A case with some clinical findings overlapping to Rubinstein-Taybi, Rubinstein-Taybi-like syndrome or multiple pterygium syndrome: coincidental findings or a new entity?

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SUMMARY: Kargı AE, Balcı S, Aköz T, Kargı Ş, Erdoğan B. A case with some clinical findings overlapping to Rubinstein-Taybi, Rubinstein-Taybi-like syndrome or multiple pterygium syndrome: coincidental findings or a new entity? Turk J Pediatr 2001; 43: 166-171.

We report a case with broad, deviated thumb and big, duplicated, deviated toes resembling Rubinstein-Taybi syndrome. But the patient did not have severe mental retardation as in Rubinstein-Taybi syndrome and had no microdeletions on chromosome 16 by FISH-based assay. This patient had mild webbing as seen in multiple pterygium syndrome, but broad-deviated thumb has not been reported in this syndrome. We discuss whether these are coincidental or overlapping findings or whether this is a possible new clinical entity.

Key words: Rubinstein-Taybi syndrome, Rubinstein-Taybi-like syndrome, multiple pterygium syndrome, FISH-based assay for Rubinstein-Taybi syndrome.

In 1963, Rubinstein and Taybi[1] described a new syndrome characterized by typical facial appearance, broad thumbs and halluces, and angulation deformities of thumbs and halluces, rarely hexadactyly of the feet and partial cutaneous syndactyly of the toes[1]. Since then, these cases have been called Rubinstein-Taybi syndrome (RTS)[2-6]. A submicroscopic deletion in chromosome 16p13.3 has recently been found in RTS patients. But it is only detected in one-fourth of these patients[7].

Multiple pterygium syndrome is characterized by webbing of the knee, elbow, axillary region, and neck, and flexion contractures of the joints[8,9].

In this report we present a new case with some classical findings of RTS such as broad and deviated thumb and some typical findings of multiple pterygium syndrome or Rubinstein-Taybi-like syndrome. Interestingly, we could not demonstrate a microdeletion of chromosome 16 in our patient by FISH-based assay.

Case Report

A nine-year-old male child was referred to the Plastic and Reconstructive Surgery Department because of malformations involving his face, hands and feet. He was the second child of nonconsanguineous parents with no family history of similar conditions, and he had two healthy brothers. He was born normally at term after an uneventful pregnancy. At birth, he weighed 3100 g (25^{th} - 50^{th} percentile) with a length of 45 cm ($<5^{th}$ percentile) and a head circumference of 35 cm (50^{th} - 75^{th} percentile). He grew regularly at about -3SD for height and weight until nine years of age. He attended school at seven years of age with average achievement.

He had severe webbing neck and cup-shaped ears. His cup ear malformation was operated under general anesthesia at eight years. He was also operated for webbing neck at eight years.

On admission, physical examination showed short stature with height 120 cm (3^{rd} percentile), and span 112 cm. His weight was 24 kg (10^{th} - 25^{th} percentile) and occipitofrontal circumference (OFC) was 52 cm. He had frontal bossing, hypertelorism (intermedial canthal distance 37 mm), wide palpebral fissures, upper eyelid ptosis, loss of hair on the lateral parts of eyebrows, depressed and enlarged nasal bridge, short and upturned nose and prominent columella, long philtrum, large and triangular mouth with

downturned corners, low-set ears with hypoplasia of scafal and helical configurations and a cup ear like malformation of the 1/3 upper part of both ears, small and recidive chin, gingival hyperplasia, dental abnormalities, bifid uvula, and short frenulum (Fig. 1). Operation scar for the webbed neck can be seen on the lateral view (Fig. 2). He had a short, bilaterally webbed neck and a low posterior hairline was noted (Fig. 3).

Distal phalanges of both thumbs were broad and radially deviated. There was incomplete syndactyly involving the fourth web of both hands. There was fifth finger clinodactyly on the right side (Figs. 4, 5). His feet were deviated laterally and he had big toes and preaxial duplication on the right side (Fig. 6). His joints were hyperextensible and hypermobile with range of motions wider than normal. The external genitalia were hypoplastic with bilateral retractile testes and inguinal hernia on the right side (Fig. 7).

He had pectus excavatum, bilateral inverted nipples and hypoplastic umbilical region. Another web involving apparently his right anterior axillary region and mildly on the left side was noted (Fig. 8).

Other systems were normal, and particularly no cardiac, renal or vertebral anomalies were noted. Routine laboratory tests, karyotyping, and ultrasonography of the abdomen and pelvis revealed normal findings. By FISH based assay and by using five cosmids covering the entire CBP gene on 16p; all cosmids, RT 100, RT 191, RT 102, RT 203, and RT 166 were present on both copies of 16p in our patient, excluding a microdeletion [Personal communication; Breuning MH, 1998].

Radiological studies showed delayed bone age. Hand radiographs showed split distal phalanx and abnormal angulation of the thumbs, clinodactyly of the right fifth finger, and hypoplasia of the proximal and middle phalanges. Feet radiographs showed preaxial duplication of the toe on the right side and abnormal angulation of the halluces (Figs. 9, 10).

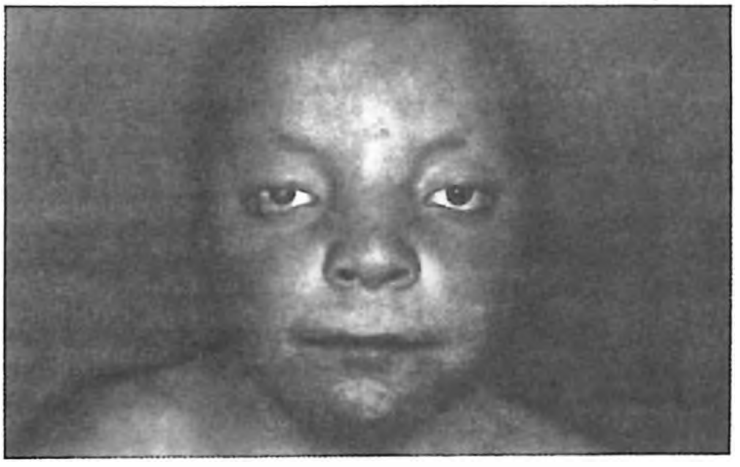

Fig. 1: Facial appearance (anterior view).

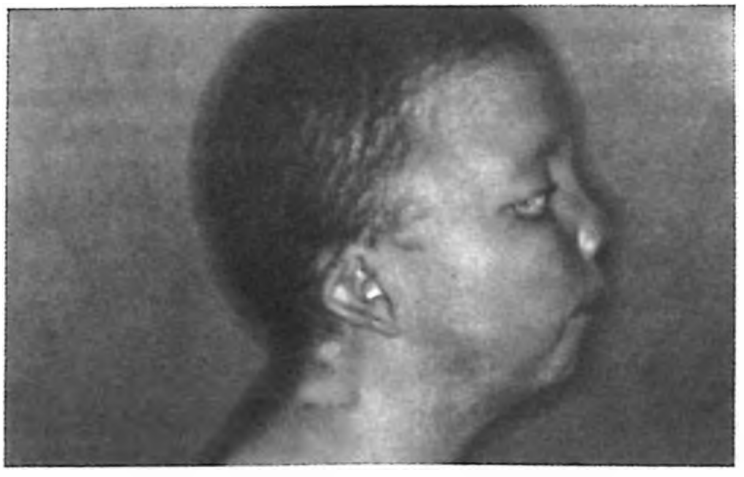

Fig. 2. Facial appearance (lateral view).

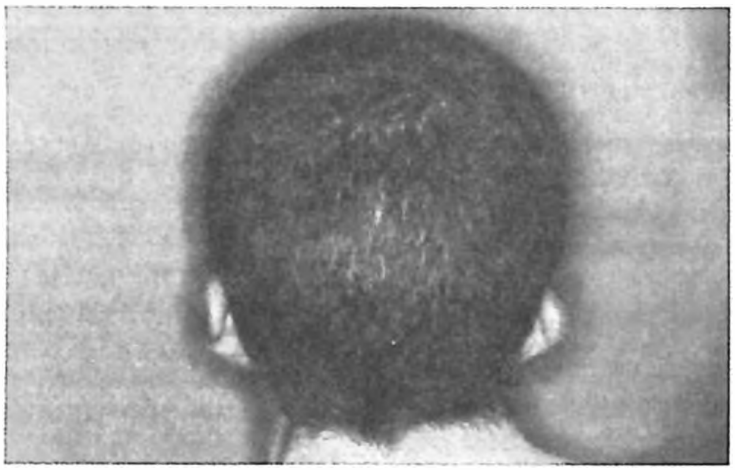

Fig. 3. Posterior view of the head.

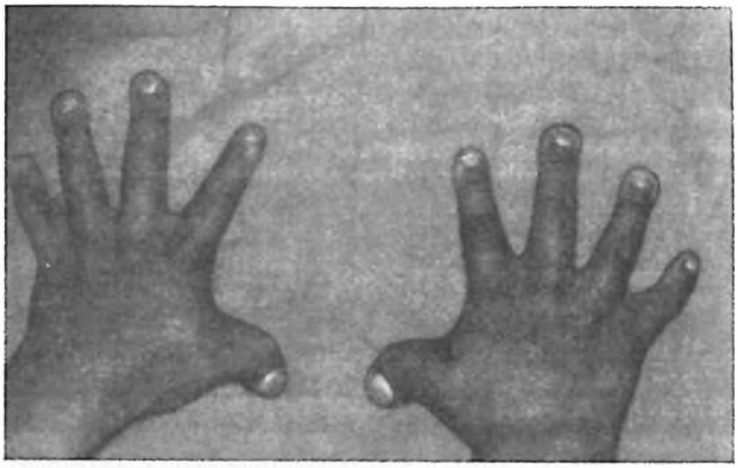

Fig. 4. Hand deformities (dorsal view).

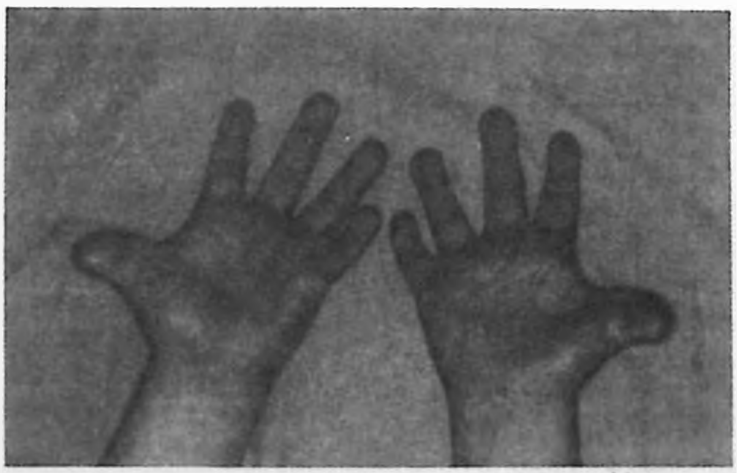

Fig. 5. Hand deformities (palmar view).

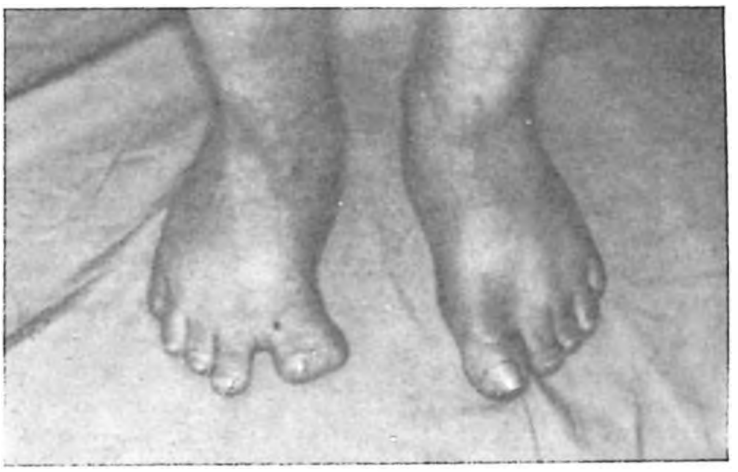

Fig. 6. Patient's feet.

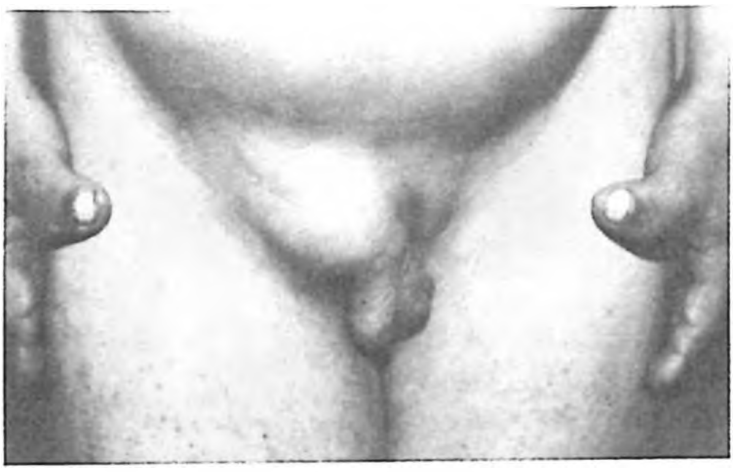

Fig. 7. Patient's genital region.

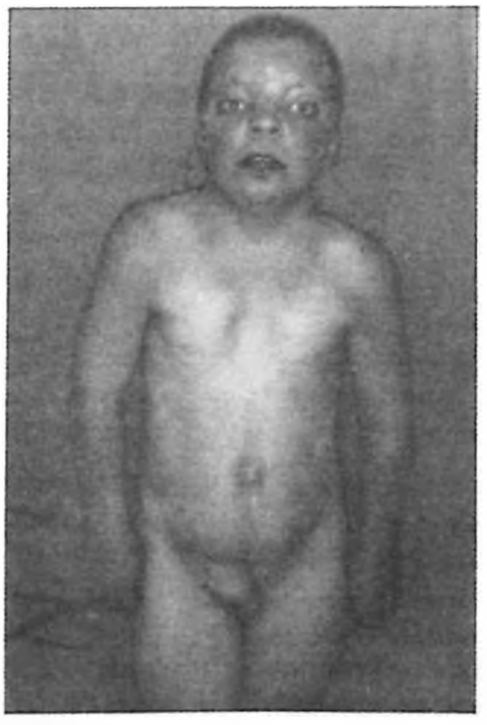

Fig. 8. Anterior view of the patient's body.

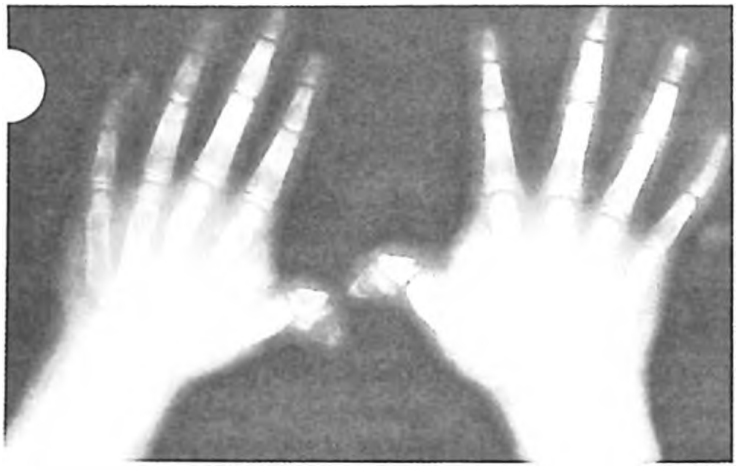

Fig. 9. Radiographs of the hands showing bilaterally abnormal angulation of the thumbs and the right split distal phalanx.

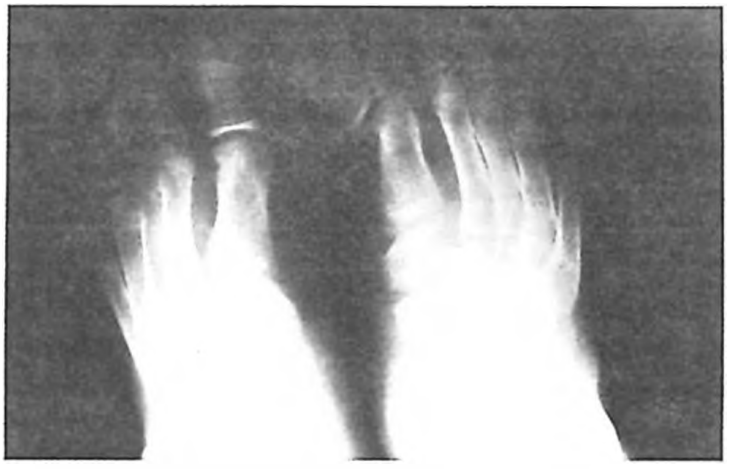

Fig. 10. Radiographs of the feet demonstrating preaxial duplication of the toe on the right side and angulation of the halluces.

Discussion

We present here a new case with some characteristic findings of RTS, some of multiple pterygium syndrome and some of Rubinstein-Taybi-like syndrome, and discuss whether findings of our case are coincidental or whether this is possibly a new entity.

Rubinstein-Taybi syndrome is characterized by specific facial appearance, psychomotor retardation, small stature and anomalies of the hands and feet with broad distal phalanges, especially of the thumbs and halluces[3,10,11].

Our patient's hand and feet abnormalities were very similar to that seen in RTS. He had mild mesomelic shortening of extremities. Both thumbs were broad with radial angulation. There was also syndactyly between the fourth and fifth fingers and clinodactyly on both hands. His feet were deviated laterally and he had big toes with preaxial duplication on the right side. These hand malformations are characteristics of RTS[3,10,11]. Our patient also had delayed bone age and we detected split distal phalanx of the thumbs, and hypoplasia of the proximal and middle phalanges of the hands by radiological studies, as is common in RTS. Other locomotor system abnormalities in RTS are laxity of joints and joint dislocations[6]. Our patient also had mildly hyperextensible joints.

While the hand and feet abnormalities in this patient are highly suggestive of RTS, facial findings not consistent with RTS suggested another syndrome. Again, our patient's intelligence was not severely affected. Recently, a more definite diagnosis of RTS has been made possible with FISH technique to determine the presence of microdeletion on chromosome 16p13.3. Though detected in one-fourth of RTS patients, further cytogenetic studies did not confirm this diagnosis in our case[7].

Though our patient's facial appearance suggested Robinow's syndrome, this patient did not have any vertebral malformations or mesomelic dysplasia, which are seen in that syndrome[12,13]. In 1993, Balcı et al.[14] noted a new hand malformation in Robinow's syndrome, such as split hand, and they also noted syndactyly between the fourth and fifth fingers and toes, such as in our case.

Multiple pterygium syndrome is another clinical entity characterized by webbing of the knee, elbow, axillary region, and neck, and flexion contractures of the joint. Webbing has never been reported in Robinow syndrome or in RTS. Neck and right axillary region webs of our patient were suggestive of multiple pterygium syndrome. Minor facial anomalies of this syndrome are ptosis, antimongoloid slant, low-set ears, and epicanthus, and some of these were present in our case. Other characteristics of multiple pterygium syndrome are vertebral anomalies, syndactyly, camptodactyly, and short stature[8,9,15]. However, these hand and feet abnormalities have never been reported in multiple pterygium syndrome in medical literature. In our patient, inverted hypoplastic nipple seen in multiple pterygium syndrome and pectus excavatum seen in RTS are remarkable[8-10].

This case should also be differentiated from Rubinstein-Taybi-like syndrome. In the syndrome reported by Cotsirilos and Pavone[16,17], facial features were not like RTS, while hand and feet abnormalities were similar to that seen in RTS. Reported facial features of this syndrome as also seen in our patient, were low-set ears, hypertelorism, ptosis of eyelids and palpebral fissures downward slanted down[16,17].

In conclusion, we report a possible new entity which had some clinical findings of RTS, Rubinstein-Taybi-like syndrome and multiple pterygium syndrome. RTS could not be definitely excluded cytogenetically. The question to be answered is whether these findings are overlapping or just coincidental or whether this is a new entity. Further similar studies are needed to resolve the question.

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