# A Case of Rubinstein-Taybi Syndrome with Tetralogy of Fallot

## Fallot Tetralojili Bir Rubinstein-Taybi Sendromu Olgusu

Helen BORNAUN,[a]
Kazım ÖZTARHAN,[a]
Şükrü CANDAN[b]

[a]Clinic of Pediatric Cardiology, İstanbul Kanuni Sultan Süleyman Training and Research Hospital, İstanbul
[b]Clinic of Medical Genetics, Balıkesir Atatürk State Hospital, Balıkesir

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Yazışma Adresi/*Correspondence:*
Şükrü CANDAN
Balıkesir Atatürk State Hospital, Clinic of Medical Genetics, Balıkesir, TÜRKİYE/TURKEY
sukru.candan@yahoo.com.tr

**ABSTRACT** Rubinstein-Taybi syndrome is a rare autosomal dominant syndrome characterized by facial dysmorphism, broad thumbs and halluces, short stature, intellectual disability and variable organ anomalies such as eye, genital, renal and cardiac anomalies. The characteristic facial features are high arched eye brows, downslanting palpebral fissures, ptosis, epicanthal folds, an extended columella, high arched palate, and dental abnormalities. Broad thumbs and halluces are distinctive features for Rubinstein-Taybi syndrome. A variety of congenital heart defects are reported in Rubinstein-Taybi syndrome. Tetralogy of fallot have been reported very rare in Rubinstein-Taybi syndrome so far. Here we report a 8 years old male with classic Rubinstein-Taybi syndrome that has accompanied tetralogy of fallot.

**Key Words:** Rubinstein-Taybi syndrome; tetralogy of fallot

**ÖZET** Rubinstein-Taybi sendromu nadir bir otozomal dominant sendrom olmakla birlikte fasyal dismorfizm, geniş el ve ayak baş parmakları, boy kısalığı, mental retardasyon ve çesitli iç organ anomalileri ile karakterizedir. Özellikle bu iç organ anomalileri göz, genital ve kardiyak sistemlerdedir. Fasyal dismorfik özellikleri; yay şeklinde kaşlar, aşağı çekik palpebral fissürler, pitoz, epikantus, geniş kolumella, yüksek damak ve dental anomalilerdir. Geniş el ve ayak baş parmakları Rubinstein-Taybi sendromu için ayırt edici özelliktir. Çeşitli kalp anomalileri Rubinstein-Taybi sendromunda bildirilmiştir. Fakat fallot tetralojisi ile birlikteliği çok nadirdir. Biz bu yazıda klasik Rubinstein-Taybi sendromu ve fallot tetralojisi birlikteliği olan 8 yaşında erkek bir olgu sunacağız.

**Anahtar Kelimeler:** Rubinstein-Taybi sendromu; fallot tetralojisi

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Rubinstein-Taybi syndrome (RS-T) is an autosomal dominant congenital disease. Its prevalence is about 1 in 100.00 to 125.000 live births.[1] RS-T syndrome is a rare genetic syndrome that consists of facial dysmorphism, microcephaly, short stature, moderate to severe intellectual impairment. The remarkable trait in this syndrome is the presence of broad thumbs and toes that are frequently angulated.[2]

*CREEBP* and *EP300* are the only genes that are known to cause this syndrome. Both genes are responsible for about half of the cases of RS-T syndrome.[3] Associated anomalies including eyes, skeletal and genitourinary system and cardiac anomalies can accompany this syndrome. In about one

third of the cases, cardiac and vascular anomalies such as atrial and ventricular septal defect, patent ductus arteriosus and capillar hemangioma could be detected.[2] Herein, we present a case with RS-T syndrome associated with Tetralogy of Fallot (TOF).

## CASE REPORT

A male patient was born at 39 weeks gestation by way of spontaneous delivery. The birth weight was 3850 g (50$^{th}$ percentile), height was 51 cm (50$^{th}$ percentile) and head circumference was 33.5 cm (25-50$^{th}$ percentile). He was the first child of healthy 26 year old parents with no consanguinity. He was referred to a cardiology unit when he was six days old with the detection of a 2-3/6 systolic murmur and the presence of a dysmorphic appearance. On physical examination, dysmorphic features such as a prominent forehead, bilateral ptosis (marked on the right) and epicanthus, low placed dysplastic ears, high-arched palate, everted lower lip, mild micrognathia, broad nasal bridge, hypertelorism, and the down slanting palpebral fissures were detected (Figure 1).

The terminal phalanges of the thumbs and the toes were big and broad on clinical examination and X-ray imaging (Figure 2).

On cardiovascular examination, blood pressure was 75/50 mmHg, heart rate was 130/min, first and second heart sounds were normal, a systolic ejection murmur was heard along the left sternal border that was most pronounced at the second left intercostal area. Electrocardiography showed sinusal rhythm. Transthoracic echocardiographic imaging of the patient revealed malalignement ventricular septal defect, overriding aorta, pulmonary valvular and infundubuler stenosis with peak systolic pressure gradient of 63 mmHg, echocardiographic examination revealed TOF (Figure 3).

He was diagnosed as RS-T syndrome associated with TOF when his physical findings were taken into consideration. He was operated for unilateral cryptorchidism when he was 11 months. A cardiac angiography was performed and he was operated for TOF at the age of 1 year. At 8 years old, his weight was 22.5 kg (10$^{th}$ percantile), his height was 120 cm (10$^{th}$ percentile) and head circumference was 43 cm (<3$^{rd}$ percentile).

## DISCUSSION

RS-T syndrome is a very rare congenital syndrome characterized by facial dysmorphism and broad

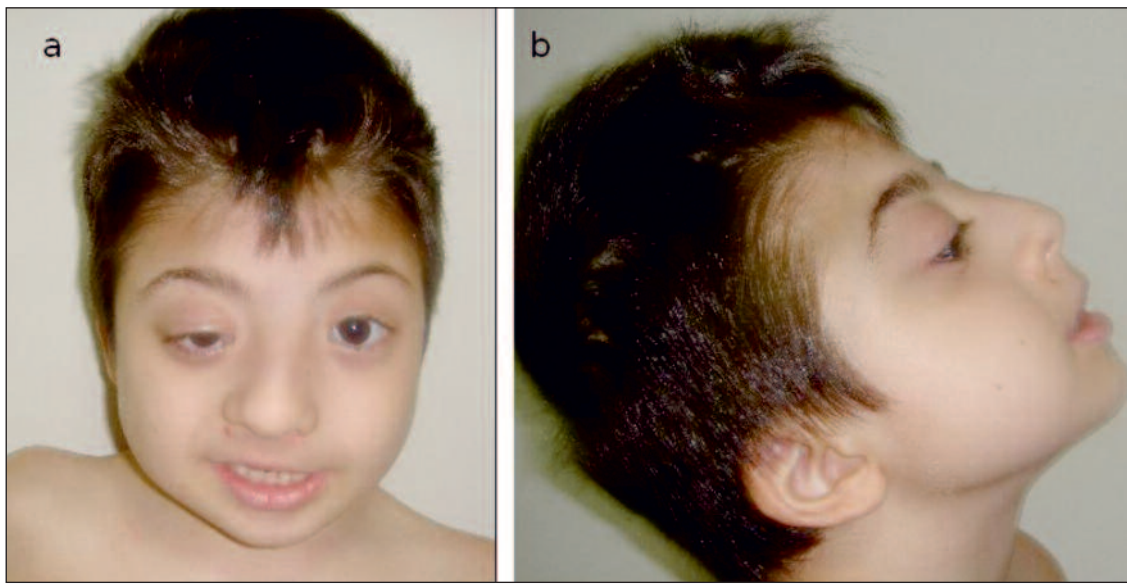


**FIGURE 1a,b:** Characteristic facial features of Rubinstein-Taybi syndrome when the patient was 8 years old.
(See color figure at http://www.turkiyeklinikleri.com/journal/pediatri-dergisi/1300-0381/)

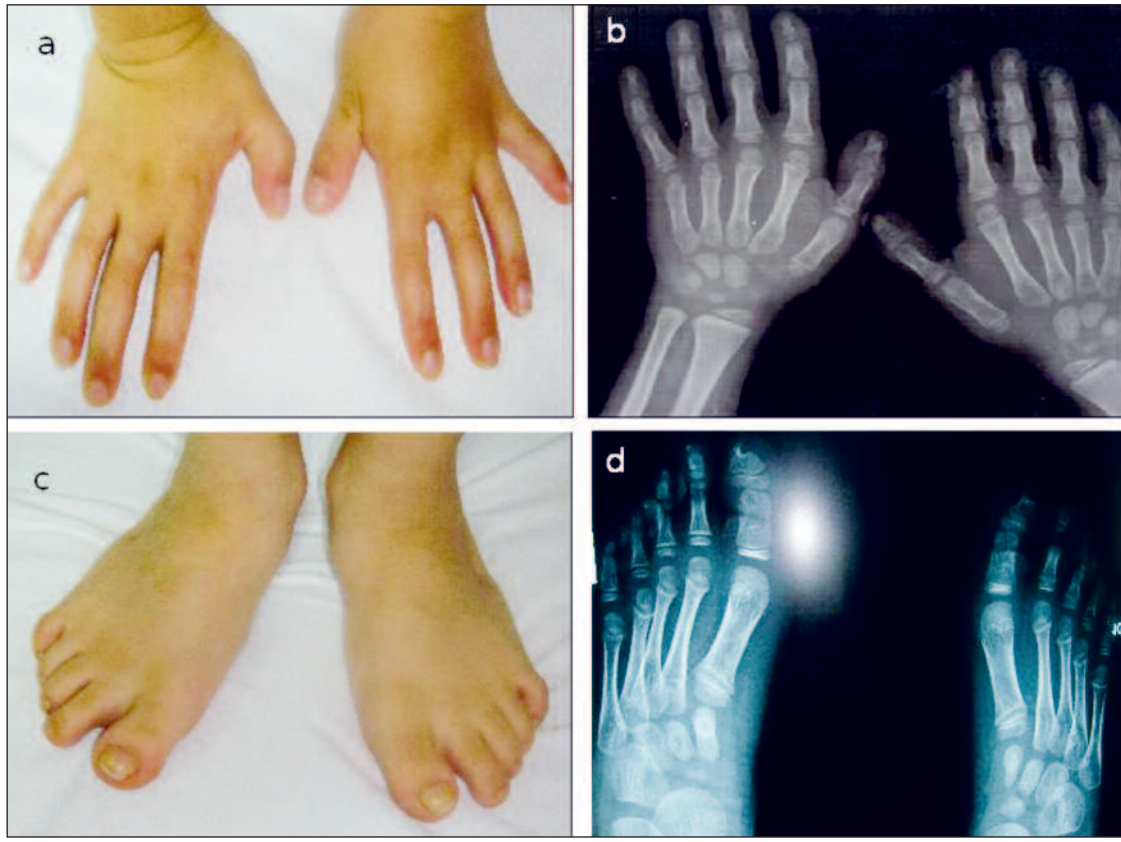


**FIGURE 2:** Broad thumbs **(a, b)** and broad toes **(c, d)** are remarkable.
(See color figure at http://www.turkiyeklinikleri.com/journal/pediatri-dergisi/1300-0381/)

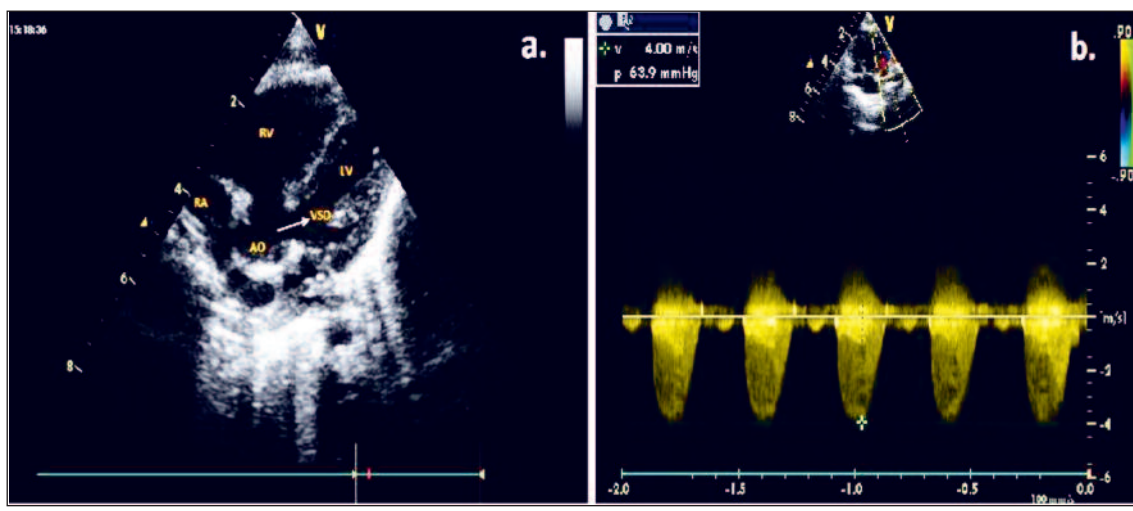


**FIGURE 3:** Echocardiography in RS-T syndrome with TOF when he was at the age of 6 days. **(a)** subaortic, ventricular septal defect, overriding aorta, **(b)** Pulmonary infundibular, valvular stenosis with mean pressure gradient: 63 mmHg.
(See color figure at http://www.turkiyeklinikleri.com/journal/pediatri-dergisi/1300-0381/)

thumbs and toes.[1] Additionally, it occurs short stature, intellectual disability and visceral defects.[2] Congenital heart anomalies of different types accompany in one third of Rubinstein-Taybi syndrome patients. The frequently detected atrial and ventricular septal defect. Also reported rarely others heart defect with RS-T syndrome such as hypoplastic left heart, patent ductus arteriosus,

coarctation of the aorta, pulmonic stenosis and bicuspid aortic valve.[4-6]

TOF comprise approximately 10% of cases of congenital heart disease, prevalance 3-6/10 000 at birth and is most common cause of cyanotic congenital heart disease. TOF is mostly sporadic and isolated.

TOF can be seen varies in single gene syndromes (Alagille synrome, Kabuki Make-up syndrome), chromosomal abnormality (Trisomia 21,13,18, 22q11 deletion), maternal (Phenylketonuria, Diabetes) and teratogenic effects (Fetal alcohol syndrome). Especially TOF is occur about 20% of 22q11 deletions syndromes (Di George, Velocardiofacial syndrome).[7]

We report the association a case with characteristic manifestations of RS-T syndrome and TOF syndrome. The association of these two entities is very rare and has not been reported previously in Turkey. Eventually, it is the second report of literature since 1978 all over the world.[8] In the future planning molecular study and may be possible genoype-fenotype correlation.

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