Rubinstein-Taybi Syndrome associated with congenital hypothyroidism and hypertrichosis

Konjenital hipotiroidizm ve hipertrikoziz ile birlikte olan Rubinstein-Taybi sendromu

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Abstract
Rubinstein-Taybi syndrome is a genetic syndrome characterized by broad thumbs and large toes, growth retardation, mental deficiency and dysmorphic facies. We report a case of Rubinstein-Taybi Syndrome associated with congenital hypothyroidism and hypertrichosis, because of its rarity.

Key Words: **Congenital hypothyroidism; Hypertrichosis; Rubinstein-Taybi syndrome.**

Özet
Rubinstein-Taybi Sendromu extremite anomalileri, mental retardasyon ve dismorfik yüz görüntüsüyle karakterizedir. Rubinstein-Taybi Sendromu ile birlikte konjenital hipotiroidi ve hipertrikozizi olan bir yenidoğan vakası nadir olması nedeniyle sunuldu.

Anahtar Kelimeler: **Rubinstein-Taybi Sendromu; Konjenital hipotiroidizm; Hipertrikoz.**

Introduction

Rubinstein-Taybi syndrome (RTS) refers to a specific pattern of physical features and developmental disabilities, which occur together in a consistent fashion. Individuals with RTS have short stature, developmental delay, similar facial features, and broad thumbs and large toes. Rubinstein and Taybi first described the condition in 1963 (1). Prevalence in the general population is estimated to range from 1 in 300,000 to 700,000. The condition occurs with equal frequency in males and females (2). We report the association of RTS with congenital hypothyroidism and hypertrichosis.

Case report

An eighteen-hour–old male infant having respiratory distress was admitted to Gevher Nesibe Hospital. The baby was born by spontaneous vaginal delivery at 34 weeks of gestation. He was the 4th child of healthy 35-year-old mother and 36-year-old father. There was no consanguinity between parents.

On admission, the baby was cyanotic and tachypneic with sternal and intercostal retractions, and grunting on expiration. Oxygen therapy was administered and his clinical findings improved. He developed jaundice on the 2nd day of life because of ABO incompatibility, and was treated with exchange transfusion. His weight was 1812 g (10-25 percentile), height was 40 cm (<3 percentile) and head circumference was 26 cm (<3 percentile). He had an unusual dysmorphic facial appearance with microcephaly, prominent forehead, downslanting palpebral fissures, epicanthal folds, hypertelorism, beaked nose, broad nasal bridge, hypoplasia of the philtrum and micrognathia (Fig. 1). He had also broad short thumbs, broad terminal phalanges of other fingers, large toes, in addition to syndactyly of the 2nd and 3rd fingers (Fig. 2). Bilateral testes were not in the scrotum. The child was noticed to be excessively hairy at birth with fine long hair all over the body (Fig. 3). He was diagnosed as RTS, based on the presence of dysmorphic facial features, broad thumbs, large toes and hypertrichosis.

Laboratory investigations were normal, including hemoglobin, hematocrit, serum calcium, phosphorus, alkaline phosphatase, BUN, creatinine, electrolytes, blood sugar, SGOT, SGPT, acid-base values and urine analysis. Total testosterone was 584.57 ng/dl (normal range: 100-500) and free testosterone was 47.42 pg/ml (normal range: 1.5-31). Thyroid function test result were; free T_3 2.33 pg/ml, free T_4 0.01 ng/dl, TSH 67.30 IU/ml and thyroglobulin 365.33 ng/ml. Thyroid volume was 0.8 ml (in normal range). Sex hormone binding globulin concetration was 1.1 mg/dl (normal range: 1.5-6.3 mg/dl). The serum insulin level was 20.6 mU/ml (normal range: 2.0-13.0 mU/ml), and 17 α hydroxy progesterone, androstenedion, and dehydroepiandrosterone sülfat concentrations were all normal. Ultrasonographical examinations of adrenal and testes were normal. Magnetic resonance imaging showed hypoplasia of the corpus callosum. His karyotype was normal (46,XY).

Total testosterone, free testosterone, insulin and sex hormone binding globulin levels of the infant were normalized around the end of the 3rd month of life with replacement treatment of thyroxine. During 3 months his hypertrichosis resolved progressively.

Discussion

Rubinstein-Taybi syndrome is a rare congenital syndrome comprised of mental and growth retardation, broad thumbs and large toes, and an unusual face. The classical facial appearance is well-established, striking and easy to recognize. It includes puffiness, down slanting of the palpebral fissures, epicanthal folds, and a prominent and/or beaked nose with nasal septum sometimes extending below the alae, and a narrow, high arched palate. They are frequently microcephalic. The ears are low set and often malformed. There is abundant dark hair, with low anterior and posterior hairlines. Eyebrows are heavy and eyelashes long. When typical features are present, newborns with RTS can be readily recognized. The facial features change with age, and diagnosis may be more difficult later in infancy (2).

Hypertrichosis is defined as an increase in the non-androgen-modulated hair on the body and may be congenital or acquired, localized or generalized (3). Congenital hypertrichosis is an all-inclusive term for excessive hair growth on a child at birth. The hair growth may involve the entire body with a mass of fine long hair, diffuse excess hair, or may be restricted to a specific area. Causes of congenital hypertrichosis vary and may be associated with various genetic syndromes (4). A characteristic facial appearance in a child with hypertrichosis may lead to the recognition of one of a number of dysmorphic syndromes, such as Brachmann-de Lange syndrome, Coffin-Siris syndrome, Rubinstein-Taybi syndrome, Seckel syndrome, cerebro-

oculofacioskeletal syndrome, Gorlin syndrome, Schinzel Giedion midface retraction syndrome or Barber Say syndrome (5).

Rubinstein-Taybi syndrome has rarely been described in association with skin lesions except for medial telangiectatic nevi, multiple or giant keloids and multiple pilomatricomas (6-9). In our patient, we also detected hypothyroidism and published the association of congenital hypothyroidism and RTS (10). Stimulation of the growth of hair via adrenal androgens by thyroid stimulating hormone may be the pathophysiological mechanism in our patient. Shoupe et al (11) reported that serum testosterone showed a positive correlation with insulin resistance, and sex hormone binding globuline showed a negative correlation. Of our patient's hormones, two of increased (the serum levels of insulin and testosterone), and one decreased (the serum level sex hormone binding globulin). Hypertrichosis might also be related to free testosterone on account of hyperinsulinism in our patient. The etiology of hyperinsulinism shown in our patient could not be explained.

In conclusion, we detected congenital hypothyroidism concomitant with hypertrichosis in an infant with RTS.

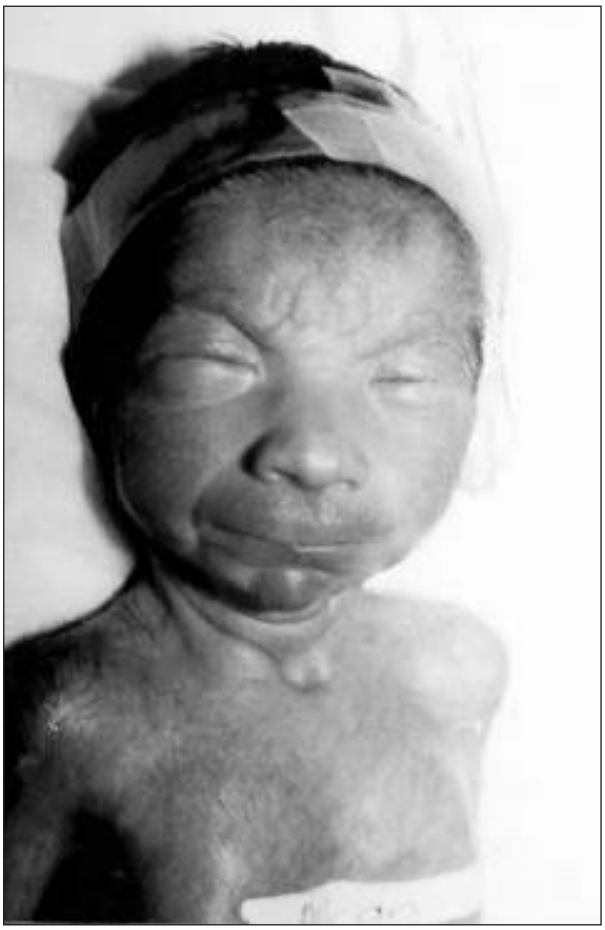

Fig. 1. The appearance of the face is peculiar to Rubinstein Taybi Syndrome (8-day-old).

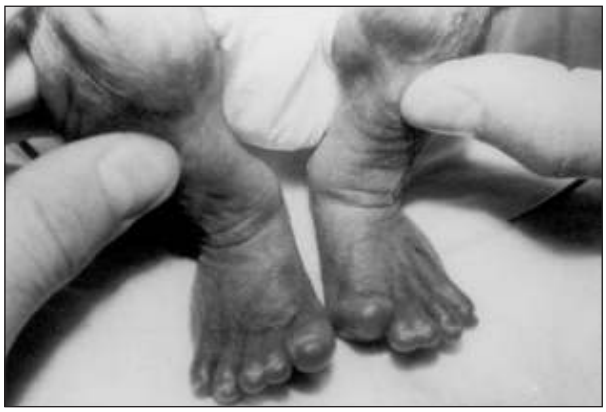

Fig. 2. Large toes of the baby

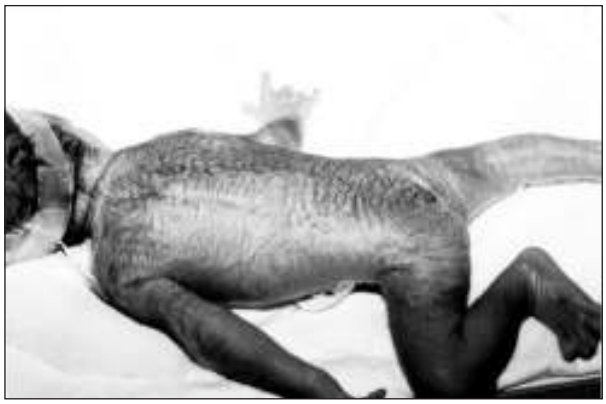

Fig. 3. Generalized hypertrichosis of the newborn

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