

CASE REPORT

An Attempt to rehabilitate a Case of Rubinstein–Taybi Syndrome: A Rare Disorder

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ABSTRACT

Rubinstein–Taybi syndrome (RSTS) is a genetically heterogeneous, rare, neurodevelopmental condition with the usual stigmata of facial dysmorphism, broad thumb and hallux, multisystem involvement, and developmental delay, which are themselves clinically diagnostic in the absence of standard criteria. Amidst all these physical features, the sensory, cognitive, behavioral, intellectual, and sometimes autistic features of the condition often escape attention. This case illustrates that the management of all these different aspects remains an integral part of rehabilitation.

Keywords: Autistic disorder, Intellectual disability, Occupational therapy, Rubinstein–Taybi syndrome.

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INTRODUCTION

Rubinstein–Taybi syndrome, formerly known as the broad thumb hallux syndrome, is a rare, congenital, neurodevelopmental disorder. The syndrome was first described by Rubinstein, a pediatrician, and Taybi, a radiologist in 1963. The RSTS is characterized by typical craniofacial dysmorphism, skeletal abnormalities like broad thumbs and first toes, postnatal growth retardation,¹ delay in intellectual and psychomotor development, and other associated systemic malformations.

The prevalence is estimated to be 1 in 100,000 to 125,000 worldwide,² and both genders are affected equally.

There are no established diagnostic criteria for RSTS. Hence, identification of the striking, characteristic features around the face and limbs and detailed clinical examination remain the cornerstone of diagnosis. The occurrence is generally sporadic with *de novo* mutation. However, cytogenetic or molecular abnormalities like a microdeletion of chromosome 16p13.3, or mutation in either the cyclic adenosine monophosphate response element-binding protein (CREB)-binding protein (CBP) or E1A-binding protein (EP300) can be detected in 55 to 78% of RSTS patients.^{3,4} However, a negative result does not exclude the diagnosis. Database search is a useful supportive tool as well.

Life expectancy seems to be normal and therapeutic approaches are symptomatic.

CASE REPORT

A two-and-half-year -old male child, who was unable to stand or walk independently or speak bisyllables until date, was brought to the outpatient department of National Institute for Locomotor Disabilities by his parents in September 2013. Careful history taking and physical examination were followed by relevant hematological, radiological, and ophthalmological investigations. The child was born out of nonconsanguineous marriage, had normal perinatal history, but recurrent upper and lower respiratory tract infection. He had microcephaly, high arched eyebrows, down-slanting palpebral fissure (Fig. 1A) with long eyelashes, broad nasal bridge with beaked nose, thin upper lip, grimacing type of smile with eyes almost closed, low-set ears, high arched palate, and talon cusps on upper incisors. He had broad thumb (Fig. 1B) and broad first toes (Fig. 1C) along with pes planus. Tone, power, and deep reflexes of the limbs were normal. He was overweight and had global developmental delay. There was slow development of gross, fine motor, and sociocognitive skills and borderline speech and language developmental delay (monosyllables at 12 months). Psychological assessment showed a developmental and social age of 1 year and 7 months, developmental quotient (DQ) was 70, and social quotient was 71 (Vineland social maturity scale). The parents were interviewed and the child was

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Figs 1A and B: (A) Low palpebral fissure; (B) Broad thumb

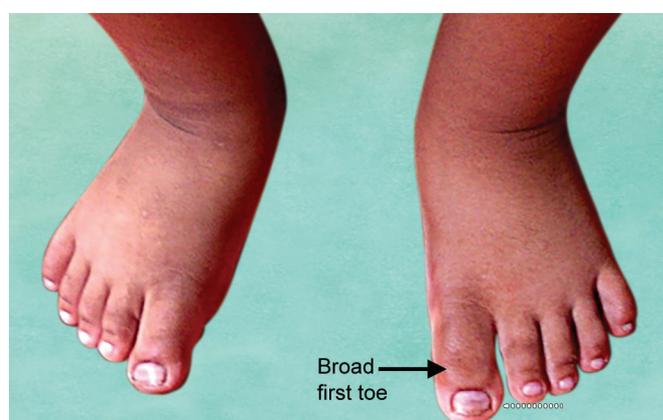


Fig. 1C: Broad first toe



Fig. 2: Sensory integration therapy

carefully observed in the pediatric occupational therapy setup. He was hyperactive, occasionally aggressive, and showed repetitive motor stereotypies. He demonstrated tactile hyperresponsivity of all four limbs and gravitational insecurity. On application of the Childhood Autism Rating Scale (CARS), he was found to be moderately autistic with a score of 35 (30–36). Bilateral cryptorchidism with both testes in the inguinal region was found on ultrasonography. Serum level of 25-hydroxy vitamin D3 [25(OH)D3] was low. No ocular, hearing, dermatological, cardiac, renal, or neoplastic abnormalities were found. Based on extensive literature search and database (Online Mendelian Inheritance in Man) search, the clinical features of the index case gave strong suspicion of the diagnosis of a case of RSTS. It was then agreed upon by a team of pediatricians adept at dealing with syndromes and genetic disorders on a regular basis. The fluorescent in situ hybridization for 16p13.3 and CREB could not be done due to financial constraints.

MANAGEMENT

Parental counseling was done and guidance for genetic counseling was provided. Shoes were modified bilaterally

with medial arch support and Thomas heel for pes planus. The mainstay of the occupational therapy was sensory integration therapy (SIT) (Fig. 2). The rehabilitation program included developmental therapy, balance training, training for activities of daily living, play therapy in groups, and activities with toys, beads, and shapes to improve hand function and fine motor coordination skills. Child was evaluated by psychiatrist and psychologist and behavioral therapy for autistic features was started. He underwent a course of speech therapy simultaneously. An 8-weekly dose of vitamin D3 (60 k) was given followed by four monthly doses. Bilateral orchidopexy was done as well.

RESULTS

After 6 weeks of therapy (November 2013), there was noticeable decrease in tactile hyperresponsiveness and gravitational insecurity.

After 8 months of therapy (May 2014), the CARS score improved to 30, especially in domains of verbal and non-verbal communication, activity level, body use, object use,

adaptation to change, taste/smell/touch appreciation, and general impression. The child was able to stand, walk, and run independently. There was improvement in hand function. The 25(OH) D3 level was corrected to 42.5 ng/mL.

After another 1 year of behavioral and speech therapy (June 2015), the CARS score improved to 28 with further improvement in areas of emotion, adaptation to change, communication level, and listening response. However, obsession with smell and occasional aggressiveness persisted.

At present, the child goes to a regular school. He has mild age-inappropriate intellectual response with some learning disability.

DISCUSSION

The RSTS is a rare, plurimal formative, genetically heterogeneous syndrome. Microcephaly with down-slanting palpebral fissures and long eyelashes, highly arched and thick eyebrows, low-set dysplastic ears, beaked nose with columella extending well beyond the nares, atypical grimacing smile, high arched palate, and micrognathia are the usual characteristic craniofacial features. Broad thumb and broad first toes are present in almost all cases² and are radially deviated in about one-third of the cases. Cryptorchidism affects 78 to 100% of the male infants⁴ and talon cusp are frequently found.^{4,5} Congenital cardiac, renal, dermatological, skeletal, and ophthalmological abnormalities may be present. There is an increased risk of developing tumors,³ mainly meningioma,⁶ which tends to occur before 15 years of age, hence needing regular follow-up as per the guidelines.⁴

Growth and speech delay are common. Intellectual disability is almost universally present⁴ and the reported intelligence quotient range is between 25 and 79.^{1,7,8} In this patient, the DQ was 70. In spite of variable cognitive impairment, children with RSTS are generally friendly with good capability to develop social and communication skills. However, Rubinstein and Taybi had mentioned hyperactivity in their original report in 1963. Hennekam et al³ noted behavioral problems in 25% cases, Waite et al⁷ found a relation with repetitive behavior and Galéra et al⁸ described short attention span, poor coordination, and motor stereotypies in RSTS. The abnormality in CREB BP gene is probably related to the impaired motor skills learning.^{3,8} On application of the CARS, we found autistic behavior in the index case. Sensory processing dysfunction, especially tactile sensitivity, is commonly found in autism.⁹ The SIT by providing tactile, proprioceptive, vestibular, visual, and auditory input increases attention, decreases defensiveness, and improves fine motor skills in autism.¹⁰ The authors found SIT along with behavioral

therapy to be extremely efficacious in the RSTS child with autistic features.

Although most cases are sporadic, somatic mosaicism has been noted in the rare familial RSTS described in literature.⁴ The recurrence risk has been estimated to be about 0.5 to 1%.¹

CONCLUSION

A rare genetic multisystem disorder like RSTS is essentially a clinical diagnosis and needs a multidisciplinary approach. The authors have attempted to utilize this approach, with emphasis on behavioral therapy and SIT. There is a dearth of published literature on the management of this syndrome, especially from the developing world, which makes this case unique.

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