Rubinstein-Taybi Syndrome: When Phenotype is the Key

Mafalda Matias, Inês Ganhão, Catarina Lacerda, Susana Rocha

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A 9-month-old girl was referred to neuropediatric consultation due to motor delay. She was the first child of a non-consanguineous couple. It was an uneventful pregnancy with normal fetal ultrasound scans and eutocic term delivery, with Apgar scores 9/10. She presented with short stature (<5th percentile), microcephaly (< percentile 5), a peculiar face (Figs. 1 and 2) with highly arched palate, short neck, large angulated thumbs (Fig. 3) and halluces, delayed psychomotor development and a distinctive grimacing smile. The DNA sequencing of the *CREBBP* gene confirmed the diagnosis of Rubinstein-Taybi syndrome, detecting a *de novo* and unidentified variant: an heterozygous mutation of *c.3182_3183dup (p.Glu1062Argfs*38)*. Further investigation found an atrial septal defect, obstructive sleep apnea, Chiari malformation type I and a butterfly-shaped dorsal vertebra. She developed a marked impulsivity and a binge eating disorder, leading to obesity. Her latest evaluation, at 36 months, established a developmental profile between 13 and 27 months, with fine motor skills and expressive language being the most affected areas.

Rubinstein-Taybi syndrome is a congenital and polymalformative neurodevelopmental disorder.[1-3] This rare syndrome, with an incidence of one in 100,000-125,000 births, has no preference for race or gender.[1,3-5] It is an autosomal dominant disease mainly caused by mutation in the *CREBBP* gene, which is essential for normal fetal development.[1,3-5] Rubinstein-Taybi syndrome is characterized by microcephaly, low anterior hairline, low-set ears, down slanted palpebral fissures, protruded beaked nose with a prominent columella, and angulated broad thumbs and halluces. This syndrome is often associated with failure to thrive, hypotonia, and psychomotor developmental delay.[1-5] Heart, vascular, renal, and skeletal malformations are frequently present. There is also a higher susceptibility to recurrent respiratory infections, dysphagia, obstructive sleep apnea,[1,3-5] and both benign (*e.g.* meningioma, pilomatrixoma) and malignant tumors (*e.g.* neuroblastoma, rhabdomyosarcoma).[3]

This case highlights the importance of the phenotypic features to diagnose Rubinstein-Taybi syndrome. Although, in most cases, a genetic confirmation is required, early recognition will allow an eclectic and timely intervention, and better prognosis.

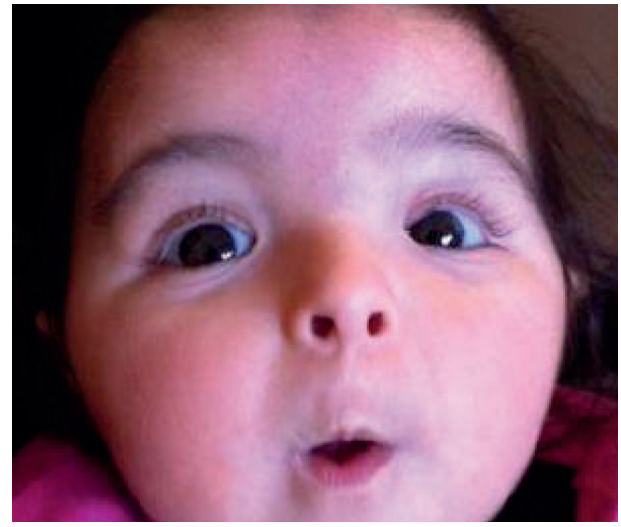

Figure 1. Typical facial features: low anterior hairline, frontal salmon patch, hypertelorism, convergent strabismus, down slanting palpebral fissures, inverted epicanthus, long philtrum, a small mouth, and thin upper lip.

Figure 2. Typical facial features: beaked nose and mild retrognathia.

Department of Pediatrics, Centro Hospitalar Barreiro-Montijo, Barreiro, Portugal
Corresponding Author
Mafalda Matias
https://orcid.org/0000-0001-8639-5338
mafaldamatias@gmail.com
Serviço de Pediatria, Centro Hospitalar Barreiro-Montijo, Avenida Movimento das Forças Armadas, 2834-003 Barreiro, Portugal
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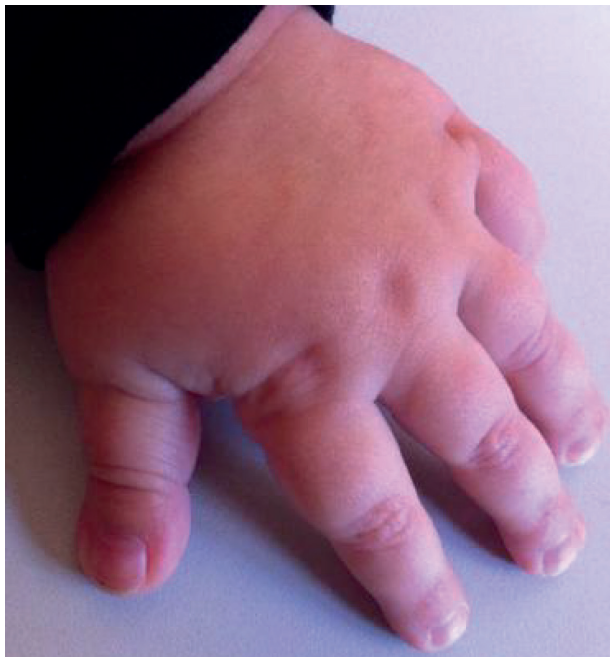

Figure 3. Broad and angulated thumb, broad distal phalanges of the third and fourth fingers.

Keywords: Child; Phenotype; Rubinstein-Taybi Syndrome/diagnosis; Rubinstein-Taybi Syndrome/genetics

WHAT THIS REPORT ADDS

- The presence of broad and flattened thumbs, a beaked nose, and short stature should raise the suspicion of this syndrome in a child with developmental delay.
- Behavior disturbances and obesity are common issues with advancing age that require close monitoring.
- Half of cases are caused by mutations of the *CREBBP* gene.
- Establishing a correct diagnosis will help clinicians minimize any complications or comorbidities associated with Rubinstein-Taybi syndrome.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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Consent for publication was obtained.

Confidentiality of data

The authors declare that they have followed the protocols of their work centre on the publication of patient data.

Awards and presentations

A previous version of this case was presented as a poster at the Excellence in Pediatrics conference in London, in 2016.

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