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CASE REPORT

# Cytogenetic diagnosis of Roberts SC phocomelia syndrome: First report from Kashmir



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## KEYWORDS

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**Abstract** There are several syndromes in which specific mitotic chromosomal abnormalities can be seen, like premature centromere separation, premature (sister) chromatid separation, and somatic aneuploidies. Identifications of such specific cytogenetic findings can be the key factor that leads towards the diagnosis of syndromes like Roberts SC phocomelia. The case presented here as Roberts SC phocomelia syndrome was identified as a child with multiple congenital anomalies and dysmorphic features. Conventional cytogenetic analysis of the case revealed premature sister chromatid separation. The premature centromeric separation was also confirmed by C banding analysis of the child. It is the first and the only case of Roberts SC phocomelia diagnosed from this part of the world. The present case report emphasizes the importance of conventional cytogenetics in the diagnosis of such syndromes.

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## 1. Introduction

Roberts SC phocomelia syndrome is an autosomal recessive developmental disorder characterized by pre and postnatal growth retardation, microcephaly, craniofacial anomalies, mental retardation and tetrphocomelia in varying degrees of severity. Robert's syndrome was initially reported by John Roberts in a male child bearing cleft lip and tetrphocomelia [1]. Later, in four individuals from two families of European descent, Herrmann et al. reported similar, but milder malformations which were referred to as SC phocomelia [2]. These two syndromes had varying phenotypic

expression and were later concluded as the same entity because of resemblance of thalidomide embryopathy with Robert's syndrome and were therefore termed as Roberts SC phocomelia syndrome [3]. The gene responsible for the syndrome called ESCO2 gene is located at 8p21.1 and was discovered by Hugo and Vega in 1995 [4]. This syndrome is rare with approximately 100 cases described in the literature [5]. Ours is the first report on Robert's syndrome from Kashmir, North India.

### 1.1. Clinical description

The proband, a two year old baby girl, is a product of non-consanguineous marriage, second in birth order and born to the parents of same geographical area of Kashmir valley. The patient had characteristic dysmorphic facies with defective

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development of all four extremities that was the main constituent of malformation complex. The craniofacial abnormalities include small low set ears, prominent frontal bones, prominent eyes, shallow orbits, hypertelorism, bilateral cleft lip and palate, micrognathia and short neck. She had severe fixed flexion deformities of all limbs. The limbs were short with hands and feet located closed to the body. The thumbs were absent bilaterally, with oligodactyly of upper and lower extremities and flexion deformity at knee joints. There was no visceromegaly and no cardio-vascular defects. The genitals were normal.

## 2. Methodology

### 2.1. G banding analysis

For G banding analysis 72 h peripheral blood lymphocyte cultures were set using RPMI 1640 medium (Sigma, St Louis, USA) supplemented with phytohemagglutinin (Himedia Labs, India) and fetal bovine serum (Himedia Labs, Mumbai, India). The cells were arrested in metaphase by colcemid treatment 2 h prior to the hypotonic shock with 0.57 M KCl solution. The cells were finally fixed with pre chilled Carnoy's fixative and slides were prepared the next day by air drop method [6]. GTG banding of one day old slides was carried out and the slides were stained using 4% Giemsa stain [7]. Thirty well spread metaphases were selected for the analysis.

### 2.2. C banding analysis

For C banding analysis three day old slides were dipped for 15 min in 0.2 N HCl and incubated in a saturated solution of barium hydroxide at 60 °C for 8–10 min. The slides were rinsed

in distilled water for 30 s and excess barium hydroxide was removed by a rapid dip in 0.1 N HCl. The slides were reincubated in a coplin jar containing 2XSSC for one hour in a 60 °C water bath. The slides were briefly rinsed in distilled water and stained in 5% Giemsa stain [8].

## 3. Results

In most of the metaphases analyzed, chromosomes were found to have premature sister chromatid separation. Almost all the chromosomes of the metaphases observed had premature sister chromatid separation. The centromeric regions of chromosomes exhibited prominent separation of sister chromatids (Fig. 1). The sister chromatid separation was also confirmed by C-banding analysis (Fig. 2). The parental metaphases analyzed did not show any such separation of sister chromatids. Besides, G-banding of the child and his parents revealed no deletion, duplication or translocation. However, aneuploidy was recorded in 5% of the metaphases of the patient.

## 4. Discussion

Conventional cytogenetics has a crucial role in the diagnosis of some genetic disorders despite being gradually abandoned in the new era of array diagnostics. There are several syndromes in which specific mitotic chromosomal abnormalities can be seen, like premature centromere separation, premature (sister) chromatid separation, and somatic aneuploidies. Identifications of such specific cytogenetic findings can be the key factor that leads towards the diagnosis of syndromes like Roberts SC phocomelia [9]. Roberts SC phocomelia is one of the rare genetic disorders where cytogenetic analysis gives a primary insight of the chromosomal morphology and a firm



**Figure 1** Karyotype of Robert's SC phocomelia syndrome showing sister chromatid separation and centromeric separation.

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