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Available online at: http://www.iajps.com ***A Case Report***

BEAULIEU BOYCOTT INNES SYNDROME (BBIS)

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Abstract:

Background: *An autosomal recessive neurodevelopmental disorder known as Beaulieu Boycott Innes syndrome (BBIS). The patient can present with dysmorphic facial features (tall forehead,shortupslanting palpebral fissures, deep-set eyes, and a long nose with overhanging columella.), delayed development, and moderate to severe intellectual disability*

Case presentation: *five months old baby boy from a Saudi consanguineous parents, a product of a cesarean section due to oligohydramnios at full term, with a birth weight of 2.2 kg, the baby is known to have failure to thrive in addition to global developmental delay, dysmorphic facial features, microcephaly, cleft palate, and congenital heart disease, the baby also has hx of feeding intolerance of both oral and NGT, in the form of vomiting and aspirations which caused him recurrent chest infections, for that the patient is on TPN, and despite receiving the maximum calories the weight gain is slow*

Conclusion: *Beaulieu-Boycott-Innes syndrome (BBIS) is a very rare genetic disease caused by homozygous or compound heterozygous mutation in the THOC6 gene (615403) on chromosome 16p13.*

Keywords: *neurodevelopmental disorder; BBIS; genetic disease.*

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INTRODUCTION:

potentially impairing its regulatory role in mRNA processing and export from the nucleus (1, 4).

In 2010, **Boycott *et al.* (1)** studied four patients with a common unique set of clinical features that suggest that this is a previously unreported syndrome characterized by developmental delay, head circumference at the second centile, congenital renal and cardiac malformations, and distinctive facial features. The facial gestalt is recognizable and involved a tall forehead, long nose, high anterior hairline, deep-set eyes with short and upslanted palpebral fissures, low-hanging columella and thick vermilion of the upper and lower lip. The congenital renal and cardiac malformations are relatively mild in these patients and have not typically required intervention. Head circumference is at the 2nd centile at birth and remains at this centile when growth is complete. Development was delayed in all the patients with the language being most significantly affected in early childhood. Academic achievement at school suggests that a specific cognitive profile is a feature of this syndrome (1).

In 2016, **Anazi *et al.*,** (3) studied a case report of a four-year-old Saudi boy who was first evaluated at the age of three years for a possible syndromic diagnosis. He was diagnosed with imperforate anus at birth and underwent anoplasty. In the NICU, he was also diagnosed with an atrial septal defect (ASD), ventricular septal defect (VSD) and patent ductus arteriosus (PDA). Renal ultrasound was normal. He had delayed development: he sat at one year, walked at two years, and had no discernible words when evaluated at three years of age. His medical history was only notable otherwise for atopic dermatitis. His parents are first cousins once removed and had had a neonatal death with congenital heart disease, and stillbirth with hydrops fetalis.

Anazi *et al.*, (3) revealed a small build and dysmorphism in the form of the broad forehead, low-hanging columella, bilateral epicanthus, thin lower lip with an infralabial groove, pointed chin, mild camptodactyly, overriding toes, and undescended testicles. The patient we describe here has a similar dysmorphology profile (broad forehead, low-hanging columella and pointed chin) and cardiac defects (VSD and PDA) to the previously described Hutterite families (3). However, **Anazi *et al.*,** (3) noted the lack of microcephaly in the THOC6- related intellectual disability in our patient, in contrast to the previously reported Hutterite families.

An autosomal recessive neurodevelopmental disorder known as Beaulieu Boycott Innes syndrome (BBIS). The patient can present with dysmorphic facial features (tall forehead,shortupslanting palpebral fissures, deep-set eyes, and a long nose with overhanging columella.), delayed development, and moderate to severe intellectual disability. Also, also patient may has other anomalies like submucous cleft palate, cryptorchidism in males, corpus callosum dysgenesis, and cardiac and renal defects (1, 2).

THOC6 gene found at chromosome 16p13.3, and it is a part of the THO complex, which plays a major role in causing the intellectual disability in the affected patient (1, 2).

A previous study suggested that the mutation of the THOC6 gene leads to impairing its regulatory role in mRNA processing and export from the nucleus (3).

CASE PRESENTATION:

we report this case of a five months old baby boy from a Saudi consanguineous parents, a product of a cesarean section due to oligohydramnios at full term, with a birth weight of 2.2 kg, the baby is known to have failure to thrive in addition to: global developmental delay, dysmorphic facial features, microcephaly, cleft palate, and congenital heart disease, the baby also has hx of feeding intolerance of both oral and NGT, in the form of vomiting and aspirations which caused him recurrent chest infections, for that the patient is on TPN, and despite receiving the maximum calories the weight gain is slow, his current weight is 2.8 kg. On examination he was found to be small for his age, with a broad forehead and epicanthus bilaterally, he also has micrognathia, low set ears and cleft palate, examination of genitalia showed undescended testes bilaterally with hypospadias. An echocardiogram was done and confirmed the presence of patent ductus arteriosus with ASD second, a whole exome sequencing was done and revealed, a homozygous pathogenic variant in the THOC6 gene, and the genetic diagnosis of autosomal recessive Beaulieu-Boycott-Innes syndrome.

DISCUSSION:

Mutations in THOC6 were a significant problem for very rare genetic diseases. THOC6 is a human morbid gene was identified in 2013 when previously described Hutterite patients with displayed developmental delay and intellectual disability, microcephaly, congenital heart disease and facial dysmorphism were found to have a homozygous missense mutation in this gene (1, 4). The missense mutation impaired nuclear localization of THOC6,

REFERENCES

1- Boycott KM1, Beaulieu C, Puffenberger EG, McLeod DR, Parboosingh JS, Innes AM. (2010) 'A Novel Autosomal Recessive Malformation Syndrome Associated With Developmental Delay and Distinctive Facies Maps to 16ptel in the Hutterite Population', American Journal of Medical Genetics, 152A(6), pp. 1349-56.

2- Amos JS1, Huang L2, Thevenon J3,4, Kariminedjad A5, Beaulieu CL2, Masurel-Paulet A3,4, Najmabadi H5,6, Fattahi Z5,6, Beheshtian M5,6, Tonekaboni SH7, Tang S8, Helbig KL8, Alcaraz W8, Rivière JB3,4, Faivre L3,4, Innes AM9, Lebel RR1, Boycott KM2; Care4Rare Canada Consortium. (2016) 'Autosomal recessive mutations in THOC6 cause intellectual disability: syndrome delineation requiring forward and reverse phenotyping', An International Journal of Genetics, Molecular and Personalized Medicine, 91(1), pp. 92-99.

3- Anazi S1, Alshammari M2, Moneis D1,3, Abouelhoda M1,3, Ibrahim N1, Alkuraya FS1 (2016) 'Confirming the Candidacy of THOC6 in the Etiology of Intellectual Disability', American Journal of Medical Genetics, 170A(5), pp. 1367-9.

4- Beaulieu CL, Huang L, Innes AM, Akimenko MA, Puffenberger EG, Schwartz C, Jerry P, Ober C, Hegele RA, McLeod DR, Schwartzentruber J. Intellectual disability associated with a homozygous missense mutation in THOC6. Orphanet journal of rare diseases. 2013 Dec;8(1):62.

In 2016, **Amos *et al.*** (2) reported three unrelated patients from distinct ethnic backgrounds from France, Iran, and the United States with deleterious-appearing bi-allelic variants in THOC6 and an overlapping spectrum of clinical features. The clinical presentation associated with recessive mutations in THOC6 included mild microcephaly to border line-normal head circumference, moderate to severe intellectual disability, and non-life threatening congenital malformations involving cardiac septal defects, cryptorchidism in males, structural renal anomalies, submucous cleft palate, and corpus callosum dysgenesis. However, most of the features are relatively non-specific, and all are observed frequently in patients assessed in a clinical genetics setting. The facial features observed in the patients included a tall forehead, short upslanting palpebral fissures deep-set eyes, long nose, low-hanging columella, retrognathia, and dental anomalies (2).

CONCLUSION:

Beaulieu-Boycott-Innes syndrome (BBIS) is a very rare genetic disease caused by homozygous or compound heterozygous mutation in the THOC6 gene (615403) on chromosome 16p13. It is an autosomal recessive neurodevelopmental disorder characterized by delayed development, mild to severe intellectual disability, and dysmorphic facial features. Other developmental anomalies, such as renal and cardiac defects. Additionally, cryptorchidism in males, submucous cleft palate, and corpus callosum dysgenesis, may also be present.