1, 9, 16, and Y, as well as at the nucleolar organizing regions of the acrocentric chromosomes. However all chromosomes have been described as showing the phenomenon, which is best demonstrated showing the C band staining technique. Zlotogora argued that the absence of PCS exclude the diagnosis of Roberts-SC phocomelia syndrome. However Van Den Berg later reported that 21 out of 100 cases of Roberts syndrome had no PCS. Thus, the absence of this phenomenon is not an exclusion criterion. The phenotypic variability of Roberts syndrome does not correlate with the presence or absence of PCS. However, PCS is considered diagnostic when there is associated prenatal and postnatal growth retardation, symmetrical limb reduction defects, and craniofacial malformations. We think that this case may demonstrate severe expression of the Roberts syndrome even through PCS is not exhibited.

In the review of 100 cases of Roberts syndrome, Van Den Berg reported the limb involvement to vary from a complete absence of arms and legs with rudimentary digits to mild growth deficiency in the limbs. The limb involvement may be symmetrical or asymmetrical. The limb involvement of our case was symmetrical, and he showed phocomelia of upper limbs, equinus valgus deformity of ankle, fibular aplasia, and normal intelligence in which PCS was not present. This report supports that normal intelligence can make social-personal adjustment possible even all of the stigmata of Roberts syndrome is present.

REFERENCES