Case Report

Prune Belly Syndrome Associated with Interstitial 17q12 Microdeletion

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Received 18 October 2021; Accepted 17 January 2022; Published 14 February 2022

1. Introduction

Interstitial deletions involving terminal 17q12 (17q12-qterm) are rare chromosomal abnormalities associated with variable phenotypes. Previous case reports of 17q12 microdeletion characterized the patients with structural and/or functional disorders of the kidney and urinary tract, maturity-onset diabetes of the young type 5 (MODY5), and neurodevelopmental or neuropsychiatric disorders (e.g., developmental delay, intellectual disability, autism spectrum disorder, schizophrenia, anxiety, and bipolar disorder) [1–3]. To date, there are few reported cases of prune belly syndrome (PBS) and associated chromosomal abnormalities. We report a new case of PBS associated with 17q12 microdeletion, and we review the literature.

2. Case Report

A term Hispanic male neonate was born at 40-week gestation to an 18-year-old primigravida by cesarean section. Apgar scores were 9 and 9 at 1 and 5 minutes, respectively. Pregnancy was complicated by an abnormal prenatal ultrasound at 20-week gestation which revealed bilateral renal pelvis dilation, dilated ureters, thickened bladder with key-hole sign, and dilated urethra. Subsequent sonography revealed progression of the hydronephrosis and hydroureter. Genetic studies that were performed during the pregnancy had shown 17q12 microdeletion, a de novo mutation. The family history was negative for congenital anomalies, and there were no history of in utero exposure to any known teratogens and no history of consanguinity.

Physical examination revealed a weight of 3470 grams (45th centile), length of 50 cm (40th centile), and head circumference of 35 cm (45th centile). Anomalies noted at birth included marked abdominal distension with a thin, wrinkled, and flaccid abdominal wall and bilateral undescended testes (shown in Figures 1 and 2). A Foley catheter was placed on day of life (DOL) 0, and the infant was started on amoxicillin for urinary tract infection (UTI) prophylaxis. Ultrasound of the kidneys and bladder on DOL 0 showed severe right hydroureronephrosis, moderate left hydroureronephrosis, thick-walled urinary bladder, and dilatation of the posterior urethra. There was a cystic structure noted in the prostate (shown in Figure 3). An abdominal ultrasound found bilateral testes in the midabdomen. Voiding cystourethrogram (VCUG) performed on DOL 2 revealed grade 5 left vesicoureteral reflux and grade 1 right vesicoureteral reflux. The cystic structure in the prostate represented the prostatic utricle cyst on VCUG. The posterior urethral
The infant Upon discharge on DOL 21, serum creatinine was 0.8 mg/dL. The infant was discharged on DOL 21, and orchiopexy at 1 month. Right and left nephrostomy tubes were placed on DOL 8 and 15, respectively. The infant was noted secondary to anterior urethral valve (shown in Figure 4). A MAG-3 renogram with Lasix on DOL 6 revealed split function of 43% in the left kidney and 57% in the right kidney without significant clearance after Lasix administration, which was consistent with bilateral obstruction. Echocardiogram showed a small patent ductus arteriosus and patent foramen ovale, and a neurosonogram was normal. The serum creatinine was monitored daily for the first few days of life and then twice weekly, peaking at 1.1 mg/dL on DOL 2 and 8.

Right and left nephrostomy tubes were placed on DOL 8 and 15, respectively. After the procedures, he developed Enterobacter cloacae pyelonephritis despite UTI prophylaxis. Upon discharge on DOL 21, serum creatinine was 0.8 mg/dL. The infant’s feeds consisted of breastmilk or Similac PM 60/40. Bilateral nephrostomy tubes remained in place until planned bilateral pyelostomy for the prevention of urinary tract infection. He was discharged to a subacute hospital for continued management.

The pathogenesis of PBS has been debated and currently proposed with two prominent thoughts: mesenchymal developmental failure or urinary tract obstruction [10]. Higher incidence in males and cases of familial PBS lead to the speculation of a possible sex-influenced inheritance pattern. Murray et al. and Haeri et al. reported 2 cases of PBS.

4. Discussion

Aplasia of the abdominal wall muscle was described by Froehlich in 1939, which is considered the first description of PBS [1]. The incidence of PBS is estimated about 1/30,000 to 1/50,000 live births [2–4], with the incidence decreasing likely due to improvement of prenatal detection and elective termination of affected pregnancies. Most of the cases of PBS are male (3-5% being female), prevalence is higher in the black population, and incidence is higher in infants born to younger mothers [5, 6]. The triad of PBS manifestation included (1) dygenesis and partial or complete aplasia of muscle of the abdominal wall, (2) undescended testes, and (3) complex malformations of the urinary tract [7].

There are other findings apart from the triad, which are present in 75% of the PBS cases. Pulmonary abnormalities, e.g., pulmonary hypoplasia (not parenchymal lung disease), are present and related to prenatal oligohydramnios. Gastrointestinal complications included malrotation, intestinal atresia/stenosis, volvulus, and obstruction occurring in about 30% of PBS patients [8]. 10% of PBS cases have associated cardiac anomalies: septal defects, tetralogy of Fallot, and patent ductus arteriosus [3]. Musculoskeletal abnormalities, usually lower extremities: club feet, congenital hip dislocation, and hypoplasia of the leg or foot, were seen in 5% of the PBS cases [2, 9].

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3. Cytogenetic and Molecular Studies

Whole genome SNP (single-nucleotide polymorphism) microarray analysis was performed using the SNP oligonucleotide microarray analysis (SOMA) CytoScan HD platform which uses over 743,000 SCN probes and 1,953,000 NPCN probes with median spacing of 0.88 kilobase (kb). Total genomic DNA was extracted from the patient’s blood sample and digested with NspI and ligated to NspI adaptors. Polymerase chain reaction (PCR) products were purified and quantified. Purified DNA was fragmented and biotin labeled and hybridized to the CytoScan HD GeneChip. There was a 1.49 megabase (MB) interstitial deletion of the long arm of chromosome 17: arr [hg19] 17q22 (34,822,465-36,307,773) x1 and 826 kilobase (kb) interstitial duplication in the long arm of chromosome 7: 7q12.1 (98,230,688-99,056,822) x3.

The SNP microarray analysis identified an interstitial deletion of 17q22.1, and this deleted interval includes numerous Online Mendelian Inheritance in Man (OMIM) genes starting from ZNHI T3 to TBC1D3H. Deletion of this region has been reported to be associated with the following phenotypes: cystic renal disorders, pancreatic atrophy, liver abnormalities, cognitive impairment and structural brain abnormalities, maturity-onset diabetes of the young (MODY), Müllerian aplasia/Mayer-Rokitansky-Küster-Hauser syndrome in females, and epilepsy (OMIM 189907).

Whole genome SNP microarray (Reveal) analysis identified an interstitial duplication of 7q12.1; this interval includes 10 OMIM genes (NPTX2, TRRAP, SMURF1, KPNA7, ARPC1A, ARCP1B, PDAP1, BUD31, PTCD1, and CPSF4). There has been no report of clinically established disorders with duplication of this region.
with interstitial deletions of chromosome 17q12, suggesting the role of *HNF1B (TCF2)*, a gene that is responsible for mesodermal and endodermal development in different tissues, in PBS [11–13]. However, 17q12 deletion has also been reported in association with other congenital abnormalities of the kidney and urinary tract (CAKUT) without the PBS phenotype: agenesis, hypoplasia, dysplasia, multicystic dysplastic kidney (MCDK), and horseshoe kidney, collecting system abnormalities (duplicated collecting systems, ureteropelvic junction obstruction, isolated hydronephrosis, or hydroureter) and tubulointerstitial disease of the kidney [14–18].

### 5. Conclusion

We report a case of a neonate with 17q12 microdeletion that is associated with PBS. Our report supports the genetic basis in PBS, and the screening for *HNF1B* gene mutations/deletions on chromosome 17q12 could help identify the patient.
of PBS and lead to preventing and improving the treatment of this rare disease.

**Data Availability**

All data pertaining to this article are available from the authors.

**Consent**

Written informed consent was obtained from the parents of the patient for publication of this case report and any accompanying images. A copy of the written consent is available for review by the editor-in-chief of this journal.

**Conflicts of Interest**

The authors declare no conflict of interest.

**Authors’ Contributions**

All authors are equally involved in drafting, literature search, and writing the paper.

**References**

[1] F. Froehlich, "Der Mangel der Muskeln, insbesondere der Seitenbauchmuskeln," Zürn, Wuerzburg, 1839.

[2] F. J. Greskovich and L. M. Nyberg, "The prune belly syndrome: a review of its etiology, defects, treatment and prognosis," Journal of Urology, vol. 140, no. 4, pp. 707–712, 1988.

[3] R. S. Sutherland, R. A. Mevorach, and B. A. Kogan, "The prune-belly syndrome: current insights," Pediatric Nephrology, vol. 9, no. 6, pp. 770–778, 1995.

[4] T. Hoshino, Y. Ihara, H. Shirane, and T. Ota, "Prenatal diagnosis of prune belly syndrome at 12 weeks of pregnancy: case report and review of the literature," Ultrasound in Obstetrics & Gynecology, vol. 12, no. 5, pp. 362–366, 1998.

[5] S. Hassett, G. H. Smith, and A. J. Holland, "Prune belly syndrome," Pediatric Surgery International, vol. 28, no. 3, pp. 219–228, 2012.

[6] G. Tonni, V. Ida, V. Alessandro, and M. P. Bonasoni, "Prune-belly syndrome: case series and review of the literature regarding early prenatal diagnosis, epidemiology, genetic factors, treatment, and prognosis," Fetal and Pediatric Pathology, vol. 31, no. 1, pp. 13–24, 2013.

[7] R. E. Stevenson, J. G. Hall, and R. M. Goodman, Human Malformations and Related Anomalies, Oxford University Press, New York, 1st edition, 1993.

[8] V. Zugor, G. E. Schott, and A. P. Labanaris, "The prune belly syndrome: urological aspects and long-term outcomes of a rare disease," Pediatric Reports, vol. 4, no. 2, article e20, 2012.

[9] R. T. Loder, J. P. Guiboux, D. A. Bloom, and R. N. Hensinger, "Musculoskeletal aspects of prune-belly syndrome. Description and pathogenesis," American Journal Disease of Childhood, vol. 146, no. 10, pp. 1224–1229, 1992.

[10] A. M. Arlen, C. Nawaf, and A. J. Kirsch, "Prune belly syndrome: current perspectives," Pediatric Health Medicine and Therapeutics, vol. Volume 10, pp. 75–81, 2019.

[11] P. J. Murray, K. Thomas, C. J. Mulgrew, S. Ellard, E. L. Edghill, and C. Bingham, "Whole gene deletion of the hepatocyte nuclear factor-1 gene in a patient with the prune-belly syndrome," Nephrology, Dialysis, Transplantation, vol. 23, no. 7, pp. 2412–2415, 2008.

[12] S. Haeri, P. L. Devers, K. A. Kaiser-Rogers et al., "Deletion of hepatocyte nuclear factor-1-beta in an infant with prune belly syndrome," American Journal of Perinatology, vol. 27, no. 7, pp. 559–563, 2010.

[13] C. F. Granberg, S. M. Harrison, D. Dajusta et al., "Genetic basis of prune belly syndrome," screening for HNF1β gene," Journal of Urology, vol. 187, no. 1, pp. 272–278, 2012.

[14] M. W. Mitchell, D. Moreno-De-Luca, S. M. Myers et al., "17q12 recurrent deletion syndrome," Dec 8, 2016 [Updated 2020 Oct 15], in Gene Reviews®, M. P. Adam, H. H. Ardinger, R. A. Pagon, S. E. Wallace, L. J. H. Bean, K. W. Gripp, G. M. Mirzazai, and A. Amemiya, Eds., University of Washington, Seattle, Seattle (WA), 1993-2021, https://www.ncbi.nlm.nih.gov/books/NBK401562/.

[15] C. P. Chen, S. D. Chang, T. H. Wang et al., "Detection of recurrent transmission of 17q12 microdeletion by array comparative genomic hybridization in a fetus with prenatally diagnosed hydronephrosis, hydroureter, and multicystic kidney, and variable clinical spectrum in the family," Taiwan Journal of Obstetrics & Gynecology, vol. 52, no. 4, pp. 551–555, 2013.

[16] R. Li, F. Fu, Y. L. Zhang, D. Z. Li, and C. Liao, "Prenatal diagnosis of 17q12 duplication and deletion syndrome in two fetuses with congenital anomalies," Taiwan Journal of Obstetrics & Gynecology, vol. 53, no. 4, pp. 579–582, 2014.

[17] Y. L. Jiang, Q. W. Qi, X. Y. Zhou et al., "Prenatal diagnosis of 17q12 microdeletion syndrome in fetal renal abnormalities," Zhonghua Fu Chan Ke Za Zhi, vol. 52, no. 10, pp. 662–668, 2017.

[18] X. Y. Jing, L. Y. Huang, L. Zhen, J. Han, and D. Z. Li, "Prenatal diagnosis of 17q12 deletion syndrome: a retrospective case series," Journal of Obstetrics & Gynecology, vol. 39, no. 3, pp. 323–327, 2019.