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Case Report .

A Severe Case of Robert Syndrome: 4 Limbs Anomalies and Maxillofacial Deformities

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ABSTRACT

Robert SC syndrome is a very rare inherited disorder, considered as an autosomal recessive genetic disease characterized by skeletal and facial anomalies, growth retardation, mental retardation, cardiac and renal abnormalities, caused by the mutation of the ESCO2 gene which is located at 8p21.1,and encodes a protein essential in establishing sister chromatid cohesion during S phase. Infants with a severe form of Roberts's syndrome are often stillborn or die shortly after birth. Mildly affected individuals may live into adulthood. A condition called SC phocomelia syndrome was originally thought to be distinct from Roberts's syndrome; however, it is now considered to be a mild variant."SC" represents the first letters of the surnames of the two families first diagnosed with this disorder. Thereare approximately 100 cases reported in the literature. It is important to identify the syndrome and provide an accurate genetic counseling with the risk of recurrence between sibling and possible prenatal diagnosis. This is a case report of four years old girl with complex multiple congenital anomalies and dysmorphic features. The Overall clinical and radiographic findings confirm our patient's diagnosis with Robert syndrome.

Key words: Roberts SC syndrome. Tetraphocomelia. Cleft palate, premature centromeric separation.

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INTRODUCTION

Robert-SC syndrome is a very rare developmental disorder, it is considered as an autosomal recessive genetic disease. It was described for the first time in 1919 by John Roberts who reported a case of bilateral cleft lip and tetraphocomelia in a boy infant.[1]

In 1966, the combination of malformations was defined as a syndrome by Appelet and coworkers.In 1969, Herrmann et al[2], reported a similar case but with milder malformations which were called pseudothalidomide or SC Syndrome. These two syndromes had varying phenotype. Zergollern and Hitrec[3] were later concluded that Roberts Syndrome and SC phocomelia are considered the same entity due to resemblance of thalidomide embryopathy. Therefore, it termed as the Roberts-SC Phocomelia Syndrome. In 1995, ESCO2 gene was discovered by Hugo and Vega.[4] It is responsible for the syndrome and located at 8p21.1.

Robert-SC syndrome is rare. There are approximately 100 cases reported in the literature, and therefore the incidence is unknown.[5] The typical clinical features in patients with Roberts Syndrome are pre-natal and post-natal growth delay, bilateral limb shortening, corneal opacity, cleft lip and palate, malar hypoplasia, micrognathia, head and neck hemangioma, ear anomalies, congenital heart anomalies and cystic kidneys.[6,7] The Upper limbs are more affected than lower limbs and there is parental consanguinity in 49% of the cases.[8-11]

CASE REPORT

An apparently normal 13 year old obese boy presented to the Pediatric outpatient clinic complaining of recurrent headache since the last 5 months. His mother also complained that since the onset of headache his school performance had decreased. The boy studied in 9th standard and had been doing fairly well before that. Previously during the course of illness, he was seen by many physicians and was advised various NSAIDs and ophthalmological checkups. There was no history of trauma. The child did not suffer from diabetes or hypertension. There was no we present here the case of 4-year-old girl is a product of consanguineous marriage. There were no complications during

the pregnancy, infections, use of medications or exposure to radiation. She is product of full term, C-Section, GBS was not done, unknown APGAR score, and respiratory supports (intubation and CPAP) were unknown. The vaccination and developmental histories are not clear. Our patient is the third conception product of full term and C-Section due to breech presentation. Her family history is positive of one child with Robert syndrome out of two. Both parents are normal. The mother age is 35 years, G6P3+3 and 2 abortions. Last pregnancy 4 months was terminated by the mother as the baby has the same condition as our patient. The patient presented with complex multiple congenital anomalies. On physical examinations, the growth parameters; weight was 9.830 kg and length was 75 cm. The noticed anomalies are as follow: severe dysmorphic feature, ectodermal dysplasia, midline defect with bat ears, dysmorphic conjunctives and severe cleft lip and palate, the oropharynx and nasopharynx are one big cavity, retrognethia and significantly hypoplastic nasal structure with normal neck. The other major congenital anomaly involves the eye lids. She has poorly formed eye lid evident on the right side with the lower eye lid almost missing, which results in exposure of the cornea and possible keratitis partly related the self-irritation with her hands (Figure 1).

The upper extremities anomalies manifest in complicated complete multiple syndactyly of both hands in a form of Mitten hands. The lower extremities have synostosis at the level of the feet with severely fixed knees and pterygium formation at the flexor aspect of the lower extremities bilaterally (Figure 2).The patient apparently doesn't have internal organs anomalies.

Radiological assessment was done and showed left and right hands deformities, as described with absent first metacarpal bones bilaterally and small right second metacarpal bone. There is evidence of severe congenital deformity involving the phalanges and digits (Figure 3).Skeletal survey showed appearance of lacunar skull, and bilateral radial deformity as describe above. Persistent flexion of both lower extremities with abnormal appearance of the knee joints, with difficult evaluation of the feet (Figure 4).CT scan of chest, abdomen and pelvis showed no evidence of anomaly at the structure of thorax or abdomen.

Fig 1: A 4 years old girl baby showing craniofacial Abnormalities with cleft lip and palate.

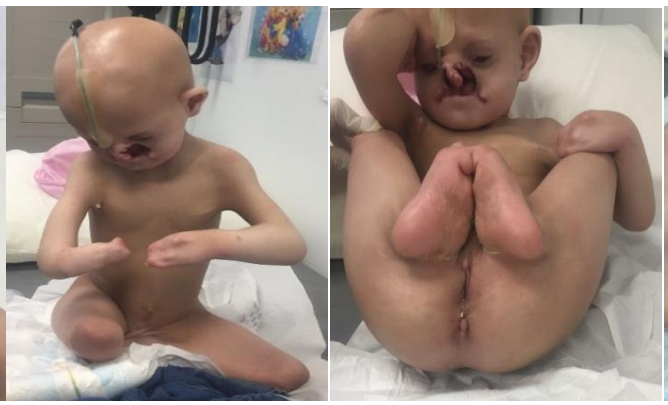

Fig 2: The lower extremities have synostosis at the level of the feet with severely fixed knees.

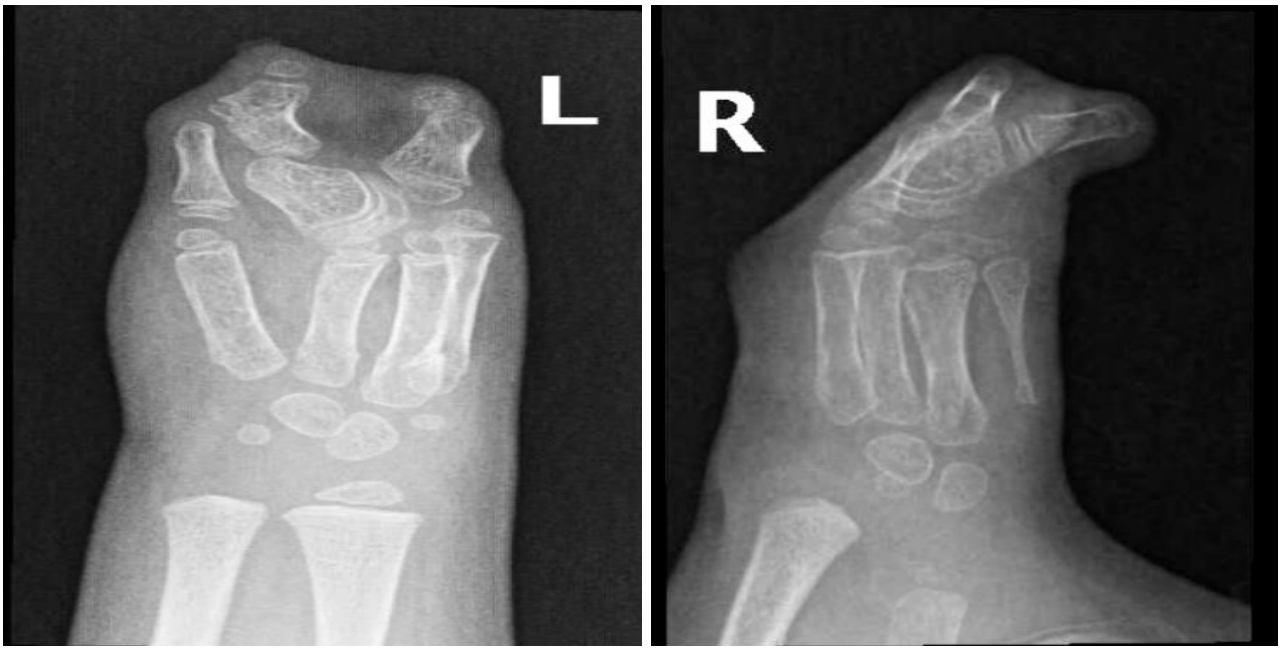

Fig 3: Hands X-Ray showing severe congenital deformities with absent of first metacarpal bones bilaterally

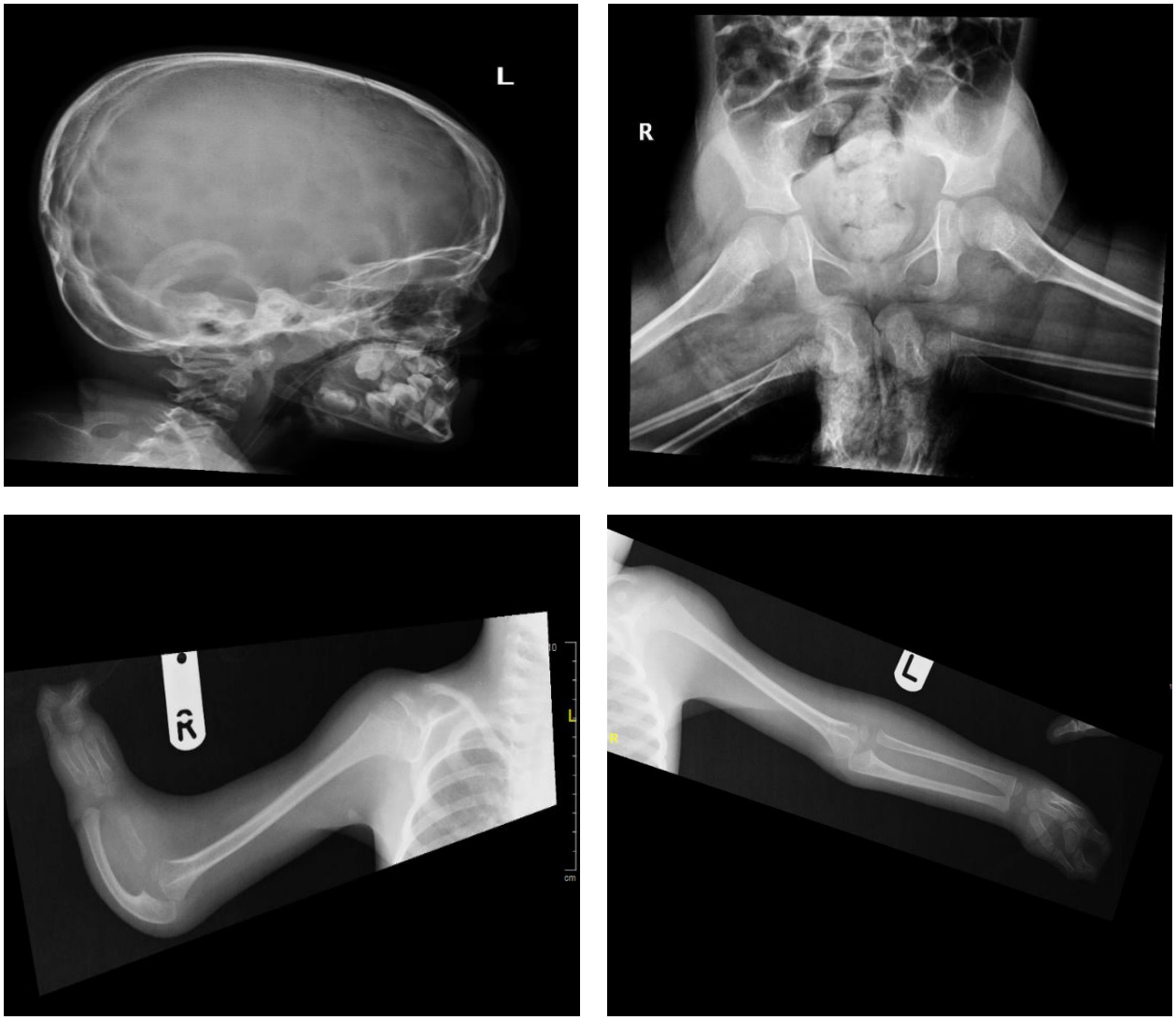

Fig 4: Skeletal survey showed appearance of lacunar skull, Persistent flexion of both lower extremities and bilateral radial deformity.

DISCUSSION

Robert syndrome has described in previous literature with different presentations. Most of the Robert syndrome patients are diagnosed before the age of 5 years involving similar presentation. Other patients who are diagnosed late or at adulthood have presented with much less severe form of Robert syndrome. The early diagnosed patient has mainly presented with growth retardation, symmetrical undeveloped limbs, craniofacial anomalies (microcephaly, cleft lip and palate, micrognathia, hypertelorism, etc.[12,13] It may be associated with other abnormalities like mental retardation/learning difficulties, dimorphism, sever fixed flexion, ambiguous genitalia, absence of pelvic bone, and other thoracic or abdominal organomegaly.[9,14,15] Robert syndrome (RS) is the result of ESCO2 gene mutation which present at chromosome 8p21. This gene product is necessary for the sister chromatid cohesion in S phase and mitosis.[12] It also participates in DNA damage repair, gene expression, and chromosome condensation.[16] It is found that there are 26 possible mutations at this gene which might explain the presence of different forms of this syndrome.[9] It is associated with some cytogenetic abnormality during cell division.

Premature separation of heterochromatin at centromere (PS) has been observed in 50% of the cases and it is correlated with the development of more anomalies.[9,17-20] Robert syndrome can be diagnosed by cytogenetic testing for PS or molecular genetic testing for ESCO2 gene, but negative result of cytogenetic testing of PS does not exclude RS which makes molecular testing the mainstay diagnostic test for RS. In a study, a histopathology examination of lung tissue and placenta in a severe form of Robert syndrome, which is 745_746delGT mutation of ESCO2 gene, done and revealed "thickened interalveolar septa, alveoli with eosinophilic granular debris and desquamated cells, rare macrophages" and "vascular lumens with ectasia and thrombosis, perivillous and basal plate fibrin deposition, intervillous thrombi, microcalcifications".[15] The recurrence of future pregnancy with Robert syndrome in cobles carrier for the mutation is 25%. There are many methods and tests can be done during pregnancy for a fetus of high risk cobles. At age of 8 weeks of gestation a sample of chorionic villus can be cytogenetically tested, but this does not necessarily exclude Robert syndrome. At age of 12 weeks, ultrasound can be performed.

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