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BRIEF COMMUNICATION

Antenatal Diagnosis of Prune Belly Syndrome

Ashutosh Gupta[1] · Renu Raina Sehgal[2] · Nandini Vasdev[3] · Sanjay Mehta[4] · Pankaj Saini[4]

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Abstract Prune belly syndrome (PBS) is a rare congenital abnormality characterized by classical triad of urinary tract abnormalities, deficient abdominal musculature, and bilateral cryptorchidism. We present a prenatally diagnosed case of PBS identified at 12 weeks. Antenatal ultrasound study showed fetal bladder and abdomen to be enormously enlarged filling up whole of fetal abdomen with bilateral clubfeet. Gross examination showed very thin parchment-like defective anterior abdominal wall with protrusion of the abdominal contents. Microscopic examination showed hypoplasia of the abdominal muscle with overlying thin layer of epidermis. The histopathology examination of the abdominal wall muscles demonstrates a pattern of developmental arrest rather than one of atrophy consequent to early and severe obstruction. There is also absence of aponeurotic layer. Antenatal suspicion of PBS was corroborated on postnatal gross examination of the fetus and further confirmed on histopathological examination of the fetus.

Keywords Urinary tract abnormalities · Deficient abdominal musculature · Cryptorchidism

✉ Ashutosh Gupta
dr_ashutosh75@rediffmail.com

[1] Fetal Medicine and Clinical Genetics, Max Super Speciality Hospital, West Block, 1 Press Enclave Road, Saket, New Delhi 110017, India

[2] Department of Obstetrics and Gynecology, Artemis Hospitals, Gurgaon, Haryana, India

[3] Department of Pathology, Artemis Hospitals, Gurgaon, Haryana, India

[4] Department of Radiology, Artemis Hospitals, Gurgaon, Haryana, India

Introduction

Prune belly syndrome (PBS), also known as Eagle–Barrett syndrome, is a rare congenital abnormality with incidence of 1:30,000 [1]. It affects males in about 96 % of cases. It is characterized by the classical triad of urinary tract abnormalities, deficient abdominal musculature, and bilateral cryptorchidism. We present the diagnosis of this disorder at 12 weeks of gestation.

Report of Case

A primigravida with spontaneous planned conception presented at the department of Foetal Medicine, Artemis hospital for nuchal translucency scan at 12 weeks. There was no significant medical or surgical history. Transvaginal ultrasound examination showed fetal bladder and abdomen to be enormously enlarged, with trabeculations within the urinary bladder filling up whole of fetal abdomen. Both kidneys were normal in anatomical location but slightly increased in size with back pressure changes, dilated pelvicalyceal system, and hyperechogenic renal parenchyma. Visibility of the fetus was also sub-optimal due to co-existing oligohydramnios; fetus had bilateral clubfoot. Lungs and heart were grossly normal. Both nasal bones were seen to be hypoplastic measuring 2.2 mm with increased nuchal translucency measuring 3.5 mm. There was no obvious major cardiac abnormality. Figure 1 shows the abnormalities observed on ultrasonography. The consultand was counseled regarding the high likelihood of PBS. After further discussions and deliberations the couple decided to terminate the pregnancy. During the process of delivering the fetus, the parchment-like membrane replacing the anterior abdominal wall gave way.

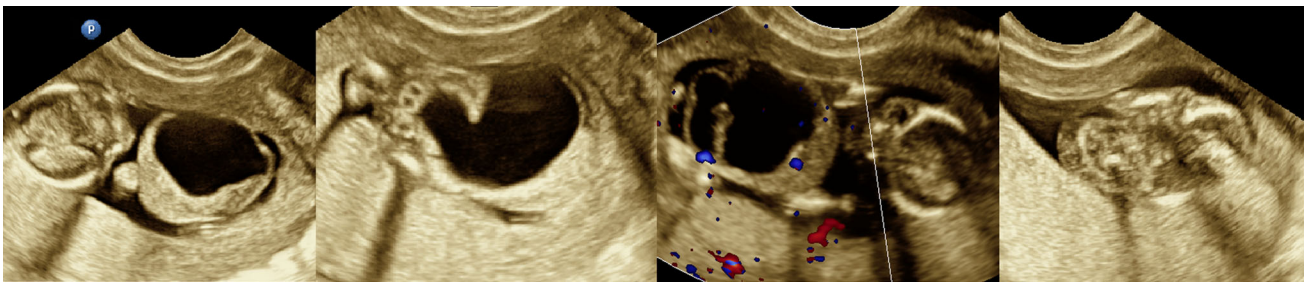

Fig. 1 Ultrasound findings—enormously enlarged fetal bladder and abdomen with trabeculations, dilated renal pelvic system with hyperechogenic parenchyma, and increased nuchal translucency

Gross Examination of the Fetus

There was a very thin parchment-like defective anterior abdominal wall with protrusion of the abdominal contents. Thoracic cavity appeared intact, but the anterior neck muscles were hyoplastic. Urinary bladder was not clearly identified; however, liver, kidneys, adrenals, and intestines appeared normal on gross evaluation. The lower limbs were curved backwards with bilateral clubfeet. Figure 2 depicts gross appearance of the fetus.

Microscopic Examination

Sections of the anterior abdominal wall showed normal skin with absence of skeletal muscle. Both kidneys were dysplastic with primitive tubules, fibrous tissue, and cortical cysts. On low power hematoxylin and eosin stain (H&E stain), the section showed hypoplasia of the abdominal muscle with overlying thin layer of epidermis (Fig. 3). High power microscopic view confirmed the hypoplastic muscles. The histopathology examination of the abdominal wall muscles demonstrated a pattern of developmental arrest rather than one of atrophy consequent to early and severe obstruction. There was also absence of aponeurotic layer. Thus, the antenatal suspicion of PBS was corroborated on postnatal gross and histopathological examination of the fetus.

Discussion

Prenatal diagnosis of the PBS is difficult and uncommonly reported at an early gestational age. We confidently identified the large bladder and PBS at 12 weeks of gestation [2].

Definitive timing and mode of treatment of PBS has not been established. PBS can present with a spectrum of abnormalities ranging from severe urogenital and pulmonary problems resulting in stillbirth, to mild urological abnormalities that require no treatment other than orchidopexy to correct the undescended testes. Poor abdominal muscle tone leads to a poor cough mechanism leading to increased pulmonary infections to constipation due to inability to perform the Valsalva maneuver, which helps push the stool out of the rectum during defecation. The mortality rate associated with PBS is 20 %. Osmolality and sodium content of fetal urine has a bearing on the underlying renal functions. Hypotonic urine and urine sodium

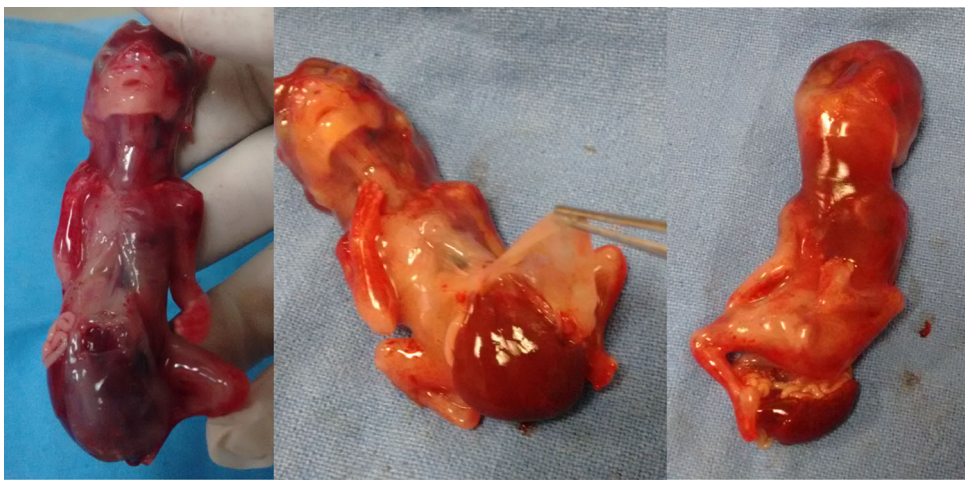

Fig. 2 Gross examination of the fetus with very thin parchment-like defective anterior abdominal wall with protrusion of the abdominal contents, and anterior abdominal muscles replaced by parchment membrane with bent right leg and bilateral clubfeet

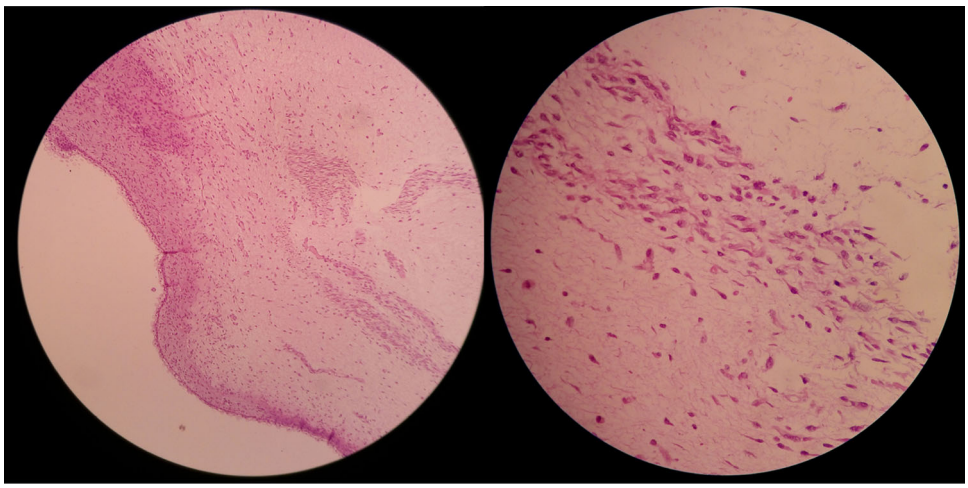

Fig. 3 Microscopic examination—low power H&E stain showing hypoplasia of the abdominal muscle with overlying thin layer of epidermis and high power showing hypoplastic muscle

below 50 mmol/L has a better prognosis. Some authors have advocated vesicocentesis as a modality of treatment for the same [3]. There are reports that affected people have survived to adulthood after undergoing abdominal reconstruction and urinary tract diversion [4].

Associated Anomalies

PBS has been found to be associated with broad spectrum defects involving musculoskeletal, cardiovascular, pulmonary, and genital malformations [5]. The incidence of cardiovascular malformations is about 10 %, especially tetralogy of Fallot and ventriculoseptal defects [5, 6].

PBS is divided into three categories: Category I patients are characterized by pulmonary hypoplasia, pneumothorax, oligohydramnios, renal dysplasia, urethral obstruction, patent urachus, and clubfeet. This category has the worst prognosis [7, 8] and the patients usually do not survive. Category II encompasses a moderately severe condition with severe renal impairment, while pulmonary functions are normal. These patients are prone to eventual renal failure overtime. Category III is the mildest of the lot and both the pulmonary and renal functions are not critically affected.

A prune belly-like variant is a close differential to the classical PBS. This is characterized by abdominal wall defect without urologic abnormalities. This entity involves the abdominal wall muscles; internal and external oblique and transverse abdominis muscle but the rectus muscles are spared which is classically involved in PBS.

Etiology

It is varied, multifactorial, and not fully understood. Three theories have been advanced to explain the pathogenesis.

1. *Mesodermal defect theory* proposes that the defect lies in the underlying mesoderm of the anterior abdominal wall and urinary tract resulting in patchy muscular hypoplasia or deficiency in the anterior abdominal wall and urinary bladder [9]. This theory is supported by the histologic findings in the abdominal wall in the present case, a pattern suggestive of developmental arrest with absence of aponeurotic layer, which is formed by joining of both rectus muscles. The abundance of fibrous tissue, collagen, and connective tissue with sparsely placed smooth muscle is suggestive more of a mesodermal differentiation abnormality rather than one of bladder outflow obstruction. Absence of the aponeurotic tissue also differentiates it from prune belly variant.
2. *Urethral obstructive malformation sequence /High pressure voiding and reflux theory* proposes that severe and early urethral obstruction leads to massive distension of the bladder and ureters, which explain the upper tract deformities. The huge distension of the urinary bladder interferes and hampers the descent of the testes and explains bilateral cryptorchidism as a component of the triad [6]. The complex morphogenesis of the male urethra with possible obstructive anomalies at several levels explains higher incidence of PBS in males.
3. *Yolk sac theory* is based on the overdevelopment of the allantoic diverticulum which grows out from the yolk sac but is contiguous with the body stalk. It becomes enlarged and is incorporated into the urinary tract as a redundant and enlarged urachus, bladder, and prostatic urethra.

Genetic Defect

PBS has been described in association with chromosomal defects such as trisomy 13, 18, and 45, XO [10–12]. Haeri et al. identified an underlying micro-deletion of 1.3

megabase at 17q12, disrupting the hepatocyte nuclear factor-1-beta gene. Halpoinsufficiency of this factor led to prostatic and ureteral hypoplasia resulting in severe obstructive uropathy with urinary and abdominal distension, leading to PBS [13]. Weber et al. [14, 15] described a consanguineous Turkish family in which five brothers had posterior urethral valve/PBS and identified a 35-cM region of homozygosity on chromosome 1q41–q44. Whole exome sequencing identified a homozygous frame-shift mutation in CHRM3 gene on chromosome 1q43, that segregated with the disease and was not found in 374 Turkish control chromosomes. The gene codes for muscarinic G protein-linked 7-transmembrane receptors, which are present throughout the body in smooth muscles, cardiac muscles, exocrine glands, and neurons of the central and peripheral nervous systems [16].

Risk of Recurrence

The risk of recurrence of this condition is unknown; multifactorial or polygenic inheritance has also been proposed. Parents should be counseled regarding the possibility of familial recurrence, as both X-linked [17], as well as autosomal recessive inheritance have been described [18]. An association between PBS and twinning has also been documented like the incidence of twinning in the general population is 1:80, and in PBS, it is 1:23 [19].

Compliance with Ethical Standards

Conflict of interest None.

Informed consent Informed consent was obtained from all individual participants included in the study.

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