ECRONICON OPEN ACCESS

EC PAEDIATRICS
Case Report

Tatton Brown Rahman Syndrome with Congenital Abdominal Wall Defect. A Rare Case Report

Mohamed Shoukry*

Department of General Surgery, University of Malta, Malta

***Corresponding Author:** Mohamed Shoukry, Department of General Surgery, University of Malta, Malta.

Received: July 18, 2023; **Published:** July 31, 2023

Abstract

This is a case report of a 4-year-old girl with Tatton Brown Rahman Syndrome (TBRS), a rare syndrome caused by a mutation in the DNMT3A gene. This congenital anomaly is characterized by skeletal overgrowth, macrocephaly and characteristic facial features.

The patient was referred to paediatric surgery in view of uncomplicated hernia via centrally located abdominal wall defect which presented since birth. After full investigations performed, she underwent the surgical repair of cardiac defects, medical optimisation and systems clinical review, the patient was scheduled for an elective repair of the congenital abdominal wall defect.

The hernia was corrected surgically without using a mesh, and the postoperative period was uneventful. Regular follow-up revealed no residual defects.

This case is unique because it describes the first documented case of a congenital hernia of the umbilical cord associated with TBRS, a rare congenital anomaly. Despite several similar overgrowth disorders associated with intellectual disabilities, TBRS is caused by a constitutive variant of the DNMT3A gene. Since TBRS is caused by a *de novo* pathogenic variant, most cases represent simplex cases. In conclusion, this case report highlights the importance of identifying and managing associated congenital anomalies in TBRS, particularly when they are rare and have not been reported previously.

Keywords: *Tatton Brown Rahman Syndrome (TBRS); DNMT3A Gene; Congenital Abdominal Wall Defect*

Introduction

Tatton Brown Rahman Syndrome (TBRS) is a syndrome initially identified in 2014 and is caused by a *de novo* mutation in the DNMT3A gene [1]. TBRS is a congenital anomaly that manifests with skeletal overgrowth, macrocephaly, and characteristic facial features [2]. None of the documented cases reported association with congenital abdominal wall defect so far.

Case Presentation

A 4-year-old girl, known case of TBRS, was referred to paediatric surgery clinic in view of a painless but fully reducible hernia via large anterior abdominal wall defect in the umbilical area noted since birth.

The patient was born in 2019 at term via emergency LSCS in view of no progress during 2nd stage of labour at 40+1 weeks and weighing 4.36 kg, with an APGAR score of 9 and 9.

She was a large-for gestational age baby. No report was made of an umbilical defect or swelling seen on antenatal US scanning.

On her second day of life, she had episodes of hypoglycaemia which persisted and jaundice and was transferred to neonatal intensive care. She was noted to have positional talipes at birth.

At the age of 6 weeks of life, it was noted to have recurrent daily episodes of tachypnoea with upward eye rolling, facial grimacing, twitching and abnormal sigh or cry. In Addition to this, there were concerns regarding neurodevelopmental delay including head support, poor visual fixation and hypotonia. Further investigations have been carried out, Echo showed congenital cardiac abnormality - 9 mm ASD with left to right flow and a small PDA with good ventricular function.

The patient had multiple hospital admissions due to recurrent bronchiolitis, pneumonia, bradycardia, seizures, and COVID pneumonia. She was investigated for GORD and metabolic disorder with high levels of methylmalonic acid. Her brain MRI showed white matter volume loss with dilatation of lateral ventricles. Her EEG telemetry showed no epileptic changes. In addition to the nerve EEM reported reduced amplitude and conduction velocity of right median sensory response. On the other hand, her sleep study concluded that she needed oxygen requirements of 0.2 L/min in view of hypoventilation.

Her chest CT showed multifocal gas trapping with atelectasis and bilateral perihilar soft tissue attenuation, likely lymphatic in origin. The Abdominal US documented unicornuate uterus. Otherwise, normal solid organs and urinary system.

She underwent the surgical repair of the cardiac anomalies on February 2020 successfully. ASD secundum closure with autologous pericardial patch and PDA closure. Predischarge echo showed no residual ASD, unobstructed pulmonary venous return, good biventricular systolic function, no residual PDA, unobstructed aortic arch, dysplastic mitral and tricuspid valve leaflets with mild MR and TR.

That was followed by repair of the Talipes equinovarus anomaly on July 2021 with satisfactory outcome. Her abdominal wall defect and subsequent hernia of the cord corrected surgically on October 2022. A supra-umbilical incision was performed that allowed extension laterally during surgery, dissection around sac, separation of umbilical stump, ligation of umbilical vessels and sac was opened and redundant part was excised. Anatomical repair using 3-0 absorbable sutures then closure into layers followed by closure of skin and creation new umbilical dimple.

Pressure dressing was applied for few days.

This anatomical repair carried out successfully without need of mesh. Post-operative period was uneventful. No residual defect reported on regular follow-up till the current report. BIPAP was switched to sick settings post-op as advised by paediatric respiratory physician as well as had intensive chest physiotherapy to avoid atelectasis and LRTI after GA.

Patient returned home in 48 hours and followed up in the out-patient's clinic routinely.

Discussion

TBRS is a congenital anomaly syndrome characterised with skeletal overgrowth, macrocephaly, and abnormal facial features [2]. The major clinical features are overgrowth (defined as height and/or head circumference at least 2 standard deviations above the population mean) associated with intellectual disability.

The syndrome is diagnosed based on the presence of these two major clinical features, as well as a constitutive variant of the DNMT3A gene [2]. No gender predominance was reported in literature review.

Since TBRS is usually caused by a *de novo* pathogenic variant - most probands represent simplex cases; the first case in the family [3].

Other common clinical features which may be seen in 20 - 80% of individuals with TBRS, include joint hypermobility, obesity, hypotonia, kyphoscoliosis, and afebrile seizures.

TBRS is one of several overgrowth disorders associated with intellectual disability, with other examples including Sotos syndrome and Weaver syndrome.

Despite all these disorders having similar clinical phenotypes they are caused by distinct genetic abnormalities [4].

We report a case of a 4 year old girl who presented with an anterior abdominal wall defect. To date, there are approximately 80 reported cases worldwide of TBRS and this is the first documented case which also includes a congenital hernia of the umbilical cord - which is a rare congenital anomaly with a quoted incidence of 1:5000. This patient is the only known patient with this presentation on top the TBRS syndromic association.

Congenital hernia of the umbilical cord is defined as "herniation of small bowel and occasionally other viscera into umbilical cord while the rest of the anterior abdominal wall is usually normal" [5].

During the 3rd week of intrauterine life, there is a communication between the intraembryonic gut and the yolk sac as the development proceeds this communication narrows into a tube known as the omphalomesenteric duct, and it usually obliterates by the end of the 7th week. There is physiological herniation of the midgut into the umbilical coelom during 5 - 6th week of gestation and herniated gut then returns during 10 - 12th week of gestation into the abdominal cavity. At 10 - 12 weeks' gestation a part of the midgut fails to return completely into the abdomen and thus is retained at the base of umbilicus resulting in hernia of umbilical cord [6].

Congenital hernia of umbilical cord is anatomically and structurally different from postnatal diagnosed umbilical hernia. The contents of the hernia sac never returned inside the abdominal cavity, abnormal poorly developed umbilical stump placed on the dome of the sac, roomy and relatively capacious hernia sac protruding via facial defect of anterior abdominal wall close to midline but could be either sides of midline. The edge of the defect is smooth and distinct eventually integrated with the abdominal wall at the base. The sac has thick wall and adherent to skin. The contents reported are omentum stuck to the dome and lateral aspect of the sac. Nevertheless, bowel loops of jejunum and mid transverse colon [7].

It has been reported that there is a poor association between umbilical cord hernias and intestinal anomalies, malrotation, and volvulus [7].

A type III abdominal wall defect was noted - corresponding with a congenital hernia of umbilical cord.

Conclusion

This case of a 4 year old girl with TBRS, who also presented with a congenital hernia of the umbilical cord - raises the question whether this may be a previously unrecognized feature of this syndrome - especially due to congenital hernias of the umbilical cord often being misdiagnosed as a small omphalocele, as well as the rarity of TBRS.

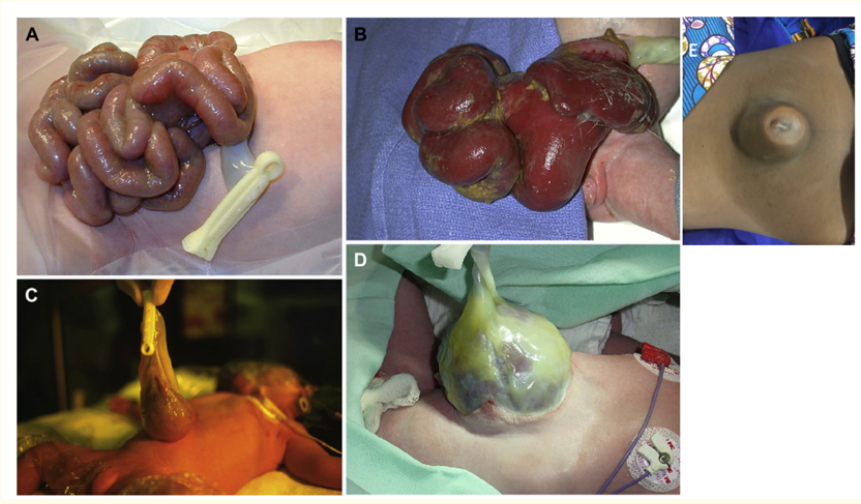

Figure 1: *Types of congenital abdominal wall defects [8]. (A) Gastroschisis with relatively normal bowel. (B) Gastroschisis with significantly damaged bowel. (C) Small omphalocele. (D) Giant omphalocele with liver out. (E) Congenital hernia of the umbilical cord.*

Despite this being an uncomplicated surgery, the patient centred care required implementation of multidisciplinary team management in view of high risk of complications due to hypoventilation syndrome, neurodevelopmental delay and other hidden or undiscovered associated anomalies.

Bibliography

1. Tatton-Brown K., *et al*. "The Tatton-Brown-Rahman Syndrome: A clinical study of 55 individuals with *de novo* constitutive DNMT3A variants [version 1; referees: 3 approved]". Wellcome Open Research (2018).
2. Yokoi T., *et al*. "Tatton-Brown-Rahman syndrome with a novel DNMT3A mutation presented severe intellectual disability and autism spectrum disorder". *Human Genome Variation* (2020).
3. Ostrowski PJ and Tatton-brown K. "Tatton-Brown-Rahman Syndrome". *Gene Reviews* 1-20 (2022).
4. Lane C., *et al*. "Tatton-Brown-Rahman syndrome: cognitive and behavioural phenotypes". *Developmental Medicine and Child Neurology* (2020).
5. Raicevic M., *et al*. "Hernia of the umbilical cord associated with a patent omphalomesenteric duct". *Journal of Postgraduate Medicine* (2017).
6. Achiron R., *et al*. "Fetal midgut herniation into the umbilical cord: improved definition of ventral abdominal anomaly with the use of transvaginal sonography". *Ultrasound in Obstetrics and Gynecology* (1995).
7. Raju R., *et al*. "Congenital hernia of cord: An often misdiagnosed entity". *BMJ Case Reports* (2015).
8. Christison-Lagay ER., *et al*. "Neonatal abdominal wall defects". *Seminars in Fetal and Neonatal Medicine* 16.3 (2011): 164-172.

Volume 12 Issue 8 August 2023