International Journal of Contemporary Pediatrics
Jagtap SS et al. Int J Contemp Pediatr. 2022 Nov;9(11):1109-1111
http://www.ijpediatrics.com
pISSN 2349-3283 | eISSN 2349-3291

DOI: https://dx.doi.org/10.18203/2349-3291.ijcp20222630

Case Report

Rubinstein–Taybi syndrome: a case report

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Received: 27 September 2022
Revised: 10 June 2022
Accepted: 10 July 2022

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ABSTRACT

Rubinstein Taybi syndrome (RTS) is a rare genetic condition caused by a mutation or deletion in the CREBBP and/or EP300 gene located on chromosome 16. It is characterized by short stature, moderate to severe learning difficulties, distinctive facial features and broad thumbs and toes. It occurs in estimated 1 in 1,25000 to 3,00000 births. Diagnosis mainly depends upon the presence of distinctive features, abnormal facies, abnormalities of limbs. These patients are also at increased risk of developing meningioma, other brain tumours and leukaemia, thus early diagnosis and recognition of malignancy can aid in successful life-saving interventions.

Keywords: Rubinstein Taybi syndrome, Genetic condition, CREBBP gene, EP300 gene

INTRODUCTION

A syndromic disorder, Rubinstein Taybi syndrome (RTS) is otherwise called broad Thumb-Hallux syndrome was initially described by Michail et al in 1957. The incident rate of the syndrome has been calculated to be 1 in every 300,000 newborns.[1] Syndrome is distributed equally amongst males and females. The main distinctive features commonly associated with this syndrome are abnormal facies (prominent forehead, well developed prominent arching eyebrows, anti- mongoloid slant of eyes, prominent nose, long overhanging columella, fullness of cheeks, characteristic grin on opening the mouth), abnormalities of limbs (abnormal thickening of distal phalanges, bilaterally abnormal thick and stubby thumb, radial deviation of thumb, bilaterally abnormal squared shape great toe).[2] The other features associated with this syndrome could be undescended testis, low IQ, renal anomalies and cardiovascular system (CVS) anomalies (ASD and VSD). One important aspect is the fact that RTS patients are prone to develop tumours. Neuroblastoma, medulloblastoma, oligodendroglioma, meningioma, seminoma, odontoma, choristoma, and polimatrixtomas were the reported tumours in RTS patients. These tumours have a pattern of neural and developmental origin.

CASE REPORT

Our patient, a 12-year-old female child was brought to our outpatient department (OPD) with complains of incoherent speech. Patient was admitted and a thorough history was noted. There was delay in attainment of milestones during infancy and childhood but the child is currently developmentally normal. On head-to-toe examination, the child had dysmorphic facies. The child had large forehead with arching and well-developed eyebrows, large columella leading to beaked nose appearance, puffed cheeks and abnormal grin on opening mouth. She had short fourth metacarpal and abnormally broad distal phalanges. The hallux was broad and square shaped with short fourth metatarsal. All these classical clinical features pointed towards the diagnosis of Rubinstein Taybi syndrome. The incoherent speech was attributed to tongue tie that was present.

The patient was thoroughly investigated. Ultrasonography (USG) abdomen and 2D echo was normal. Pediatric

surgery reference taken i/v/o tongue tie and got operated. Speech therapy started. Mouth rehabilitation done i/v/o dental caries. Ear, nose and throat (ENT) and ophthalmological evaluation done, which was normal. Patient advised IQ testing and procurement of disability certificate according to the results. Patient was directed for vocational training. Parents were counselled regarding the syndrome and the necessity of remaining in follow up.

Figure 1: Rubinstein-Taybi syndrome-showing distinctive clinical features like large forehead, high arched eyebrows, long columella, abnormal grin.

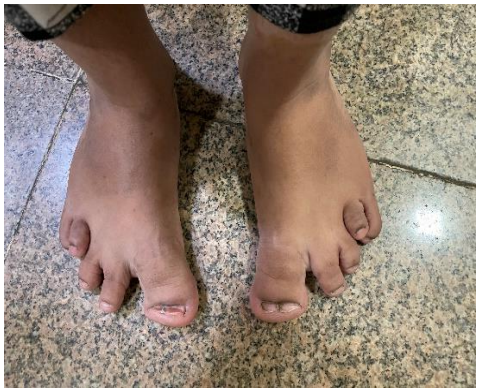

Figure 2: Rubinstein Taybi syndrome- showing bilaterally abnormal square shaped great toe.

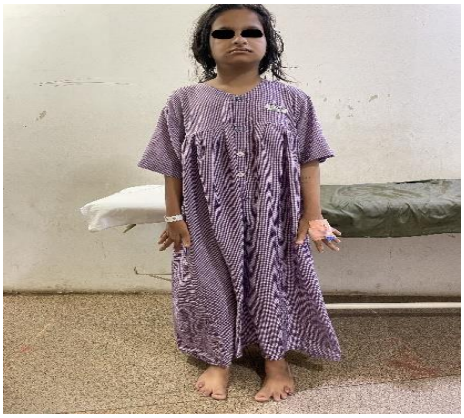

Figure 3: Rubinstein Taybi syndrome - showing abnormal facies and limb abnormalities.

DISCUSSION

RSTS is characterized by distinctive facial features, broad and often angulated thumbs and halluces, short stature, and moderate-to-severe intellectual disability. The characteristic craniofacial features are downslanted palpebral fissures, low-hanging columella, high palate, grimacing smile, and talon cusps. Prenatal growth is often normal, then height, weight, and head circumference percentiles rapidly drop in the first few months of life. Short stature is typical in adulthood. Obesity may develop in childhood or adolescence. Average IQ ranges between 35 and 50; however, developmental outcome varies considerably. Some individuals with EP300-RSTS have normal intellect. Additional features include ocular abnormalities, hearing loss, respiratory difficulties, congenital heart defects, renal abnormalities, cryptorchidism, feeding problems, recurrent infections, and severe constipation.

The diagnosis of RSTS is established in a proband with characteristic clinical features. Identification of a heterozygous pathogenic variant in CREBBP or EP300 confirms the diagnosis if clinical features are inconclusive.[3]

Early intervention programs, special education, vocational training to address developmental disabilities, referral to behavioral specialists/psychologists, and support groups/resources for family members; standard treatment for eye abnormalities, hearing loss, sleep apnea, cardiac anomalies, renal anomalies, cryptorchidism, and dental anomalies; aggressive management of gastroesophageal reflux and constipation; surgical repair of significantly angulated thumbs or duplicated hall.[4] Monitoring of growth and feeding, especially in the first year of life; annual eye and hearing evaluations; routine monitoring for cardiac, renal, and dental abnormalities.

RSTS is inherited in an autosomal dominant manner. RSTS typically occurs as the result of a de novo pathogenic variant in the family; most individuals represent simplex cases (i.e., the only affected member in a family). In most instances, the parents of an individual with RSTS are not affected. When the parents are clinically unaffected, sibs are still presumed to be at increased risk for RSTS because of the possibility of a mild phenotype in a heterozygous parent or parental somatic and/or germline mosaicism. The empiric recurrence risk for sibs is less than 1%. Individuals with RSTS rarely reproduce. The risk to offspring is 50%. Once the pathogenic variant has been identified in an affected family member, prenatal testing for a pregnancy at increased risk and preimplantation genetic testing are possible.

CONCLUSION

A thorough work up of all syndromic patients is essential to rule out complications. Such patients should be kept in

regular follow up to keep a watch on progression of abnormalities. Early intervention programs, vocational training to address developmental disabilities help the patients in leading a near normal life.

Funding: No funding sources
Conflict of interest: None declared
Ethical approval: Not required

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Cite this article as: Jagtap SS, Inamdar P, Pal R, Rai RK. Rubinstein–Taybi syndrome: a case report. Int J Contemp Pediatr 2022;9:1109-11.