

Rubinstein Taybi Syndrome - A Case Report from India

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Authors' contributions

This work was carried out in collaboration among all authors. Author KD did the concept, design, drafting and critical revision of the article. Author SSS did clinical/radiographic data, literature review and revision. Authors BS, RS and AV managed the literature review and revision. All authors read and approved the final manuscript.

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Case Report

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ABSTRACT

Rubinstein – Taybi syndrome (RTS) otherwise called as Broad Thumb-Hallux syndrome is considered to be a genetic disorder characterized by facial dysmorphism mental deficiency and growth retardation. Presented here is a case report of the patient with RTS with comprehensive oro-dental treatment. This case report describes the clinical features of a 25-year-old female with RTS, who had multiple dental problems such as multiple missing teeth, dental caries, periodontal disease and severe malocclusion. Physical findings were similar to those previously described in other reports. In this case report, the extraoral and intraoral features of this patient are discussed.

Keywords: Rubinstein taybi syndrome; thumb-hallux syndrome; genetic disorder.

1. INTRODUCTION

A Neuro-developmental 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. Both males and females

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have been equally distributed. It is due to the noticeable clinical features such as broad thumb and toes [1].

The main distinctive features most commonly associated with this syndrome are postnatal growth deficiency, typical dysmorphic facies, downward sloping palpebral fissures, broad thumbs and halluces, and psychomotor developmental delay, typical altered facial features, a prominent forehead, hypertelorism, and mental disability [2]. 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.

Oral findings of this syndrome include retro/micrognathia, limited mouth opening, a high arched and narrow palate, a pouting lower lip, cleft uvula and palate, and rarely a cleft upper lip [3]. Dental abnormalities occur in 67% of individuals with RTS and can include hypodontia, maintenance of deciduous teeth, talon cusps, and enamel hypoplasia. Dental caries and periodontal disease have been reported in these patients [4].

2. CASE STUDY

A female patient aged 25 years, accompanied by her parents reported to the Department of Oral Medicine and Radiology complaining of missing teeth in the upper and lower front jaw region for the past 2 years.

The patient had a past medical history of preterm birth of 28 weeks. She also had primary complex and jaundice during her childhood. The family history was contributory as the younger sister also had a similar complaint of multiple missing teeth. Her parents were of low socioeconomic status.

The general examination revealed delayed expressive speech and developmental milestones. The patient had short stature (135 cm) and weighed (38.5 kg). The patient is moderately nourished and moderately built and had an average of 100 scores in IQ test.

On extraoral examination, signs of paleness in the bulbar conjunctiva. The patient had sparse hair on the scalp, excess hair growth on the face.

The bridge of the nose wide and appears beaked with septum extending below the alae of the nose. Thin upper lips evident.



Fig. 1. Patient showing micrognathic mandible, increased intercanthal distance, the beaked nose showing extended septum, wide bridge of the nose, hirsutism



Fig. 2. Lateral profile of the patient showing microstomia, thin upper lip, beaked nose with septum extending below alae of the nose, sparse hair on the scalp

The intraoral examination showed micrognathia with a limited mouth opening of 40 mm. Pale oral mucosa evident with shallow vestibular depth in the upper and lower arch. The maxillary arch has a high arched palate and the mandibular arch showed a shallow floor of the mouth with short lingual frenum. Multiple missing teeth in relation to 18,13,12,23,28,38,31,41,42,45,48 and

morphologically altered premolars and anterior teeth. Generalized microdontia was evident. Multiple morphologically altered teeth seen such as Talon's cusp in 11,21, Peg lateral -22 and hypo mineralized tooth with altered cuspal morphology in 14. Dental caries was also present in 36,37,46. Grade III mobility was seen in 11 and 21.



Fig. 3. Short stature of the patient

Due to multiple missing teeth, the patient underwent radiographic investigation. Orthopantomogram showed idiopathic external root resorption in multiple teeth, multiple morphologically altered shape of crown and roots of teeth, an ill-defined radiolucency showing periapical abscess 44. There was the presence of a single root and a single root canal with two crowns joined together in 14 similar to gemination. The crown of the teeth is enlarged at the expense of the root to 16,17,26,27,36,37, 46,47 resembling taurodontism. Altered condylar morphology and curved styloid process were seen bilaterally. There was an increased width of the mandibular canal bilaterally. Increased radiopacity evident in the left maxillary sinus with altered morphology of maxillary sinus bilaterally. Chromosomal mutation analysis was done using

Serial single-gene testing. The sequence analysis result showed small intragenic deletions detected when performed in CREB Binding Protein.

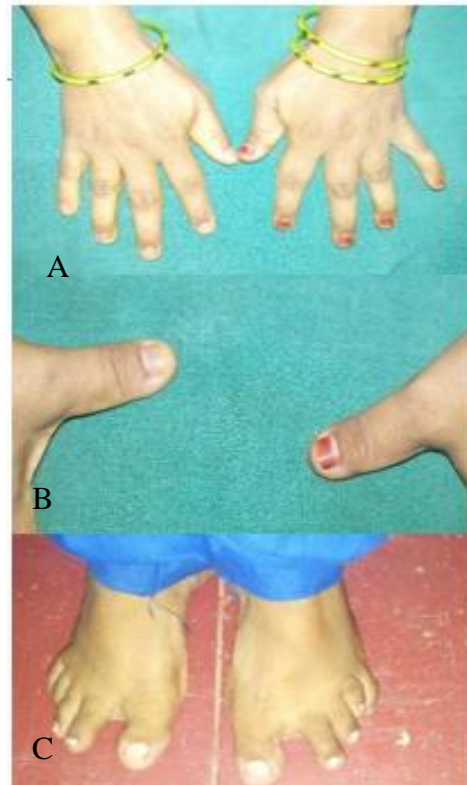


Fig. 4. A. Short digits. B. Broad thumb. C. Broad big toe with increased distance between first and second toes



Fig. 5. Small maxillary arch with the high arched palate, shallow vestibular depth, multiple missing teeth to 18,13,12,23,28 and morphologically altered premolars and anterior teeth



Fig. 6. Small mandibular arch with the shallow floor of the mouth, short lingual frenum, multiple missing teeth to 38,31,41,42,45,48



Fig. 7. Morphologically altered teeth seen with Talon's cusp in 11 and 21 peg lateral to 22



Fig. 8. Orthopantomogram showing idiopathic external root resorption, the morphologically altered shape of crown and root of teeth, periapical abscess -44, gemination -14, taurodontism -molars, altered condylar morphology, curved styloid process, increased width of the mandibular canal, obliteration of maxillary left sinus

The proposed treatment plan included full mouth rehabilitation, the vision of thorough oral prophylaxis, preventive sealing of deep fissures adjacent to talon cusps, restoration of carious teeth, removal of periodontally weaker teeth, replacement with implant prosthesis and supervised home oral care. Patient was referred to general physician for further investigation and management is required.

3. DISCUSSION

Rubinstein Taybi Syndrome is the occurrence of multiple congenital anomalies. There are eighteen varieties of chromosomal anomalies that have been observed in various studies in patients with this syndrome. The most occurring anomaly is either by a microdeletion at 16p13.3, or mutations in the CREB-binding protein (CREBBP or CBP) or EP300 gene (at 22q13) [4].

A mutation in the CREBBP gene (OMIM 600140) at the chromosomal locus 16p13.3 is detectable by the FISH technique in about 15% of persons with RSTS (RSTS1). With sequence analysis, this figure rises to 30-50%. In a minority of individuals, the EP300 gene (OMIM 602700) at 22q13 has been implicated (RSTS2) [5].

In this case, the patient showed extraoral features of broad thumb and big toe, short stature, short digits, hirsutism, alopecia. Also, intraoral features such as micrognathia, multiple missing permanent teeth, talon's cusp in upper anterior teeth, reduced buccal and lingual sulcus depth. Morphologically altered teeth and malocclusion were also evident. Various systemic abnormalities occur which manifest from early childhood in RTS patients. The most significant features are Broad thumb and first toes, short stature, vertebral abnormalities. Broadening of the thumb and big toe may be judged subjectively when the facies are suggestive. Also, broad thumbs may occur independently in a mentally handicapped person, either as part of normal variation or as dominantly inherited brachydactyly type D. The case for autosomal dominant inheritance seems as yet unproven. Since no subject showing all the classic hallmarks of the syndrome has reproduced, there remains the possibility of the full-blown syndrome arising from a dominant mutation. Mental handicap or developmental delay is universally present with IQ estimations ranging from 20 to 80. The mean in those diagnosed young is probably around 50 [3].

Some cardiac abnormalities have also been mentioned in some studies such as congenital heart diseases like ASD, VSD, PDA, coarctation of the aorta, pulmonic stenosis, bicuspid aortic valve, pseudotruncus, aortic stenosis, dextrocardia, vascular rings, and conduction problems [5]. 24–38% of children with RTS have cardiac abnormalities. If an abnormality is found, on-going care and monitoring by a cardiologist is warranted [6].

Most patients who have this syndrome may have to necessarily carry out dental treatment under sedation or general anaesthesia. So, it is important to know that these patients might have an obstruction in the upper respiratory tract during sleeping or sedation because of the abnormal anatomical characteristics of their head and neck region [7]. Obstructive sleep

apnea may lead to hypertension in patients with RTS. Polysomnography in individuals with RTS and hypertension should be considered. Children with RTS are more challenging to intubate due to their relatively anterior larynx and easy collapsibility of the laryngeal wall. Intubation with anaesthesia is important due to the high risk of aspiration during induction and emergence [8].

The most common dermatologic are multiple large keloids. Cutaneous features of RTS are a tendency to form keloids, pilomatrixoma, ingrown toenails, paronychia, hypoplastic toenails, keratosis pilaris, atopic eczema, seborrheic dermatitis, and hirsutism.[9] They are more prone to tumours such as Meningioma, neuroblastoma, medulloblastoma, oligodendroglioma, seminoma. [10] The facies is sometimes reminiscent of that seen in Treacher-Collins syndrome or occasionally Seckel or Hallermann-Streiff syndromes.[10] Ocular findings in individuals with RTS that mimic glaucoma include corneal lesions, megalocornea, colobomatous or cystic optic nerve, excavation of papilla, and large cup-to-disc ratio. Intraocular pressure monitoring should be obtained at the time of concern. Other eye anomalies have been shown as strabismus, Mongoloid slanting palpebral fissures, refractory errors, ptosis, coloboma, ptosis, cataracts, nystagmus. The remarkable facial appearance is the small head, frontal prominence, beak-shaped nose with the nasal septum extending below the alae, highly arched palate, and mild micrognathia. Other findings may include long eyelashes, nasolacrimal duct obstruction, ptosis of eyelids, congenital or juvenile glaucoma and refractive error. Low-frequency abnormalities have included bifid uvula, submucous palatal cleft, bifid tongue, macroglossia, short lingual frenum, natal teeth, and thin upper lip [11].

The common dental abnormalities are crowding teeth, malocclusion, multiple caries, hypodontia, hyperdontia, talon cusps occur. Due to multiple malocclusions and structural defects in the maxillofacial regions. Crowding was very frequent and expressed. Crossbite was the main finding. Several patients experienced problems with oral hygiene, mainly inadequate brushing because of irregularly formed and placed teeth, the small opening of the mouth, and poor hand dexterity and coordination [12]. Anomalies of tooth structure are demarcated enamel opacities and hypoplasia, white tips of cusps on the first permanent molars, and white lines on the upper central incisors have been noticed [13]. Talon

cusps, so-called because it resembles an eagle's talon in shape, refers to a developmental dental anomaly consisting of an accessory cusp like structure projecting from the cingulum area (rear) of the upper or lower anterior teeth [13]. Talon cusps have been observed in over 90%, necessitating specific dental care. Talon cusps are found in 1% of the normal population. RTS patients have specific oral-dental features, and especially the presence of talon cusps can help in establishing the clinical diagnosis [14].

4. DIFFERENTIAL DIAGNOSIS

Although many components of the syndrome may occur as isolated findings or as features of various other syndromes, the overall pattern of anomalies is sufficiently distinctive to permit diagnosis in most instances. The facial features also show resemblance to Floating-Harbor syndrome and Gorlin-Chaudhry-Moss syndrome [1]. The facies are sometimes reminiscent of that seen in Treacher-Collins syndrome or occasionally Seckel or Hallermann-Streiff syndromes [12]. Broadening of the thumb and big toe may be judged subjectively when the facies are suggestive. Also, broad thumbs may occur independently in a mentally handicapped person, either as part of normal variation or as dominantly inherited brachydactyly type D. Broad thumbs may be observed in Apert syndrome and Pfeiffer syndrome [14].

5. CONCLUSION

RTS is a rare congenital disorder and reports describing this syndrome are scarce in the literature. Moreover, the diagnosis of RTS is still essentially clinical. Rubinstein-Taybi Syndrome has specific medical conditions in children and adults that occur with greater frequency than the normal people. RTS patients have specific oral-dental features, and especially the presence of talon cusps can help in establishing the clinical diagnosis. Knowledge of the oral-dental features will also be helpful for adequate management.

CONSENT

As per international standard written informed patient consent has been collected and preserved by the authors.

ETHICAL APPROVAL

As per international standard, written ethical permission has been collected and preserved by the author(s).

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The patient's parents gave their consent for photographs of her daughter to be taken and used for teaching purposes.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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