INTRODUCTION

Roberts syndrome is a rare autosomal recessive genetic disorder. It carries the name of John Roberts, who reported the case of a male infant with bilateral cleft lip and tetraphocomelia. The combination of malformations was recognized as a syndrome in 1966 by Appelet and coworkers. 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. In 1995, two Colombian geneticists Hugo and Vega discovered the Roberts gene, called ESCO2 gene which is located at 8p21.1.

Typical clinical features of Roberts syndrome are pre-natal and postnatal growth retardation, bilateral symmetric limb reduction and craniofacial abnormalities. This syndrome is rare with approximately 100 cases described in the literature and only a single case reported from Pakistan in 1993.

CASE REPORT

A 22 days old male baby from the province of Punjab was admitted via emergency department with acute watery diarrhea and assessment of multiple malformations. He was born to a 20-year-old mother and 17-year-old father who were first cousins. The infant was the first child born via spontaneous vaginal delivery at hospital and had no history of birth asphyxia.

Both parents were healthy. There was no history of any congenital malformation in family. There was no history of any illness (like fever, rash, hypertension) and no drugs/teratogens exposure was noted during pregnancy. The course of pregnancy was reportedly unremarkable although she did not have regular antenatal care or ultrasounds. There was no history of abortion or still birth.

On presentation the growth parameters were below 4th centiles; weight was 1.7 kg, length was 44 cm and the head circumference was 30 cm. The patient had characteristic dysmorphic facies with defective development of all four extremities that was the main constituent of malformation complex (Figure 1). The craniofacial abnormalities included prominent frontal bones, microbrachycephaly, small low set ears, prominent eyes, shallow orbits, hypertelorism, unilateral cleft lip and palate, hypoplastic ala nasi, micrognathia, short neck and down slanting palpebral fissures. He 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 (Figure 2) and flexion deformity at knee joints. Corneae were clear. There was no visceromegaly and no cardio-vascular defects. He had intact cranial nerves, and normal genitals.

Radiographic examination showed agenesis of radii and ulna, fusion of 4th and 5th metacarpal with hypoplasia of distil phalanx. Pelvis and iliac bones were normal; there was bilateral fibular aplasia with shortening of tibia (Figure 3). Other tests including echocardiography and abdominal ultrasound were normal. Complete blood count was normal with no thrombocytopenia. Cytogenetic

ABSTRACT

Roberts syndrome is a genetically determined rare birth defect causing, skeletal deformities, particularly symmetrical limb reduction and craniofacial anomalies. For any child with limb and craniofacial bony malformations, this syndrome should be considered in the differentials. Although this syndrome represents only a small proportion of the total number of individuals with limb deficiency, it is important to be identified in order to give accurate genetic counselling including recurrence risk in siblings and possible prenatal diagnosis. This is the case report of a 22 days old male infant who presented with defective development of all four extremities and craniofacial abnormalities. The overall clinical and radiological features were suggestive of Roberts syndrome.

Key words: Roberts SC phocomelia syndrome. Tetraphocomelia. Cleft palate.
studies could not be done due to unavailability of facilities. Diagnosis of Roberts syndrome was made on the basis of craniofacial malformations and limb deformities (tetraphocomelia) and prenatal growth retardation. The couple was provided genetic counselling regarding the possibility of prenatal diagnosis by ultrasound for the next baby.

**DISCUSSION**

Roberts syndrome is an extremely rare condition. The affected group is diverse and spread worldwide. Typical features include symmetric underdeveloped limbs and craniofacial abnormalities. The limb abnormality varies from shortening to complete absence, mostly symmetrical, short arm bones, fused fingers and missing thumbs. Lower limbs and feet are often affected in a similar fashion as upper limbs. Craniofacial malformations occur with marked variability. They include cleft lip and palate, hypertelorism, exophthalmos due to shallow orbits, wide nasal bridge, micrognathia and thin silvery blond hair. The limb defects include tetraphocomelia which is a prominent characteristic of the syndrome with oligodactyly, radial aplasia or dysplasia. Other less common features are renal anomalies (polycystic, dysplastic kidneys), cryptorchidism, neurological anomalies like microcephaly and hydrocephalus; and femoral tibial ankylosis. Many affected infants die in the newborn period. Survivors may have mental retardation, but the intelligence can be normal as well.

At least two autosomal recessive dysmorphogenetic syndromes present clinical overlap with Roberts syndrome, the so-called pseudothalidomide (SC phocomelia) and TAR (thrombocytopenia absent radii syndrome).

The diagnosis of Roberts syndrome relies on cytogenetic testing. The characteristic abnormality on cytogenetic reveals premature centromere separation (PCS), also known as heterochromatin repulsion (HR) or puffing. These two important cytogenetic abnormalities disrupt the process of chromatid pairing and are responsible for the development of multiple structural anomalies found in Roberts SC syndrome. Molecular studies of ESCO2 confirm the diagnosis. In April 2008, there were 26 known mutations of the ESCO2 gene. Carrier status cannot be determined by cytogenetic analysis. There is no correlation between phenotypical severity of this syndrome with cytogenetical abnormalities. Prenatal diagnosis requires cytogenetic analysis of fetal cells, by chorionic villus sample, amniocentesis or cordocentesis. Confirmation of the suspected diagnosis requires cytogenetic testing. A negative cytogenetic analysis does not exclude Roberts syndrome. It has been identified that the ESCO2 gene mutation responsible for developmental abnormalities maps to chromosome 8p21.

Prenatal diagnosis of at risk pregnancies requires antenatal ultrasound as early as 12 weeks gestation. Stioui et al. detected premature centromere separations on chronic villus sampling at 8 weeks gestation in a woman at risk of recurrence of Roberts syndrome, who had one affected child. The molecular genetic testing for prenatal diagnosis of Roberts syndrome is not available in routine. However, prenatal testing may be available for families in which the disease-causing mutation has been identified. Pre-implantation genetic diagnosis may be available for families in which the disease-causing mutations have been identified. 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 cleft lip and palate, correcting orthopaedic deformities and nutritional rehabilitation is suggested along with parental counselling.
Consent: Written informed consent was obtained from parents for the purpose of publication of the manuscript and figures of the child.

REFERENCES


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