Rubinstein-Taybi Syndrome; A Case Report

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Abstract

Objective

Rubinstein-Taybi Syndrome is a rare genetic disorder with characteristic features including downward slanting palpebral fissures, broad thumbs and halluces, and mental retardation. Systemic features may involve cardiac, auditory, ophthalmic, endocrine, nervous, renal and respiratory systems. This syndrome is sporadic in nature and has been linked to microdeletion at 16p 13.3 encoding CREB-binding protein gene (CREBBP). We report a 15-years-old girl, a known case of chronic renal failure, with downward slanting palpebral fissures toward the ears, hypertelorism, short stature, beaked nose, micrognathia, strabismus, dental anomalies, large toes, broad thumbs, and mental retardation.

Keywords: Rubinstein-Taybi syndrome; chromosome 16p 13.3; mental retardation; CBP gene.

Introduction

Attention to detect neurodevelopmental delay in pediatric neurology services has a great importance to early intervention of developmental delay in children (1,2,3). According to this, diagnosis of different genetic syndromes with neurodevelopmental delay is invaluable.

Rubinstein- Taybi Syndrome (RSTS) was initially reported by Michail et al. in 1957 as the broad thumb-hallux syndrome and then was described by Rubinstein and Taybi in 1963 (4) in children with broad thumbs and toes, facial abnormalities and short stature. Since then, there have been over 250 cases documented in the literature. It has been estimated that 1 per 300-500 institutionalized persons with mental retardation over age 5 have this syndrome. Male and female individuals are affected at equal rates (5).

Typical facial features include downward slanting palpebral fissures toward the ears, hypertelorism, long eyelashes, high arched eyebrows, prominent nose, and malpositioned ears with dysplastic helices. In addition, characteristic skeletal findings are broad short terminal phalanges of the thumbs and halluces, and postnatal growth retardation with head circumference below the fiftieth percentile. Dermatologic features include capillary malformation in approximately 50 percent of patients and higher incidence of keloid formation (6) and pilomatricomas (7).

There may be systemic involvement of multiple organ systems. Of children with RSTS, 24-38 percent have cardiac abnormalities including atrial and ventricular septal defects, patent ductus arteriosus, coarctation of the aorta, pulmonic stenosis, and bicuspid aortic valve abnormalities (8). Feeding difficulties and gastroesophageal reflux disease require aggressive treatment in young children to prevent nutritional

and growth deficits. Cryptorchidism affects 78-100 percent of the male infants (9). There is an increased incidence of benign and malignant tumors as well as leukemia and lymphoma (6,10). Other organ systems that may be involved include auditory, ophthalmic, endocrine, neurologic, respiratory (9) and renal systems. Rubinsten-Taybi Syndrome is associated with a mutation in the CREB-binding protein gene (CREBBP) located on chromosome 16p 13.3. CREBBP which is essential to normal development. It has been identified as a nuclear protein that participates as a coactivator in cyclic AMP-regulated gene expression. The precise relationship between microdeletion in the CREBBP and the phenotype of Rubinstein-Taybi is yet to be elucidated (11,12). The pediatric neurologic and nephrologic community should be aware of the syndrome and its associated complications to manage patients.

The purpose of this case report was to provide more information on RSTS and its associated complications. In this report, we introduce a case with a high level of serum creatinine as a known case of chronic renal failure.

Case report

A 15-years-old girl was admitted for the follow-up of her renal problems as a known case of chronic renal failure (CRF) with a high plasma level of BUN and creatinine. The clinical history of the patient revealed that the developmental milestones were delayed and she had history of neonatal distress and respiratory infections during infancy. She went to school but had educational problems. Her parents were consanguineous. She underwent surgical repair (cystoplasty) because of vesicoureteral reflux and neurogenic bladder during childhood but because her parents did not cooperate, she was neglected and her problems progressed and became complicated to CRF. She had obstipation and prolonged constipation since infancy. She had a history of intermittent fever due to recurrent urinary tract infection during infancy.

The patient had a distinctive facial appearance with hypertelorism, a broad nasal bridge, a beaked nose, micrognathia, microcephaly, smile grimacing, a narrow and high arch palate, dental anomalies (different size and abnormal size and shape), antimongoloid palpebral fissures, strabismus, heavy and highly arched eyebrows and long eyelashes (Fig.1, 2).

On examination, short stature (short height and low weight), mental retardation and physical growth delay, stature under 50th percentile, head circumference under 50th percentile, hyperextensible joints of hands and feet, broad thumbs and large toes, and motor, mental, language and social retardation were noted (Fig.3, 4, 5)

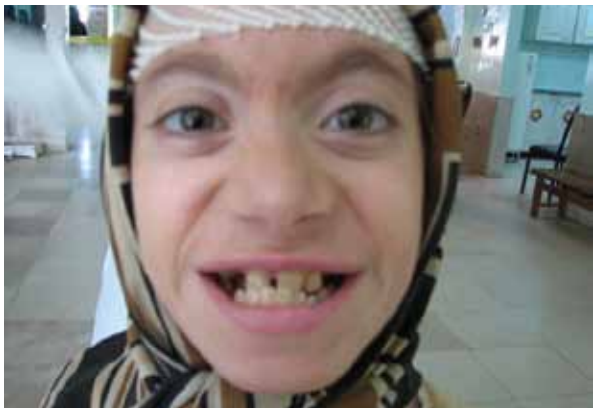

Fig 1: Patient's hypertelorism,high arched eyebrows, Dental anomalies(different size, abnormal size and shape)

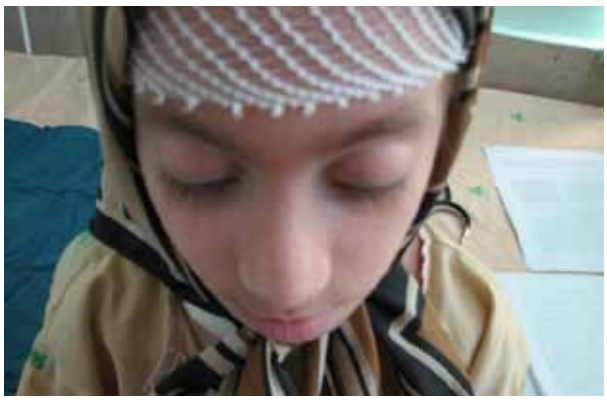

Fig2: Patient's Long eyeshades

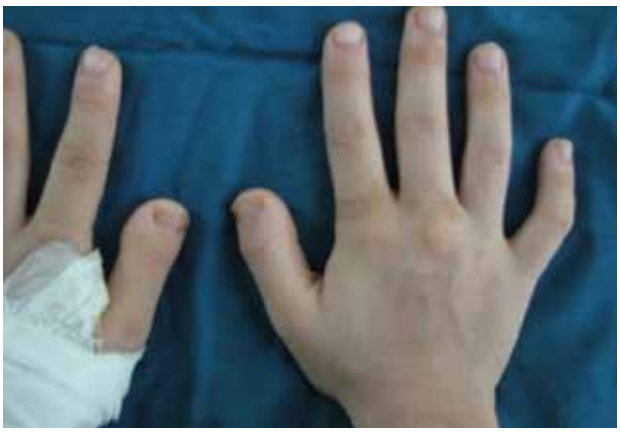

Fig3: Patient's braod thoumbs

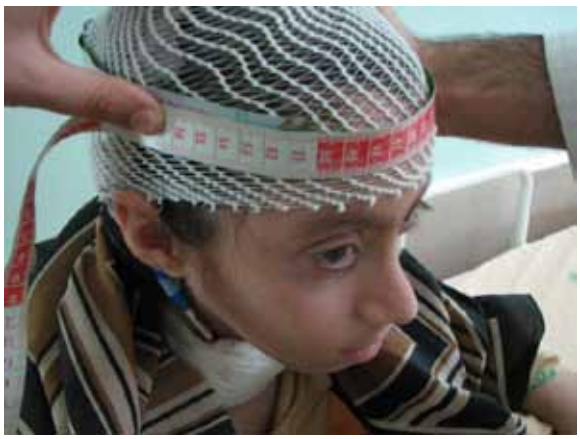

Fig 4

Fig 4, 5: Our case in comparison with another girl of the same age - Short stature (patients has microcephaly, Beaked nose, Micrognathia)

We found some properties in this patient that suggested a syndrome called Rubinstein-Taybi Syndrome (RSTS).

Discussion

Rubbinstein-Taybi Syndrome is a rare multiple congenital anomaly with approximately 700 cases reported worldwide. It appears that there is very little documented evidence regarding this syndrome in pediatric and nephrologic literature (12).

The cause of RSTS is still unclear, but it is associated with a microdeletion at 16p 13.3 region in the CREB-binding protein gene (CREBBP) in some patient, suggesting that deletion is the most probable cause of the syndrome (13). CREBBP is a transcription coactivator and functions as a potent histone acetyltransferase, both of which are essential to normal development (11).

In animal models, the mice with truncated Crb protein demonstrate clinical features of RSTS observed in humans including growth retardation, retarded osseous maturation, hypoplastic maxilla with a narrow palate, and cardiac and skeletal abnormalities (14).

More recently, the breakpoint of two distinct reciprocal translocations occurring in patients with the diagnosis of RSTS has been located in the same band 16p 13.3. However, this anomaly cannot be identified in all patients. Clinically, the difference between patients with or without deletion is minimal except for microcephaly. Band 16p 13.3 seems to be an important locus for mental retardation in patients with correct diagnosis of RSTS (9,15,16,17).

Our patient, a known case of CRF, had a high level of serum BUN and creatinine since her childhood. Urinary tract system is one of the multiple organ involvements in RST syndrome. Therefore, it was identified in our case report. She also had more characteristic features of the RSTS as explained above.

In conclusion, RSTS is a rare genetic condition that affects body shape, extremities, and many organs/systems of the body, particularly cardiac, respiratory, nervous, and renal system. This case report can help pediatricians to become more familiar with this syndrome.

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