

MEDICAL SCIENCE

To Cite:

Desai K, Taksande A, Meshram R, Jain A. Beaked nose with syndactyly: A rare case of Rubenstein-Taybi syndrome. *Medical Science* 2023; 27: e280ms3070.
doi: <https://doi.org/10.54905/disssi/v27i136/e280ms3070>

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Peer-Review History

Received: 15 April 2023

Reviewed & Revised: 19/April/2023 to 20/June/2023

Accepted: 24 June 2023

Published: 29 June 2023

Peer-review Method

External peer-review was done through double-blind method.

Medical Science

pISSN 2321-7359; eISSN 2321-7367

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Beaked nose with syndactyly: A rare case of Rubenstein-Taybi syndrome

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Apoorv Jain¹**

ABSTRACT

Rubinstein-Taybi syndrome is a rare genetic disorder characterized by facial dysmorphism along with multiple malformations. A 6 years old male child was brought to the Department with complaints of stammering speech and webbed as well as joint fingers. Extraoral features revealed characteristic facial appearance with a nasal septum extending below alae nasi i.e., beaked nose, posteriorly rotated ears, maxillary hypoplasia and the clinical features, cardiac abnormality and treatment plan of this patient are considered in this case report. Identification of multiple malformations associated with this syndrome is pivotal for an early diagnosis as multidisciplinary approach is required in the initial evaluation, treatment and follow-up among these patients.

Keywords: Rubinstein-Taybi syndrome (RTS) or (RSTS), Beaked nose, Broad thumb-hallux syndrome, Clinodactyly, Syndactyly

1. INTRODUCTION

Rubinstein-Taybi syndrome (RTS) is a congenital, rare, neurodevelopmental and plurimal formative disorder (Spena et al., 2015). It was first recognized as syndrome in the United States in 1963 when medical doctors, Jack Rubinstein along with Hooshang Taybi published the first case series consisting of seven individuals, however, this happened after Rubinstein and Taybi evaluated two children with intellectual disability who had a same facial appearance and more significant was their unusual big toes and broad thumbs. Further, they circulated the clinical profile to other colleagues and an additional five cases were discovered. The syndrome is also known as *broad thumb-hallux syndrome* because of these defining characteristics (Braaten, 2018).

Plurimalformative syndromes are named according to their low prevalence and incidence in the population and comprise of a large group of rare diseases and Rubinstein-Taybi syndrome is considered as one of these rare diseases (Milani et al., 2015). There is a lack of objective criteria for this syndrome and hence difficult to diagnose on clinical signs and symptoms. Etiology has been associated with two known genes: *CREBBP* and *EP300* (Spena et al., 2015).

The diagnostic clinical features present at birth include broad thumbs and

toes, distinct facies and mental retardation. There are certain peculiar facial features of this syndrome such as broad nasal bridge with the nasal septum extending below the alae, beaked pointed nose, epicanthal folds, microcephaly, palpebral fissures which slant downward, bossing forehead and strabismus (O'Neil et al., 1989). Here in, we discuss a case of 6 years old male child who was brought to the department with complaints of stammering speech and webbed as well as joint fingers.

2. CASE REPORT

A 6-year-old male child was brought with complaints of stammering speech and webbed and joint fingers. The clinical findings that were consistent with Rubinstein–Taybi syndrome diagnosis comprised of beaked nose, downward slanting palpebral fissure (Figure 1), maxillary hypoplasia and webbed and joint fingers (Figure 2). On observation his nasal septum was extending below alae nasi with posteriorly rotated ears, maxillary hypoplasia (Figure 1).

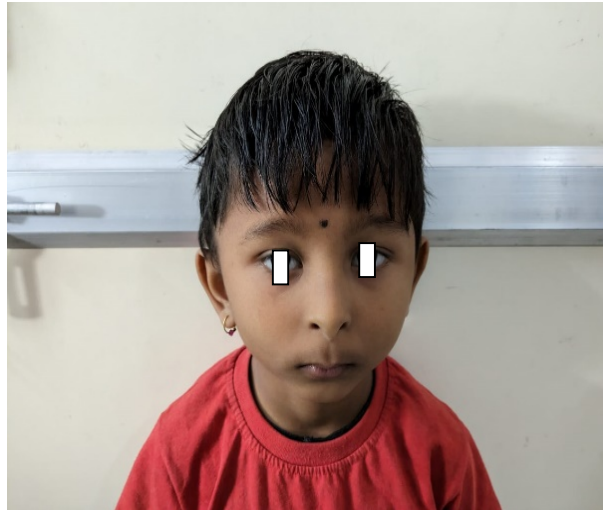


Figure 1 Beaked nose, downward slanting palpebral fissure, maxillary hypoplasia



Figure 2 Fourth finger clinodactyly on both sides, syndactyly between third, fourth and fifth fingers of hand

After evaluation of clinical features and patient's history, patient was referred for 2d echo, USG abdomen- pelvis, X-ray spine, examination of eyes with fundal examination and examination of parents was also done for various signs and symptoms, which was normal and no family history of such findings as well. Examination of hands and feet revealed fourth finger clinodactyly on both sides, syndactyly between third, fourth and fifth fingers of hand (Figure 2).

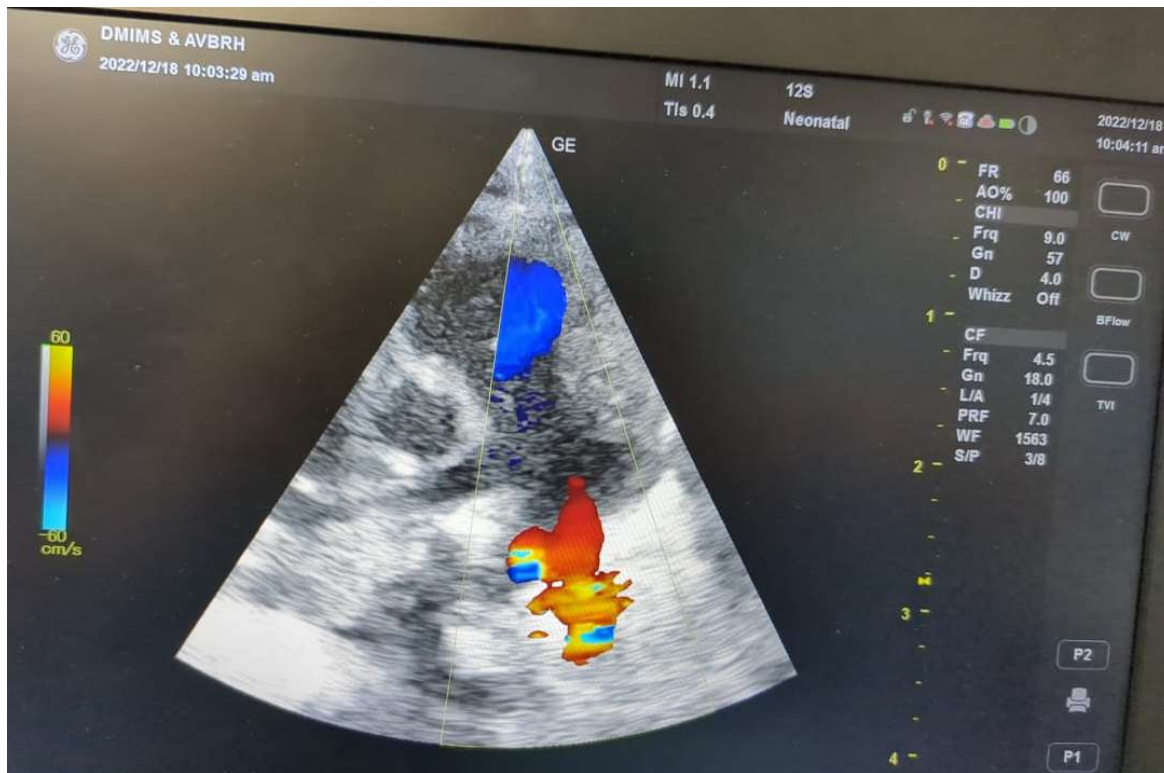


Figure 3 2D echocardiography revealed hemodynamically insignificant PDA of 4mm

On 2D echo, hemodynamically insignificant PDA of 4mm was seen (Figure 3). USG abdomen, EEG, X-ray spine, ophthalmological examination was normal. Several conditions that were included in the differential diagnosis before reaching the final diagnosis of Rubinstein-Taybi syndrome are Tricho-rhino-phalangeal syndrome, Floating Harbor syndrome and FG syndrome; however, were subsequently ruled out. PDA ligation was done and speech therapy was initiated.

3. DISCUSSION

RTS patients typically have a normal prenatal course and are acknowledged when delivered due to their characteristic facial appearance as well as hand and feet anomalies. Secondly, children affected with RTS presents with delayed mental growth showing mild to severe mental retardation and the mean intelligence quotient most probably around 35. Furthermore, approximately 50% of patients have an abnormal Electroencephalogram (EEG) and a third among most prominent features of RST patients is congenital heart defects (Chopra et al., 2019). The present patient presented with beaked nose and nasal bridge with the nasal septum lengthening below the alae, palpebral fissures which slant downward which were consistent with the typical facial appearance of this syndrome.

The various cardiac anomalies among patients affected by the Rubinstein-Taybi syndrome are atrial septal defect (ASD), ventricular septal defect (VSD), patent ductus arteriosus (PDA), coarctation of the aorta, pulmonic stenosis or bicuspid aortic valve (Stevens and Bhakta, 1995). In the present case, hemodynamically insignificant PDA of 4mm was reported on 2d echo. In a retrospective analysis of cases of 11 patients of Rubinstein-Taybi syndrome at tertiary hospital in North India by Kumar et al., (2012) had growth failure postnatally and short stature was found in about 7 patients. Developmental delay was found in 10 patients, 7 patients showed mental retardation and seizures in 1 case. In the present case no mental abnormality was detected.

Additional reported features among RTS patients comprise of hearing loss, ocular abnormalities, feeding problems, respiratory difficulties, renal abnormalities, congenital heart defects, cryptorchidism, recurrent infections as well as severe constipation (Stevens, 2019). Except congenital heart defect, no other abnormality was detected in the present case. Several conditions that were included in the differential diagnosis before reaching the final diagnosis of Rubinstein-Taybi syndrome are Tricho-rhino-phalangeal syndrome (Lüdecke et al., 2001).

Floating Harbor syndrome (White et al., 2010) and FG syndrome (Lyons et al., 2009), however were subsequently ruled out. Appropriate databases were searched along with online databases for extraction of diagnosis of the present case. Tricho-rhino-phalangeal syndrome (TRPS) is typified by a bulbous nasal tip, sparsely distributed scalp hair, a flat long philtrum, a narrow upper

vermilion border and protruding ears. Skeletal abnormalities include short stature, shortened phalanges and metacarpals, cone-shaped epiphyses at the phalanges and hip malformations (Lüdecke et al., 2001).

Floating-Harbor syndrome is characterized by low birth weight, short stature with delayed bone age, dysmorphic facial appearance and developmental delay. Facial features include deep-set eyes with long eyelashes, a large rounded bulgy nose with a wide nasal bridge, a triangular-shaped face, a broad mouth with tinny lips and a short smooth philtrum, a wide columella and broad, short or bifid thumbs (White et al., 2010). FG syndrome (FGS) is characterized by hypotonus dysmorphic facial features, retarded mental growth and abnormalities of the corpus callosum, broadened thumbs and halluces, constipation and anal anomalies (Lyons et al., 2009).

In the present case hypotonia, broad thumbs and halluces, constipation, anal anomalies, mental retardation, corpus callosum abnormalities, bifid thumbs or cone-shaped epiphysis of phalanges, sparse scalp hair, a bulbous tip of the nose, a long flat philtrum or a thin upper vermilion border, hip malformations were absent. In the neonate this syndrome can be confused with the de Lange syndrome, trisomy 13, Apert syndrome and Pfeiffer syndrome. Therefore, it is best to consider individuals without all the classic features of RTS syndrome as having an "incomplete form" rather than an incorrect. Feeding problems, upper respiratory infections and recurrent otitis media are common during infancy (O'Neil et al., 1989).

The revealed frequency is of approximately one affected individual in 100 000 newborns. Mutations in EP300 and CREBBP genes have been recognized to cause this syndrome (Roelfsema and Peters, 2007). The gene *EP300* is essential for normal cardiac and neural development, whereas *CREBBP* is essential for hematopoietic differentiation, neurulation, angiogenesis and skeletal as well as cardiac development. Hence, mutations in *CREBBP* gene results in Rubinstein-Taybi syndrome i.e., characterized by mental retardation, skeletal abnormalities and congenital cardiac defects (Bamforth et al., 2001).

Rare mutations as seen with gene EP300 are also seen. Comprehensive screening of patients has shown mutated CREBBP and EP300 genes in approximate 50% of cases. Still the cause of the various manifestations we know is unknown, other not known genes could also be involved, which are yet to be discovered (Roelfsema and Peters, 2007).

4. CONCLUSION

When compared to the general population, children and adults with Rubinstein-Taybi Syndrome have unique medical issues. Identification of multiple malformations associated with this syndrome is pivotal for an early diagnosis as interdisciplinary approach is recommended in the initial assessment, management and follow-up among these patients.

Acknowledgement

We thank the participants who were all contributed samples to the study.

Informed consent

Written & Oral informed consent was obtained from all individual participants included in the study. Additional informed consent was obtained from all individual participants for whom identifying information is included in this manuscript.

Funding

This study has not received any external funding.

Conflict of interest

The authors declare that there is no conflict of interests.

Data and materials availability

All data sets collected during this study are available upon reasonable request from the corresponding author.

REFERENCES AND NOTES

- Bamforth SD, Bragança J, Eloranta JJ, Murdoch JN, Marques FI, Kranc KR, Farza H, Henderson DJ, Hurst HC, Bhattacharya S. Cardiac malformations, adrenal agenesis, neural crest defects and exencephaly in mice lacking Cited 2, a new Tfp2 co-activator. *Nat Genet* 2001; 29(4):469-74. doi: 10.1038/ng768
- Braaten E. The SAGE encyclopedia of intellectual and developmental disorders. Sage Publications 2018.

3. Chopra SS, Chauhan A, Mitra R. Rubinstein–Taybi syndrome: A case report. *Int J Med Dent Case Rep* 2019; 6(1):1-3. doi: 10.15713/ins.ijmdcr.125
4. Kumar S, Suthar R, Panigrahi I, Marwaha RK. Rubinstein-Taybi syndrome: Clinical profile of 11 patients and review of literature. *Indian J Hum Genet* 2012; 18:161-6. doi: 10.4103/0971-6866.100751
5. Lüdecke HJ, Schaper J, Meinecke P, Momeni P, Groß S, Von-Holtum D, Hirche H, Abramowicz MJ, Albrecht B, Apacik C, Christen HJ, Claussen U, Devriendt K, Fastnacht E, Forderer A, Friedrich U, Goodship TH, Greiwe M, Hamm H, Hennekam RC, Hinkel GK, Hoeltzenbein M, Kayserili H, Majewski F, Mathieu M, Mc-Leod R, Midro AT, Moog U, Nagai T, Niikawa N, Orstavik KH, Plöchl E, Seitz C, Schmidtke J, Tranebjaerg L, Tsukahara M, Wittwer B, Zabel B, Gillessen-Kaesbach G, Horsthemke B. Genotypic and phenotypic spectrum in Tricho-Rhino-Phalangeal syndrome types I and III. *Am J Hum Genet* 2001; 68(1):81-91. doi: 10.1086/316926
6. Lyons MJ, Graham JM, Neri G, Hunter AG, Clark RD, Rogers RC, Moscarda M, Boccuto L, Simensen R, Dodd J, Robertson S, Du-Pont BR, Friez MJ, Schwartz CE, Stevenson RE. Clinical experience in the evaluation of 30 patients with a prior diagnosis of FG syndrome. *J Med Genet* 2009; 46(1):9-13. doi: 10.1136/jmg.2008.060509
7. Milani D, Manzoni FM, Pezzani L, Ajmone P, Gervasini C, Menni F, Esposito S. Rubinstein-Taybi syndrome: Clinical features, genetic basis, diagnosis and management. *Ital J Pediatr* 2015; 41(1):1-9. doi: 10.1186/s13052-015-0110-1
8. O'Neil DW, Canada RT, Clark MV, Lowe DJ. Rubinstein-Taybi syndrome: Case report. *Pediatr Dent* 1989; 11(2):158-60.
9. Roelfsema JH, Peters DJ. Rubinstein–Taybi syndrome: Clinical and molecular overview. *Expert Rev Mol Med* 2007; 9(23):1-6. doi: 10.1017/S1462399407000415
10. Spena S, Gervasini C, Milani D. Ultra-rare syndromes: The example of Rubinstein–Taybi syndrome. *J Pediatr Genet* 2015; 4(03):177-86. doi: 10.1055/s-0035-1564571
11. Stevens CA, Bhakta MG. Cardiac abnormalities in the Rubinstein-Taybi syndrome. *Am J Med Genet* 1995; 59(3):346-8.
12. Stevens CA. Rubinstein-Taybi Syndrome 2019. <https://europepmc.org/article/nbk/nbk1526>
13. White SM, Morgan A, Da-Costa A, Lacombe D, Knight SJ, Houlston R, Whiteford ML, Newbury-Ecob RA, Hurst JA. The phenotype of Floating–Harbor syndrome in 10 patients. *Am J Med Genet A* 2010; 152A(4):821-9. doi: 10.1002/ajmg.a.33294