

# Prenatal Diagnosis of Roberts-SC Phacomelia Syndrome: A Rare Case Report

Dr. Shabbir Ahmed<sup>1</sup>, Dr. Girija M. K<sup>2</sup>, Dr. Saiteja Namala<sup>3</sup>, Dr. Rajan B<sup>4</sup>

<sup>1</sup>Senior Resident, Department of Radio-Diagnosis, Dr. B. R. Ambedkar Medical College, Bengaluru, India

<sup>2</sup>Head of the Department, Department of Obstetrics and Gynaecology, Dr. B. R. Ambedkar Medical College, Bengaluru, India

<sup>3</sup>Post-Graduate Resident, Department of Radio-Diagnosis, Dr. B. R. Ambedkar Medical College, Bengaluru, India

<sup>4</sup>Head of the Department, Department of Radio-Diagnosis, Dr. B. R. Ambedkar Medical College, Bengaluru, India

**Abstract:** *Roberts syndrome/Roberts-scPhacomelia syndrome is a rare disease, with multiple limb and skeletal abnormalities (called "pseudothalidomide disease"). There are only around 150 cases described in literature. We present a case of Roberts syndrome, diagnosed in the prenatal routine anomaly scan, when a 24 years patient came for routine antenatal check-up without prior follow-up. The pregnancy was not followed due to socioeconomic and family situation and no prior ultrasound was performed. The ultrasound evaluation showed: hypoplastic inferior maxilla with micrognathia, antimongoloid palpebral slant, abnormal and lower implanted ears, oligodactyly of right hand, upper limbs phocomelia (severe on the right side), asymmetrical femur growth and intrauterine growth restriction. Roberts syndrome is a rare genetic disease with autosomal recessive transmission generated by mutations in ESCO2 gene, located on chromosome 8. The disease should be easy to diagnose by antenatal ultrasound examination, but in our case, the lack of prenatal follow-up determined anomaly scan at 24weeks. We believe this case is an argument towards introducing ultrasound-screening compulsory to all pregnancies. To identify a possible genetic mutation, further investigations of the parents are in progress, but classically the disease has a recessive autosomal transmission. The baby was terminated later on as soon as the suspicion of Roberts-SC syndrome was made. The overall radiological features were suggestive of Roberts syndrome.*

**Keywords:** autosomal recessive, Roberts SC phocomelia syndrome

## 1. Introduction

Roberts syndrome is a rare autosomal recessive genetic disorder. It carries the name of John Roberts, who first reported the case of a male infant with bilateral cleft lip and tetraphocomelia in 1919.

<sup>7</sup>The combination of malformations was recognized as a syndrome in 1966 by Appelt and co-workers. Hermann et al. reported similar but milder malformations which were referred to as 'pseudothalidomide SC syndrome' in 1969. These two syndromes had varying phenotypic expression and were later concluded as the same entity because of resemblance of thalidomide embryopathy with Roberts syndrome and were therefore termed as Roberts SC phocomelia syndrome. <sup>10</sup>In 1995, two Colombian geneticists Hugo and Vega discovered the Roberts gene, called ESCO2 gene which is located at 8p21.1. <sup>11</sup>Typical clinical features of Roberts syndrome are pre-natal and postnatal growth retardation, bilaterally symmetric/asymmetric limb reduction and craniofacial abnormalities. <sup>10</sup>This syndrome is rare with approximately 100 cases described in the literature and only a single case reported from Pakistan in 1993.<sup>3,9</sup>

Roberts syndrome is also known by many other names, including: Hypomelia-Hypotrichosis-Facial Hemangioma Syndrome, SC Syndrome (once thought to be an entirely separate disease), Pseudothalidomide Syndrome, Roberts-SC Phocomelia Syndrome, SC Phocomelia Syndrome, Appelt-Gerken-Lenz Syndrome, RBS, SCP pseudothalidomide Syndrome, and Tetraphocomelia-Cleft Palate Syndrome.

## 2. Case Report

We present a case of Roberts syndrome, diagnosed in the prenatal routine anomaly scan, when a 24 years patient came for routine antenatal check-up without prenatal follow-up. The pregnancy was not followed due to socioeconomic and family situation, and no prior ultrasound was performed. The ultrasound evaluation showed: hypoplastic inferior maxilla with micrognathia, antimongoloid palpebral slant, abnormal and lower implanted ears, superior limbs phocomelia, asymmetrical femur growth and intrauterine growth restriction.

First pregnancy was uneventful and the first child is healthy and normal. There is no history of any congenital malformation in other family members. There was history of fever in second trimester of current pregnancy for which she was treated symptomatically. No history of other illnesses like rash, hypertension and teratogen exposure during pregnancy. There is no history of abortion or stillbirth.

On presentation the growth parameters on ultrasound were:

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**Biparietal diameter (BPD): 58mm (Corresponding to 23 weeks 06 days)**

**Head circumference (HC): 213mm (Corresponding to 23 weeks 03 days)**

**Abdominal circumference (AC): 174mm (Corresponding to 22 weeks 02 days)**

**Femur length (FL) (RIGHT): 16mm (Corresponding to 14 weeks 06 days)**

**Femur length (FL) (LEFT): 19mm (Corresponding to 15 weeks 06 days)**

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weeks 05 days)

**Humerus length (RIGHT):** Bone ossification was not clearly seen on USG

**Humerus length (LEFT):** 29mm (Corresponding to 19 weeks 03 days)

**Tibia length (RIGHT):** 30mm (Corresponding to 20 weeks 05 days)

**Tibia length (LEFT):** 31mm (Corresponding to 21 weeks 03days)

**FL/AC ratio:** 9.32% (Normal Range: 20~24% > 21 weeks)

**FL/BPD ratio:** 27.84% (Normal range: 71.0 ~87%, >23 weeks)

**FL/HC ratio:** 7.61% (Normal range: 13.30 ~23.90%, 15~42 weeks)

**HC/AC ratio:** 1.22% (Normal range: 0.87 ~1.39, 13~42 weeks)

**Thoracic/Abdominal:** 93.19% (Normal)

**Circumference ratio**

**Fetal weight:** 558gms

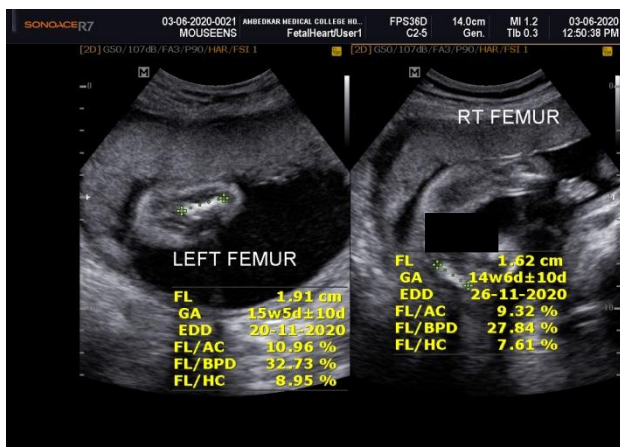
The baby had characteristic dysmorphic facies with defective development of all four extremities that was the main constituent of malformation complex. The craniofacial abnormalities included prominent frontal bones, small low set ears, prominent frontal bones, prominent eyes, shallow orbits, hypertelorism, hypoplastic inferior maxilla with micrognathia, antimongoloid palpebral slant, abnormal and lower implanted ears, oligodactyly of right hand, upper limbs phocomelia (severe on the right), asymmetrical femur growth and intrauterine growth restriction. The baby had severe fixed flexion deformities of all limbs. The limbs were short with flexion deformity a twist joints. Proptosis was present. There was no visceromegaly and no cardiovascular defects. The baby was immediately terminated and baby gram was taken after due consent from the parents (Fig 6 and Fig7).



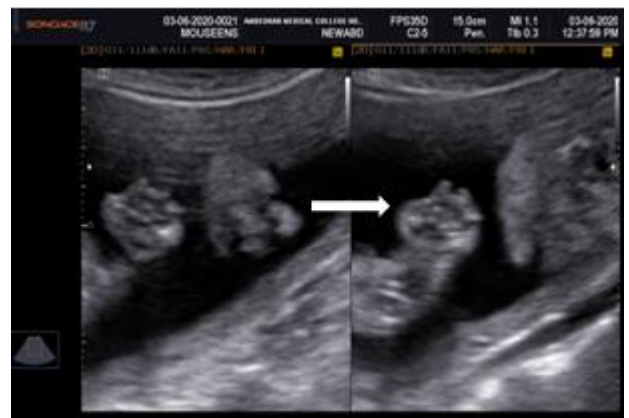
**Image 2:** USG showing hypoplastic right upper limb and phacomelic left limb



**Image 3:** USG showing hypoplastic right upper limb and left humerus



**Image 1:** Showing bilateral asymmetrical growth of the femur



**Image 4:** USG showing oligodactyly of right hand



**Image 5:** Baby characteristic abnormal lower implanted ears, upper limb asymmetry, asymmetrical femur growth, micrognathia and upper limb flexion joint contractures.



**Image 6 and Image 7:** Babygram (24weeks) showing agnesis of radius and ulna of both upper limbs, asymmetrical humerus of both the sides and bilateral shortening of femur.



Radiographic examination showed agnesis of radius and ulna of the right hand and bilateral asymmetrical humerus and bilateral shortening of femurs. Pelvis and iliacbones were normal; there was also bilateral shortening of tibia.

Complete blood count was normal with no thrombocytopenia. Cytogenetic studies could not be done due to non-availability of facilities. Diagnosis of Roberts syndrome was made on the basis of craniofacial malformations and limb deformities (phocomelia) and growth retardation.

### 3. DISCUSSION

Roberts Syndrome is a very rare congenital malformation. Its prevalence is unclear. Thus far, about 150 cases of different racial and ethnic backgrounds have been reported in the literature.<sup>4</sup> The major abnormalities required to make the diagnosis of Roberts Syndrome include: mental retardation, growth retardation with prenatal onset and continuing postnatally, midline craniofacial abnormalities, tetra-hypomelia that are more prominent in the upper extremities varying from phocomelia to simple shortness of the extremity and accompanying extremity abnormalities.<sup>4,11</sup> In 2005, the disease gene was determined by Vega et al.<sup>11</sup> All of the above findings were determined in our case except genetic analysis which was not done due to non availability.

The craniofacial and extremity abnormalities seen in this syndrome include left lip and palate, craniosynostosis, microcephalia, silver-coloured or sparse hair, micrognathia, ocular hypertelorism, exophthalmia, eyelidcoloboma, corneal blurring, cataract, mid-facial capillary

haemangioma, ear malformations, low-set ears, maxillary protrusion, malarhypoplasia, hypoplastic mandible, nasal hypoplasia and short neck bilateral symmetrical tetraphocomelia or hypomelia, brachydactyly/ oligodactyly.<sup>[1]</sup>

In Roberts Syndrome, the upper extremities are affected more frequently than the lower extremities. In our case too we had upper extremities more involved than lower extremities. Cardiac anomalies are observed in about 50% of the cases. A trial septal defect, ventricular septal defect, patent ductus arteriosus have previously been reported.<sup>5</sup> However, valvular aortic stenosis has not been mentioned in the literature. In our case there was no cardiac problem. Other less common features are renal anomalies (polycystic, dysplastic kidneys), cryptorchidism, neurological anomalies like microcephaly and hydrocephalus and femoral tibial ankylosis. The reasons for death of these patients are generally cardiac, renal anomalies and infections.

Chromosomal anomalies such as premature centromere separation [PCS, heterochromatin push] and/or ESCO2 mutations on the 8th chromosome are determined on cytogenetic evaluation and molecular studies.<sup>4, 11</sup> Despite the observation of PCS as a characteristic chromosomal finding in most of the RBS cases, there are also some reported cases with normal chromosomes. Most patients born with growth retardation, severe craniofacial and limb defects have died early in childhood. Those with less severe defects have better prognosis. Aggressive medical intervention that is correcting left lip and palate, correct in orthopaedic deformities and nutritional rehabilitation is suggested along with parental counselling.<sup>2</sup>

The unique cytogenetic abnormality called premature centromere separation which disrupts the process of chromatid pairing, is responsible for the development of multiple structural anomalies found in Robert SC Syndrome. Premature centromere separation has been reported in lymphocytes and/or fibroblasts from patients whose clinical phenotypes cover the range of the Roberts syndrome, from a severe variant to SC phocomelia syndrome at the milder end.<sup>8</sup> Jabs et al.<sup>6, 8</sup> presented evidence that Roberts syndrome is a mitotic mutant. They emphasized that, in addition to previously described changes, aneuploidy with random chromosome loss and micronuclei and/or nuclear lobulation in the inter phase cells are characteristic features of this syndrome. They suggested however, that the defect might lie in one of the proteins transiently associated with the kinetochore being involved in its function.

Stioui et al. detected premature centromere separation on chorionic villus sampling at eight weeks gestation in a woman at a risk of recurrence of Roberts syndrome. Hirschhorn and Kaffe pointed out that they had made a prenatal diagnosis of Roberts-SC syndrome in a family at risk by detection of skeletal and renal abnormalities.

#### 4. Conclusion

This case report emphasizes the importance of recognizing infants born with phocomelia syndrome. Differentiating infants with Roberts-SC phocomelia from other multiple malformation syndromes that feature intercalary limb

defects, including thalidomide embryopathy, TAR (Thrombocytopenia with absent radius syndrome), and Schinzelphocomelia is fundamental.

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