

Robinow Syndrome: a Rare Case Report from a Tertiary Care Hospital in Eastern India

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Abstract

Background

Robinow syndrome is a rare congenital disorder with phenotypically heterogeneous abnormalities. Two modes of inheritances are known for this syndrome namely autosomal recessive and autosomal dominant.

Case Report

We describe here an eighteen-month-old child who had mesomelic short stature, abnormal facial features, clinodactyly, micropenis and vertebral changes which were further supported radiologically. The case was the first of his kind, which came to our hospital. The diagnosis was challenging and ascertained only after confirmation with multiple specialties and various interdepartmental discussions.

Conclusion

The syndrome is rare and hence is less known among health care workers. Also, the prenatal testing which is available for the entity needs to be explained to the suspected mothers.

Key Words: Autosomal recessive, Child, Facial dysmorphism, Short stature.

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1- INTRODUCTION

Robinow syndrome is a rare disease simultaneously affecting many parts of the body, particularly the skeletal system. With existence of both autosomal recessive (AR) and autosomal dominant (AD) forms, it has been known to run in families. So examining other siblings if a case is suspected is justified. The condition was thought to have a geographical predilection owing to a higher documentation of such cases in Oman and Turkey (1, 2).

A one and half year old male, accompanied by his mother presented to our hospital with complains of a genital abnormality. A meticulous work up including inter-departmental interventions and imaging modalities helped us to diagnose this rare entity.

2- CASE REPORT

An eighteen-month-old male child, accompanied by his mother, a product of non-consanguineous marriage presented to the Pediatric OPD complaining of buried penis. There were no symptoms suggestive of obstruction to the urinary stream, phimosis, lack of hygiene, pain during micturition or fever. There was no history of trauma. Detailed history revealed perinatal and infancy periods had been uneventful with attainment of normal development milestones.

The patient was immunized as per National Immunisation Schedule (NIS) and was receiving adequate dietary intake consisting of mixed Indian diet. Past medical history did not reveal any abnormality.

On examination, the patient's vitals were within the normal limits. Patient had distinct facial features and routine general physical examination revealed other

abnormalities as well. He had a small face with deficient malar prominence, broad and prominent forehead, hypertelorism, flat nasal bridge, upturned nose, elongated philtrum and low set ears (**Figure.1**).

Upper lip was tented exposing the gums, which were hypertrophied with presence of bifid tongue and high arched palate. The patient was found to have a short stature with shortened limbs (**Figure.2a**), valgus deformity, absent middle phalanx of the little finger and low hairline. On roentgenography, multiple hemivertebrae, block vertebrae and presence of vertebral fusion (**Figure.3a and 3b**) were seen. It further revealed shortening of the forearms, dissociated proximal radioulnar articulation and dissociated humeroulnar and humeroradial articulation (**Figure.4**).

Ultrasonography (USG) revealed normal abdomen and urinary tract and adequately functioning kidneys, which were normal in shape, size and position.

On examination his weight was 10.8 kg (between the median and -1 SD), length was 67 cm (below -3 SD) and head circumference 44 cm (between -2 and -3 SD). The upper segment to lower segment ratio was 1.31(**Table.1**).

Cardiovascular systemic, central nervous system (CNS) and respiratory systems did not reveal any abnormality. Routine blood picture, thyroid function tests, renal function tests and electrolytes were within the normal range.

Due to the rarity of such collective findings, the patient was referred within the hospital and extensively discussed with Pediatric surgeons, radiologists and orthopedicians, following which a diagnosis of autosomal recessive Robinow syndrome was stated.



Fig.1: Clinical photograph of face showing midfacial hypoplasia, prominent and broad forehead, wide root of the nose, flat nasal bridge, elongated philtrum, hypertelorism, low set ears and tenting of upper lip.



Fig.2a



Fig.2b

Fig.2 (2a and 2b): 2a. Clinical photograph showing clinodactyly, absent middle phalanx in the little finger and shortened limb; 2b. Clinical photograph displaying genital abnormality (micropenis).



Fig.3a



Fig.3b

Fig.3 (3a and 3b): Radiographic views showing multiple hemivertebrae.



Fig. 4a

Fig.4b

Fig.4 (4a and 4b): Radiographic views showing malocclusion of teeth, shortening of the forearms, dissociated proximal radio-ulnar articulation and dissociated humeroulnar and humeroradial articulation.

Table-1: Anthropometric measurements of the index case

Variables	Observed	Expected (for chronological age 18 months)	Interpretation
Head circumference	44 cm	47.4 cm	Between -2 and -3 SD
Length	67 cm	82.3 cm	Short stature (Below -3 SD)
Weight	10.8 kg	10.9 kg	Between median and -1 SD
Mid arm circumference	12.5 cm		
Upper segment (US)	38 cm		
Lower segment (LS)	29 cm		
US/LS	1.3		

US: Upper segment, LS: Lower segment, Cm: Centimeters, Kg: Kilogram, SD: Standard deviation.

4- DISCUSSION

Robinow syndrome is an extremely rare entity in India. Globally around 200 cases have been reported (3) since it was first introduced in 1969 by clinical geneticist meinhard Robinow together with physicians Frederic Silverman and Hugo Smith in certain members of a household as a dwarfing syndrome, being characterised by short limb dwarfism, deformities in face, head and external genitalia associated with vertebral anomalies (4, 5).

Hence it is also known as Robinow-Silverman-Smith syndrome. It has also

been described as fetal facies syndrome as the facial features of the sufferers resemble with a fetus. Other synonyms used in various literatures are Robinow dwarfism, mesomelic dwarfism-small genitalia syndrome, fetal face syndrome (6) and ‘acral dysostosis with facial and genital abnormalities’. Robinow syndrome has an incidence of 1:500,000 with no gender predilection (7). A few studies have reported higher frequency of Robinow syndrome in some parts of the world especially Turkey and Czechoslovakia (1).

On the basis of inheritance both forms have been described, though till 1978, only the autosomal dominant form was known.

The severe autosomal recessive form was described later on (2). The recessive form is due to homozygous mutations localized to chromosome 9q22 whereas the autosomal dominant Robinow syndrome is due to heterozygous mutation in ROR2 gene and WNT5A gene on chromosome 3p (8). Recently Autosomal Dominant (AD) form has also been linked to DL.V3 allele related frameshift mutation (9).

Recessive form encompasses multiple morphological abnormalities characterized by severe skeletal, vertebral and craniofacial defects like limb and thorax malformation, rib and vertebral irregularity, facial and genital abnormalities, and mesomelic short stature (10). Based on the predominant skeletal dysplasia, this anomaly was previously known as costovertebral segmentation defect with mesomelia (COVESDEM) syndrome.

Features common in both the dominant and recessive forms are the characteristic facial features, gingival hypertrophy, orodental abnormalities, and maldeveloped genitalia. There is midfacial hypoplasia, short upturned nose with flattening of nasal bridge, broad and prominent forehead, hypertelorism, low set ears, inverted "V" shaped (tenting or downturned) upper lip. Both the primary and secondary sets of teeth are present causing malocclusion and overcrowding, often the incisors being exposed due to the maldevelopment of the upper lip. Usually gum hypertrophy is present from birth. Ankyloglossia and bifid tongue may be associated features.

Genital abnormalities in the form of micropenis are common in Robinow syndrome with no abnormalities of the scrotum and testis (11). Cryptorchidism and hypospadias have been reported in a few cases. In females, the clitoris is small in size and labia minora may be underdeveloped.

Since there are numerous skeletal dysplasia which may cause dwarfism, distinguishing Robinow syndrome phenotypically from the rest is important in making the diagnosis. Robinow syndrome manifests with mesomelic or acromesomelic limb shortening as compared to the other dwarfing skeletal dysplasia in which the limb shortening is rhizomelic (10).

Such patients frequently suffer from infection encompassing a wide spectrum of disorders including ear infections (12), renal (hydronephrosis, cystic dysplasia of the kidney), respiratory and gastrointestinal disorders (esophageal reflux) to name a few (13). Congenital heart abnormalities like septal defect, coarctation of the aorta, tetralogy of Fallot, severe pulmonary stenosis, tricuspid atresia and right ventricular outflow obstruction have been reported. These cardiac defects are probably the major cause of mortality in this syndrome in the first few years of life (14, 15).

Hemivertebrae and scoliosis are the distinctive features of recessive form whereas umbilical hernia, supernumerary teeth wide retromolar ridge, alveolar ridge deformation, malocclusion, gingival enlargement, dental crowding, and hypodontia are found mostly in patients with the dominant form (16). In another study, severe craniofacial abnormalities were common in the recessive variant whereas intraoral features were related to the dominant forms (17). Thoracic vertebral fusion, abnormalities of the ribs and frequent hemivertebrae result in kyphoscoliosis and chest deformity.

Robinow syndrome generally has a favorable prognosis, which is essentially attributed to the minor involvement of the nervous system. Affected females have preserved fertility and can carry out pregnancies without any hindrance most of which get delivered by Lower segment

Cesarian section (LSCS) owing to cephalopelvic disproportion (18). Since there is genetic predisposition in this syndrome, genetic testing done antenatally in suspected (especially short stature mothers) would help in early diagnosis of the disease, which can be coupled with effective genetic counseling (19). Short stature can be well detected by fetal ultrasound evaluation during the routine anomaly scan at 20 weeks gestation (19). As in the indexed case with micropenis, treatment with Human chorionic gonadotropin (hCG) can help to increase the penile length (20) apart from having beneficial effects on growth, thus tackling the short stature. Orthopedic management includes postural or surgical correction of kyphoscoliosis with justified use of braces and splints when necessary.

5- CONCLUSION

In spite of the rarity of Robinow syndrome in the literatures, pediatricians and gynaecologists should familiarize themselves with this entity. Suspected mothers should be enlightened regarding available genetic testing which will help in early diagnosis and prenatal genetic counseling. The life expectancy if affected is primarily due to the cardiovascular involvement, though quality of life is better than other syndromes as there is minimal effect on the nervous system.

6- ETHICAL CONSIDERATIONS

Approval and consent to participate and publication: Prior consent has been taken from the patient's mother. The mother approved of the study and all photographs were taken in the presence of the mother. Further care has been taken to mask the identity by covering the eyes with a computer-generated filter.

7- AUTHOR'S STATEMENTS

SS admitted the patient, did the primary examination, drafted the initial manuscript,

and approved the final manuscript as submitted. SM reviewed and revised the manuscript, was involved in the extra departmental discussions, and approved the final manuscript as submitted. All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

8- ABBREVIATIONS

- **AR:** Autosomal Recessive,
- **AD:** Autosomal Dominant,
- **OPD:** Out Patient Department.

9- CONFLICT OF INTEREST

The authors have no conflicts of interest to disclose. No funding was secured for this study.

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