

# A rare presentation of Rubinstein-Taybi syndrome

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## ABSTRACT

**Objective.** Taybi syndrome is a rare genetical disorder with the symptoms of small stature, broad thumbs and first toes, a moderate to severe intellectual handicap, and unique facial traits. The present case study aimed with diagnose and therapeutic management of pediatric patients having Rubinstein-Taybi syndrome.

**Study area.** The case study was carried out in Jawaharlal Nehru Medical College, Acharya Vinoba Bhave Rural Hospital, Sawangi Meghe, Wardha, Maharashtra, in department of Pediatrics. The present study follows case of male child, diagnosed with different degrees of compliance, in which the therapeutic approach was determined by the severity of the patient's conditions.

**Outcomes.** Case study on 3 years old male child was carried out and observed with some behavioural changes like unstable mood, distractibility and impulsivity along with attention problem, aggressive nature and self-injurious behavior etc. As the syndrome does not have a particular treatment but some therapies are applied to address issues that are frequently connected to the illness. The thumbs or toes surgically repaired might enhance grip or ease pain. The study was performed as per the scientific way, based on research literatures study.

**Keywords:** Rubinstein-Taybi syndrome, polydactyly, intellectual disability, broad thumb hallux syndrome, dysmorphic facies

## INTRODUCTION

Rubinstein-Taybi syndrome (RSTS) is also known as broad thumb hallux syndrome, was described in 1963. It is a rare genetic disorder which is characterized by dysmorphic facies, dental problems, microcephaly, cutaneous features, broad and angulated thumbs, ocular abnormalities, hearing loss, respiratory problems, cryptorchidism, growth retardation, developmental delay, skeletal deformities and intellectual disability [1]. Most cases are sporadic, but some families show autosomal dominant inheritance. Majority of the mutations are due to microdeletions. Typically, patients with suspected Rubinstein-Taybi syndrome need evaluation by pediatric geneticists who have expertise in dysmorphology. The estimated prevalence of this incredibly uncommon autosomal dominant genetic disorder is one instance per 125,000 live births [2]. Various advanced research has shown mutations in the 16p13.3 gene encoding cyclic-AMP-regulated enhancer binding protein (CREBBP) in RSTS patients [3,4] (Figure 1).

Majority of the cases are tentatively diagnosed based on the clinical picture there is no proper diagnostic criteria relevant to this syndrome available. Obesity may also be seen in childhood and adolescence in some cases. In spite of a complex and expensive clinical care required, around 90% of the patients only make it to their adulthood. In adult age, the predominance of behavioral and mental health issues (83%), gastrointestinal issues (73%), constipation being the primary symptom, and insomnia (62%) are characterize in RSTS [5]. Though polydactyly is a feature of multiple syndromes it is quite rare in Rubinstein-Taybi syndrome. The diagnosis of Rubinstein-Taybi syndrome also requires genetic mutation analysis through microarray method or Fluorescent In Situ Hybridization (FISH) technique. Foot polydactyly is one of the most common defects associated at birth. It is defined as a congenital defect associated with presence of extra phalanges that can be present with or without metatarsals. In this case, the diagnosis of Rubinstein-Taybi syndrome is established in a proband based on the

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Article History:  
Received: 30 November 2023  
Accepted: 13 December 2023

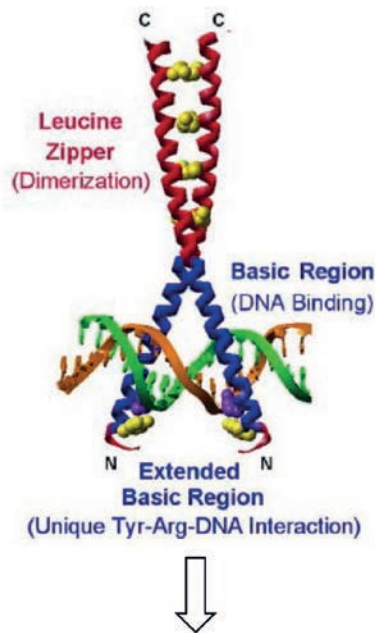


FIGURE 1. “C” insertion between “nt” 4944 and 4945 leading to frame-shift and truncation

clinical features of the patient [6]. Recently, a case study was reported in Dr. D.Y. Patil Hospital and Medical College, Mumbai, India on RSTS patient, aged of a 12-year-old female child [7]. Now the cases on the same syndrome are increasing day by day. Based on the increased cases of RSTS in India, the present case study was reported in our medical college hospital.

**CASE REPORT**

A 3 year old male child accompanied by his parents was brought to the orthopedics department

with complaints of pain and swelling over the left 6th toe following a fall at home. For above complaints the patient was first referred to orthopaedician where x-ray done was suggestive of 6th toe fracture for which 6th toe amputation was done under short general anesthesia (Figure 2). In the post-operative period, the patient developed one episode of convulsion for which the patient was referred to a us. On admission, the patient was noticed to have facial dysmorphism associated with global developmental delay with a Developmental Quotient(DQ) of 60% for gross motor and fine motor milestones and

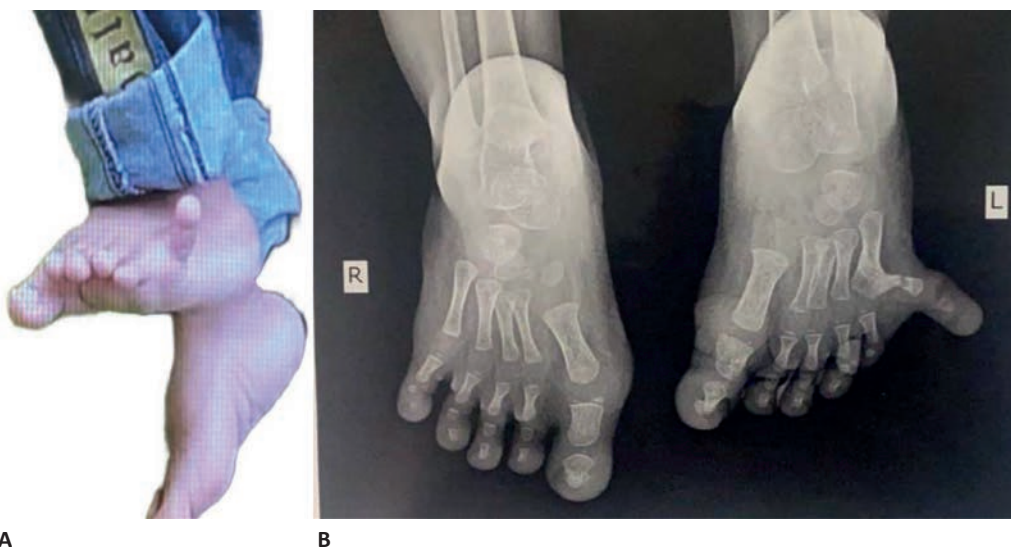
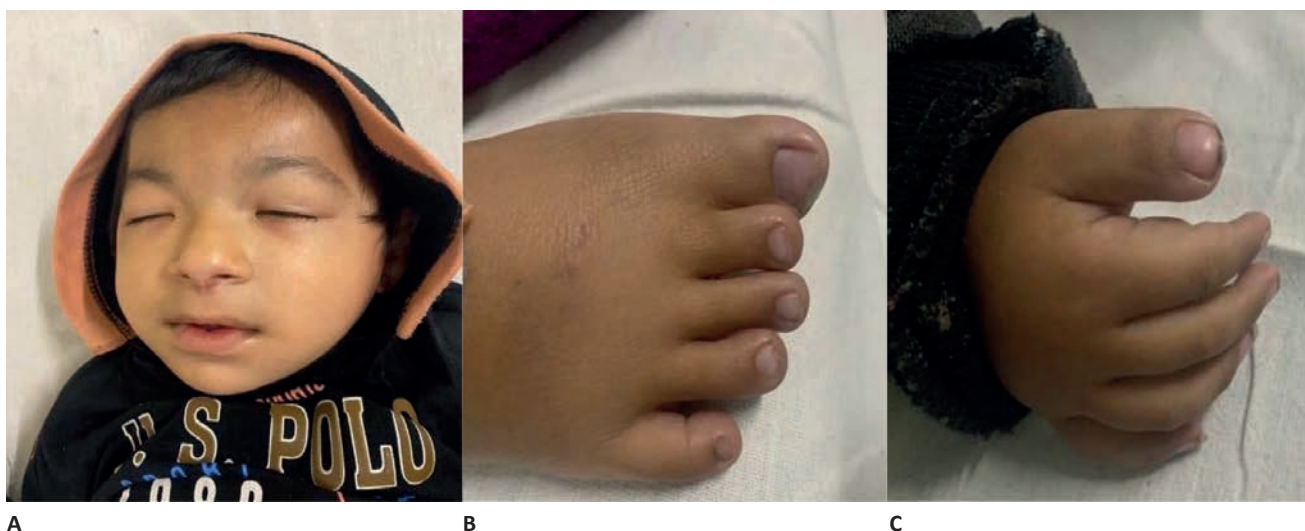


FIGURE 2. A. Post axial polydactyly; B. Fracture of extra toe



**FIGURE 3.** A. Rubinstein-Taybi Facies; B. Broad Great Toe and terminal phalanges; C. Broad Thumb

50% for social and language milestones. Facial features included slanting palpebral fissure, hypertelorism with low set ears and low columella and a prominent forehead. The child also had a high arched palate with carious dentition. Patient has broad thumbs in both hands and broad terminal phalanges of all limbs (Figure 3). MRI was done which was normal. Thyroid profile done was normal and 2D-ECHO was normal. USG abdomen and pelvis was done which was normal. No significant antenatal history given by the mother. Birth history and family history was insignificant. Clinically the child had Rubinstein-Taybi syndrome with a rare presentation of polydactyly.

## DISCUSSION

Rubinstein-Taybi syndrome is a very rare genetic disorder of autosomal dominant inheritance. The incidence of Rubinstein-Taybi syndrome is 1 in 100000 to 125000 live births [4,8]. It is mainly caused due to mutation in the gene encoding CREBBP, it is a gene encoding cyclic-AMP related enhancer binding protein located on short arm of chromosome 16 at locus of 13.3 (16p13.3), which results in characteristic features of Rubinstein Taybi Syndrome. CREBBP gene helps in basic cellular functions like DNA repair, cellular growth and differentiation, apoptosis of the cells and also aids as a tumor suppressor gene through different signal pathways. Molecular analysis for identifying CREBBP and EP300 genes is therefore essential [9]. It is characterized by differentiating facial features with typical hand and foot findings. Some of the problems that are encountered in the early life are feeding problems, poor weight gain and respiratory difficulties. There are complications related to teeth such as Talon cusps, abnormal tooth number [10,11] and enamel hypoplasia. The Talon cusps usually occur on the upper incisors of secondary dentition. Heart diseases are major

complications observed that include, Ventricular and Atrial septal defect, pulmonary stenosis, dextrocardia and disorders related to conduction [12]. A relation with hypoplastic left heart with the RSTS has also been observed in few cases [13].

Thyroid hypoplasia, congenital hypothyroidism and pituitary hypoplasia are some of the Endocrine disorders that have been studied [14,15]. Apart from these, constipation (40-74%), megacolon [10,15] and GERD have been observed with respect to the digestive system. Recurrent of abdominal pain, appearance of blood in stools have been indicated [16].

There are few growth issues like prenatal growth that is considered to be normal and begins at the initial stages of life. There is complete absence of growth in adolescence. In case of females at the age of 21, the BMI may be increased, where as it is normal in males. Obesity is observed in many adults [9]. The average height for adult females is 151.0 cm and in males it is 162.6 cm [13] and these growth charts have also been published for RSTS. Disorders related to eyes include corneal abnormalities, strabismus, glaucoma, refractory errors and coloboma etc. There can be hearing loss in some cases because of the refractory middle ear disease that may result in gradual hearing loss. The respiratory issues observed include sleep apnea that is caused, due to hypotonia, collapsibility of laryngeal walls and micrognathia. Renal problems are very common, which include UTIs, hypospadias, nephrolithiasis, hydro-nephrosis and duplications etc. Most of the boys have been observed with undescended testes. Orthopedic complications like spine curvatures, slipped capital femoral epiphysis, dislocated patellae and lax joints were commonly occurring along with vertebral abnormalities. Some neurologic anomalies such as the craniospinal abnormalities that include syringomyelia and cervical cord compression have been reported [17].

Many kinds of malignant and benign tumors were reported in few patients with RSTS. This included medulloblastoma, neuroblastoma and malignancies in blood. There was a study conducted in the Dutch population having RSTS where there was no confirmation with respect to malignancies. But the incidence of pilomatricomas and meningiomas was studied [18]. There has been delayed development in children with RSTS. An observation of the average age for walking was 30 months, speaking first words was 25 months and toilet training could happen at the age of 62 months. There was a deficit in the visuospatial working memory and verbal skill [19]. There was decreased IQ of 51 and for few it was from 25 to 79. In a study there has been a decline in the abilities of 32% in adults with RSTS. This included limited speech, decreased social interaction and effect on mobility and stamina [14].

Three RSTS cardinal features have been described in 2009 by Galèra et al. that include short attention span, poor coordination and motor stereotypies [10]. Thus in the mildest cases, main stages of development should be followed in order to initiate an individualized stimulation as early diagnosis can be difficult. Individuals with RSTS have sociable and

friendly nature and the behavioral disorders like OCD and mood swings can be observed only in adulthood [9,15]. Behavioral changes like unstable mood, distractibility and impulsivity have been frequently observed [10]. Attention problem, aggressive nature and self-injurious behavior have also been observed. Nearly 62% of the adults with RSTS were reported with autistic behavior. Others have anxiety or unknown fears. Occurrence of panic attacks and agoraphobia at higher levels has been observed [15].

## CONCLUSION

Polydactyly is a rare occurrence of Rubinstein Taybi Syndrome as mentioned above, hence, though this patient has polydactyly he was asymptomatic till he received trauma to the extra digit and underwent surgical amputation around 3 years of age. Owing to the complexity and rarity of this syndrome, multiple questions still remain unanswered about Rubinstein-Taybi syndrome. This syndrome requires extended investigations clinically focused on diagnosis and management with genotype-phenotype correlation.

*Conflict of interest:* none declared

*Financial support:* none declared

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