Case Report

Open Access Journal of
Biomedical Science
ISSN: 2690-487X

Recurrent Severe Polyhydramnios in Bartter Syndrome: A Case Report

Slagjana Simeonova Krstevska[1]*, Todor Arsov[2], Ana Marija Shpishic Pushevska[3], Tatjana Gurzanova[4], Igor Samardziski[1], Irena Todorovska[1], Vesna Livrinova[1], Iva Paneva[1], Aneta Sima[1], Daniel Milkovski[1] and Marija Joksimovic[1]

[1]*University clinic for obstetrics and gynecology, Skopje, N. Macedonia*

[2]*University institute for immunology and human genetics, Medical Faculty Skopje, University for medical science Shtip, N. Macedonia*

[3]*Special hospital for gynecology and obstetrics Mother Theresa Skopje, N. Macedonia*

[4]*PHO Newborn, Skopje, N. Macedonia*

ABSTRACT

Repetitive severe polyhydramnios is a potentially serious obstetric condition which requires detail evaluation. We present a case of a 35-year-old pregnant woman referred due to extreme repetitive polyhydramnios in 19 gestational week. She had history of two missed abortions and premature labor in 23 gestational weeks with extreme polyhydramnios and death. Pat histology report didn't show any anomaly of the organs and systems of that neonate. The actual pregnancy was conceived with IVF procedure and went uneventful until 19 GW. Combined first trimester screening and the noninvasive prenatal test went with low risk for aneuploidies. Gestational diabetes was excluded. Second trimester morphology scan and TORCH infections were within normal. She was hospitalized in 26 GW as a result of premature contractions, received tocolytic therapy on several occasions. Amnioreduction was performed twice, amniotic fluid for quantitative karyotype was done and came negative for aneuploidies (13,18,21 and sex chromosomes). Consultation with genetics and pediatric nephrologist was made due to suspicion of Bartter syndrome. Amniotic fluid as well as blood from both partners was sent to referent genetic laboratory and the molecular findings were in line with the diagnosis of SLC12A1 associated Bartter syndrome type 1 in the fetus. Corticosteroid therapy for fetal lung maturation was given and delivery was made by caesarean section in 31 gestational weeks. The neonate with weight 1180g, length 30cm, Apgar score 6/6/7, was admitted to neonatal intensive care unit. On the 7th day there was a gradual worsening in the general condition with cardiopulmonary failure and no response to reanimation resulted in neonatal death.

Conclusion: Bartter syndrome is an autosomal recessive disease characterized by severe fetal polyuria and extreme polyhydramnios. It can be cause of preterm labor and should be suspected in cases of repetitive polyhydramnios.

KEYWORDS: Polyhydramnios; Bartter syndrome

INTRODUCTION

Bartter syndrome is an autosomal recessive, heterogeneous group of salt losing renal tubulopathy with secondary hyperaldosteronism, hypokalemia, and metabolic alkalosis [1]. It was first described in medical literature in the 1960s by Dr. Frederic Bartter.

Incidence

The Bartter syndromes occurs in males and females equally and is estimated to affect approximately one in 100,000 people in the general population.

Quick Response Code:

Address for correspondence: Slagjana Simeonova Krstevska, University clinic for obstetrics and gynecology, Skopje, N. Macedonia

Received: January 16, 2023 **Published:** February 09, 2023

How to cite this article: Slagjana Simeonova K, Todor A, Ana Marija Shpishic P, Tatjana G, Igor S, et. al. Recurrent Severe Polyhydramnios in Bartter Syndrome: A Case Report. 2023- 5(1) OAJBS. ID.000542. **DOI:** 10.38125/OAJBS.000542

Classification

Subdivisions of Bartter syndrome based upon the underlying genetic mutation [2] are:

a) Bartter syndrome type 1 (SLC12A1 gene)

b) Bartter syndrome type 2 (KCNJ1 gene)

c) Bartter syndrome type 3 (CLCNKB gene)

d) Bartter syndrome type 4A (BSND gene)

e) Bartter syndrome type 4B (CLCNKA and CLCNKB genes)

f) Transitory antenatal Bartter syndrome associated with MAGED2 mutations.

Clinical Symptoms

The term antenatal Bartter syndrome refers to those cases who present before birth and is typically associated with types 1, 2, 4a and 4b. These disorders were sometimes also called hyper prostaglandin E syndromes as they are associated with elevated levels of urinary prostaglandins. Antenatal presentation associate's polyhydramnios, premature birth, postnatal polyuria, severe dehydration episodes, growth retardation, hypercalciuria and nephrocalcinosis [3].

Congenital sensorineural deafness may occur in some cases. As children grow older, growth retardation, short stature and developmental delays may occur. Some affected infants may have certain facial features including a triangularly shaped face, prominent forehead, large eyes, pointed ears. Classical form presents a milder phenotype, and diagnosis is frequently delayed from infancy to adolescence.

Diagnosis

The antenatal subtypes of Bartter syndrome can be diagnosed prenatally when polyhydramnios is detected without associated congenital malformations, and elevated levels of chloride and aldosterone are detected in the amniotic fluid. Molecular genetic testing can detect mutations in specific genes known to cause the Bartter syndromes, but is only available at specialized laboratories. Amniotic fluid biochemistry is also beneficial in the diagnosis [4,5], as well as some ultrasound markers like dilated and increased fetal bladder [6]. Differential diagnosis: Gitelman syndrome, EAST syndrome, Pseudo-Bartter syndrome, Autosomal dominant hypocalcemia type 1.

Treatment

There is no cure for these disorders which require lifelong administration of certain supplements and medications. Proper balance of fluids and electrolytes helps correction of electrolyte imbalances. Because the elevated levels of prostaglandins aggravate the polyuria and electrolyte abnormalities, treatment typically includes NSAID such as indomethacin, ibuprofen or celecoxib. as well as renin-aldosterone-angiotensin system inhibitors [7].

Successful use of growth hormone therapy has been reported in some cases for short stature associated with Bartter syndrome. Cochlear implants can be used to treat deafness associated with Bartter syndromes type 4A and 4B. Genetic counseling is recommended for affected individuals and their families. Psychosocial support for the entire family is essential as well.

CASE REPORT

We present a case of a 35-year-old pregnant woman (G4, para 1) referred to tertiary level due to extreme polyhydramnios in 19 gestational week. In obstetric history there were two first trimester missed abortions, premature labor in 23 gestational weeks with extreme polyhydramnios and exits lethalis. Pat histology report didn't show any anomaly of the organs and systems of that neonate.

The actual pregnancy was conceived with IVF procedure and went uneventful until 19 GW. First trimester screening and non-invasive prenatal test was with low risk for aneuploidies. In 19 GW extreme polyhydramnios was noted and she was referred to our clinic for second opinion. The oral glucose tolerance test (75g) and second trimester fetal morphology scan were normal (Figure 1-5).

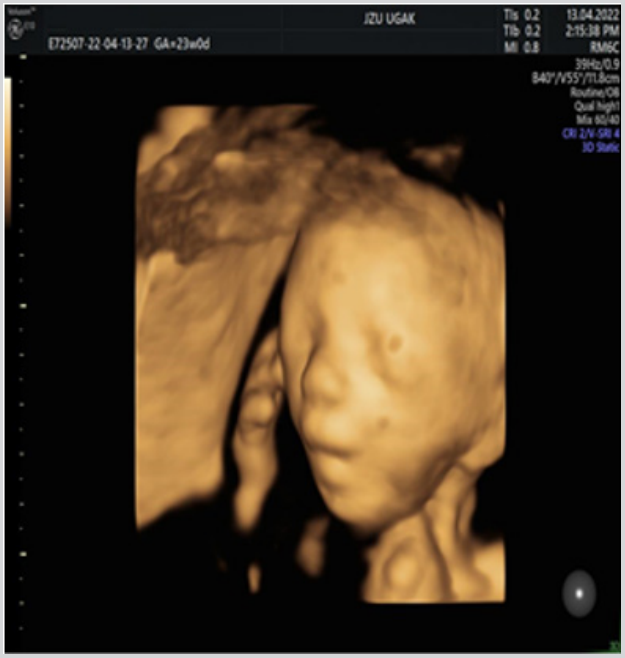

Figure 1: Fetal face.

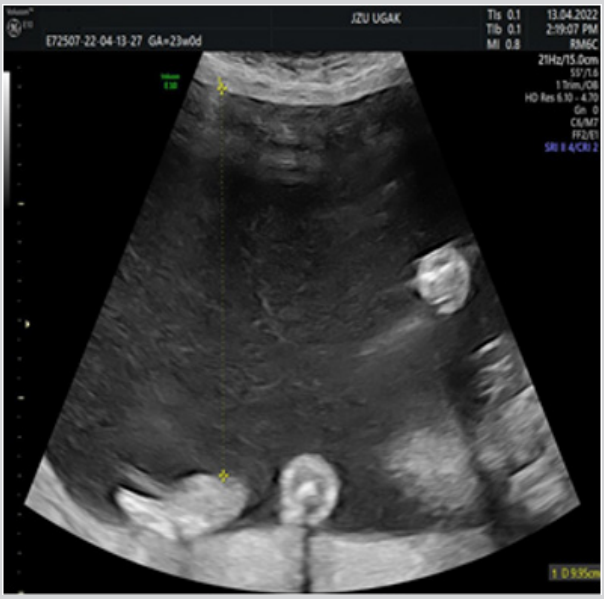

Figure 2: Polyhydramnios as single vertical pocket of more than 9cm.

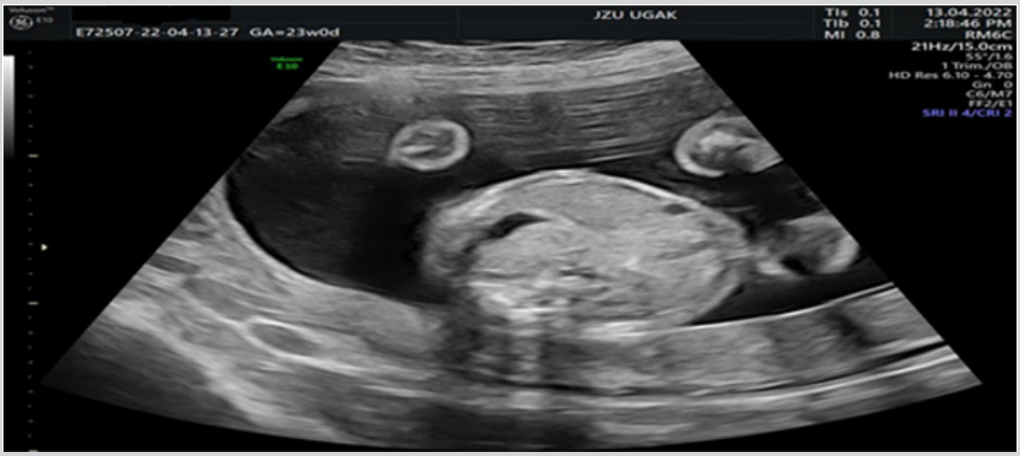

Figure 3: Abdominal circumference with fetal stomach.

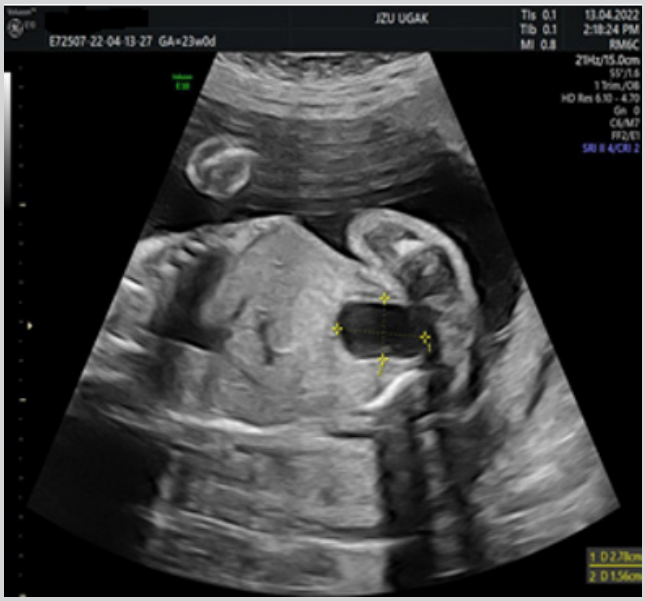

Figure 4: Fetal bladder of adequate size for gestational age.

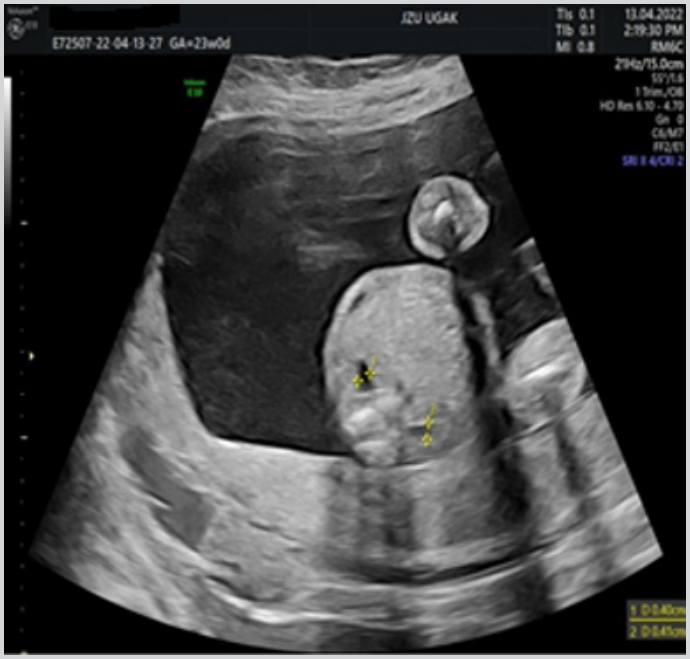

Figure 5: Fetal pylons 4mm bilaterally.

TORCH infections were excluded. Indomethacin was given orally, and she was checked in one week interval.

She was hospitalized in 26 GW as a result of premature contractions, received tocolytic therapy in several occasions (indomethacin, artesian, progesterone and magnesium sulphate). Ultrasound biometry was adequate for gestational age with cervical length of 35mm, Doppler of the fetoplacental unit was normal, amniotic fluid level around 40cm. She suffered from worsening abdominal distension, breathlessness and difficulty sleeping after 24 weeks. Amnioreduction was performed in 2 occasion when amniotic fluid for quantitative karyotype was performed and came negative for aneuploidies (13,18,21 and sex chromosomes).

Consult with genetics and pediatric nephrologist was made due to suspicion of Bartther syndrome because of repetitive polyhydramnios. Amniotic fluid as well as blood form both partners was sent to referent genetic laboratory (Institute of Human Genetics, Köln, Hereditary Kidney Diseases Group). DNA amplification using polymerase chain reaction (PCR) and subsequent Sanger sequencing analysis of the coding regions and exon-intron boundaries of the following genes: SLC12A1 (OMIM 600839; Ref Seq NM_000338.2), KCNJ1 (OMIM 600359; Ref Seq NM_000220.4) revealed that the fetus was compound heterozygote for SLC12A1 mutations c.572T>A and c.572T>A.

The mother is carrier of the SLC12A1-Variant c.572T>A and the father is carrier of the SLC12A1-Variant c.1306T>C>A. The molecular findings are in line with the diagnosis of SLC12A1 associated Bartter syndrome type 1 in the fetus. Corticosteroid therapy for fetal lung maturation was given in 26 and 31 gestational week and she was delivered in 31 gestational weeks due to podalic lie, imminent preterm delivery and non-reassuring non stress test. The neonate had weight of 1180g, length of 30cm, Apgar score 6/6/7 and was admitted to NICU, treated with oxygen support and indomethacin orally. Fetal polyuria, hydration and electrolyte balance were managed. On the 7th day there was a gradual worsening in the general condition with cardiopulmonary failure and no response to reanimation resulted in neonatal death.

DISCUSSION

Polyhydramnios occurs in 1% of all pregnancies [1]. It is diagnosed as amniotic fluid index greater than 25 cm may be caused by congenital anomalies (anencephaly, cleft palate, tracheoesophageal fistula, diaphragmatic hernia), genetic disorders of the fetus, maternal diabetes, placental abnormalities, fetal anemia or can be idiopathic. Detailed evaluation which includes ultrasonography scanning, screening for maternal diabetes or amniocentesis is usually indicated. Recurrent polyhydramnios in absence of congenital anomalies may be caused by rare conditions like Bartter syndrome [2]. Antenatal Bartter syndrome is frequently caused by mutations in the SLC12A1 or KCNJ1 genes. Bartter syndrome is inherited in an autosomal recessive manner. It is a primarily a disorder in the loop of Henle, impairment in electrolyte tubular reabsorption which results in fetal polyuria.

In antenatal Bartter syndrome severe salt losing is further aggravated by an increased incidence of proteinuria and impaired renal function at some age. In the prenatal diagnosis of Bartter syndrome besides genetics there is a possibility of other approaches. Garnier et al analyzed amniotic fluid biochemistry (total proteins, alpha-fetoprotein and electrolytes) for the prediction of Bartter syndrome [4]. In Bartter syndrome they observed significant differences for protein amniotic fluid levels. Elevated chloride levels in amniotic fluid were consistent with diagnostic finding in Bartter syndrome according to study of Narayan et al. [5]. Other amniotic fluid biochemical markers have been described, notably increased aldosterone levels and low total protein levels. Some authors like Thakur et al investigated ultrasound markers associated with Bartter syndrome. A consistent full bladder with severe polyhydramnios with onset around 24 gestational weeks like a novel finding was observed due to fetal polyuria and can be used as a clue to investigate cases with severe polyhydramnios with no structural anomaly.

CONCLUSION

This is a rare diagnosis but has significant clinical implications. Early identification and treatment may lead to prolonging the

pregnancy and reducing the morbidity associated with extreme prematurity. There is a debate whether we should offer genetic testing for all cases of recurrent idiopathic polyhydramnios. In this case of pregnancy with poor obstetric history amniocentesis and genetic diagnosis confirmed homozygous duplication in the SLC12A1 gene, associated with Bartter syndrome Type I. Although this was a case with exits lethalis in early neonatal period the prenatal diagnosis helped in the proper management and genetic counseling will follow before and during the next pregnancy.

ACKNOWLEDGMENT

The authors would like to thank Prof Velibor Tasic, MD, PhD, University Children's Hospital, Skopje, N. Macedonia and PD. Dr. med. Bodo Beck from Hereditary Kidney Diseases Group, Institute for Human Genetics, Cologne, Germany. Ethical consent from the Institutional Review Board, consent from the parents to perform genetic analysis and consent from the parents for the publication of this report were obtained.

REFERENCES

1. Fatma A, Ali F, Alberry M (2017) Bartter syndrome: a rare cause of refractory severe polyhydramnios. Ultrasound in obstetrics and gynecology.
2. Gina N, Angela C, Mi-Hye P (2021) A rare cause of refractory severe polyhydramnios: antenatal bartter syndrome. Medicina 57(3): 272.
3. Martin K, Kamel L (2017) Pathophysiology of antenatal Bartter's syndrome. Curr Opin Nephrol Hypertens 26(5): 419-425.
4. Arnaud G, Sophie D, Rosa VP, Jean FO, Alexandra B, et al. (2010) Bartter syndrome prenatal diagnosis based on amniotic fluid biochemical analysis. Pediatr Res 67(3): 300-303.
5. Narayan R, Peres M, Kesby G (2016) Diagnosis of antenatal barter syndrome. Clin Exp Obstet Gynecol 43(3): 453-454.
6. Seema T, Manisha K, Supriya M, Preeti P, Vandana T, et al. (2020) Severe polyhydramnios with consistent fetal full bladder: A novel sign of antenatal bartter's disease. J Pediatr Genet 9(4): 296-300.
7. Ramesh BY, Vinayaka G, Sreelakshmi K (2012) Antenatal Bartter Syndrome: A Review. Int J Pediatr 2012: 857136.