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Townes-Brocks syndrome In Gaza Strip

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Abstract

Townes-Brocks syndrome (TBS) is an autosomal dominant disorder with multiple malformations and variable expression. Major findings include external ear anomalies, hearing loss, limb deformity, imperforate anus, and renal malformations. A 9 month-old male is presented with the clinical findings of the autosomal dominant TBS in an otherwise unaffected family. Herein, we are report a Palestinian case of TBS with a full picture of anomalies including imperforate anus, abnormal thumb and, left dysplastic ears associated with genitourinary malformations.

Keywords: Chromosome 16q12.1; SALL1gene; Recto-Urethral Fistula; Townes-Brocks Syndrome (TBS);

Abbreviations: TBS: Townes-Brocks Syndrome; VUR: Vesico-Ureteral Reflux;

Introduction

TBS is a rare autosomal dominant congenital anomaly syndrome characterized by the triad of anorectal, hand (thumb anomalies) and external ear malformations with sensorineural hearing loss. Intelligence is usually normal, although mild-moderate mental retardation has been reported [1,2,3]. Mutations in SALL1, a gene mapping to chromosome 16q21.1, are responsible for TBS [4]. Many cases are sporadic [5]. Townes and Brocks (1972) observed a father and 5 of his 7 children who had imperforate anus, triphalangeal thumbs, and other anomalies of the hands and feet, including fusion of metatarsals, absent bones, and supernumerary thumbs. Other features included mild sensorineural deafness, and lop ears [6]. The minimal frequency of TBS is estimated at1 case per 250,000 live born, but may be misdiagnosed because its defects overlap with those of other genetic diseases [7,20].

Patient Report

A 9-month-old male boy was admitted to our hospital due to acute bronchiolitis, has abnormal thumb in the right hand (Thumb is attached by skin threads), imperforate anus, recto- urethral fistula (cloacal malformation), Solitary left pelvic (ectopic) kidney with Vesico-Ureteral reflux (VUR)-grade III, hypospadias, left dysplastic ear. Our patient was born vaginally at 38th week of gestation with a birth weight of 2,600 gm after an uneventful pregnancy. He was the first baby for a young couple with positive consanguinity. There were no affected family members. Others includes epicanthal fold, prominent forehead, microcephaly, his weight is (6kg) below the fifth percentile, head circumference 41cm (microcephaly) below the fifth percentile, and his bone age approximately 3 months.

Discussion

Our patient showed typical symptoms of the Townes-Brocks syndrome, i.e., anal atresia with recto-urethral fistula, right hand thumb is attached by threads. Genitourinary system revealsleft solitary pelvic (ectopic) kidney with Vesico-Ureteral Reflux (VUR)-grade III, hypospadias and dysplastic left ear canal. The child also showed facial dysmorphism with depressed nasal bridge and mild small ear, microcephalic, hypertelorism, epicanthal fold and broad prominent forehead. No chest cage deformity, mild wheeze chest. Heart was regular, rhythmic, no hepatosplenomegaly or palpable masses. Genitalia show hypospadias, undescended testis (inguinal canal).Child's weight was 6 kg (below the fifth centile), head circumference was 41 cm (below the fifth centile) see figures [1,2]. Skeletal survey reveals normal study without vertebral or ribs abnormalities except absence of the first metacarpal bone on the right hand, see figures [3,4]. Park S and Lee W stated that to date, at least 66 cases have been reported Worldwide [18].

TBS is characterized by the triad of imperforate anus (84%), dysplastic ears (87%); overfolded superior helices and preauricular tags or pits, microtia, frequently associated with sensorineural and/or conductive hearing impairment (65%), and thumb malformations (89%; triphalangeal thumbs, duplication of the thumb (preaxial polydactyly), bifid thumbs and toes, finger and toe syndactylyand rarely hypoplasia of the thumbs). Renal impairment (42%), were not part of the original description, including end-stage renal disease, may occur with or without structural abnormalities (mild malrotation, ectopia, horseshoe kidney, renal hypoplasia, polycystic kidneys, vesicoutereral reflux, unilateral agenesis renal, posterior urethral valves, meatal stenosis, and glandular hypoplasia [21,22]. Congenital heart diseaseoccurs in 25%, including tetralogy of Fallot, atrial septal defect, truncus arteriosus, ventricular septal defects, patent ductus arteriosus and pulmonary valve atresia [23,24,25,26]. Foot malformations (52%; flat feet, overlapping toes) and

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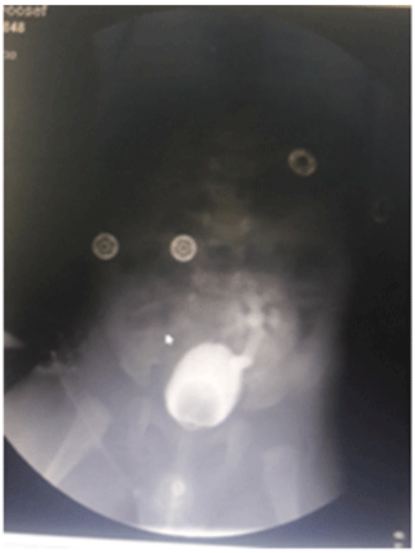

Figure 1: Micturating cystogram reveals, Left solitary pelic (ectopic) kidney with vesicoureteral reflux (VUR)-grade III

Figure 2: Right hand (Thumb is attached by skin threads).

genitourinary malformations (36%) are common. Intellectual disability occurs in approximately 10% of individuals. Rare features include iris coloboma, Duane anomaly, Arnold-Chiari malformation type 1, and growth retardation [8,9]. Reaching a correct diagnosis of as TBS is important since this condition has a 50% rate of transmission to offspring [3]. Variable expression may result in mild clinical manifestations which necessitates careful examination of both patient and parents [10]. Diagnostic criteria suggested for TBS include two or more of the following:

1. Anorectal malformation (imperforate anus, anteriorly placed anus, anal stenosis);

2. Hand malformation (pre-axial polydactyly, triphalangeal thumb, bifid thumb);

3. External ear malformation (microtia, "satyr" or "lop" ear, preauricular tags or pits) with sensorineural hearing loss;

4. A relative with the syndrome [19].

Diagnosis/Testing

The diagnosis of TBS is based on clinical findings; identification of a heterozygous SALL1 pathogenic variant on molecular genetic testing establishes the diagnosis if clinical features are inconclusive [3]. Unfortunately, we could not do gene study for our patient due to political problem with referral of the samples. But according to clinical picture, we can say our patient have Townes Brocks syndrome.

Differential diagnosis

VATER associations, although TBS does not have Tracheo-Oesophageal fistula or vertebral anomalies, and TBS has ear anomalies and deafness which are not typical of VATER [11]. VACTERL with hydrocephalus, reported as an X linked or autosomal recessive condition, may include radial and renal anomalies and imperforate anus along with other VATER features [12].

There are overlapping features in TBS and Baller-Gerold syndrome, including thumb anomalies (usually absent or hypoplastic in Baller-Gerold syndrome), imperforate anus, and urogenital anomalies. An important differentiating feature is craniosynostosis which is present in 100% of patients with Baller-Gerold syndrome [13].

Branchio-oto-renal dysplasia is a rare syndromic disorder characterized by otic malformations, branchial fistulae and branchial cleft cysts renal malformations: can range from mild renal hypoplasia to bilateral renal agenesis [14]. Fanconi anemia characterized by progressive bone marrow failure, various congenital abnormalities (including absent thumb triphalangeal thumb, cutaneous, skeletal, craniofacial, and genitourinary anomalies), and predisposition to malignancies [15,16]. Oculo-auriculo-vertebral spectrum (OAV), also has similar features to TBS, but again there are no vertebral anomalies in TBS and imperforate anus is rare in OAV [17].

Conclusion

We were able to diagnose this case of Townes-Brocks syndrome (TBS) for the first time in Gaza Strip after fulfilling all diagnostic criteria and after ruling out all related diagnoses. This case just reemphasizes the importance of though examination of babies suspected of having congenital disorders.

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