Case Report

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Anatomy Section

External Genital Aplasia with Prune-Belly Syndrome in a Female Foetus - A Rare Case Report

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ABSTRACT

The Prune-Belly Syndrome (PBS) is a rare congenital anomaly with unknown etiology that is characterised by the triad of absent or a deficient development of the abdominal muscles, bilateral cryptorchidism and an anomalous urinary tract. This condition occurs only in males in its full form. However, a similar condition occurs in females in the absence of cryptorchidism and presence of triad showing abdominal musculature deficiency, anomalies of urinary and genital system. A 22-week-old dead foetus after abortion had foetal abnormalities like Potter's facies, distended abdomen, absent genitalia, absent urethral orifice, absent vaginal orifice, talipes equino varus and gross oligohydramnios was donated to Anatomy Department, for further evaluations. On autopsy, it was found to have grossly dilated urinary bladder filling entire abdominal cavity, female internal genital organs, urethral atresia, vaginal atresia, bilateral hydroureteronephrosis, two hemivaginae entering into the urinary bladder, uterus didelphys, bowel loops on right side below the liver and hypoplastic lungs. The histopathological examination of the uterus, both fallopian tubes and ovary was done. Only few cases of female counterpart of PBS have been discussed in literature so far.

Keywords: Abdominal wall deficiency, Skeletal abnormalities, Urogenital anomalies, Urinary bladder, Urethral artesia

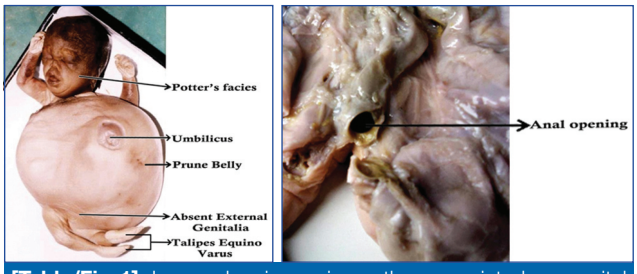
CASE REPORT

A 28-year-old female gravida II, para I, live I with six months of pregnancy came to OBG Department (not a booked case) with decreased foetal movements for two days. There was no relevant history regarding bleeding or draining per vagina or any other medical condition was reported by the patient. She had non eventful first pregnancy. Also, there was no history of consanguinity, no positive family history.

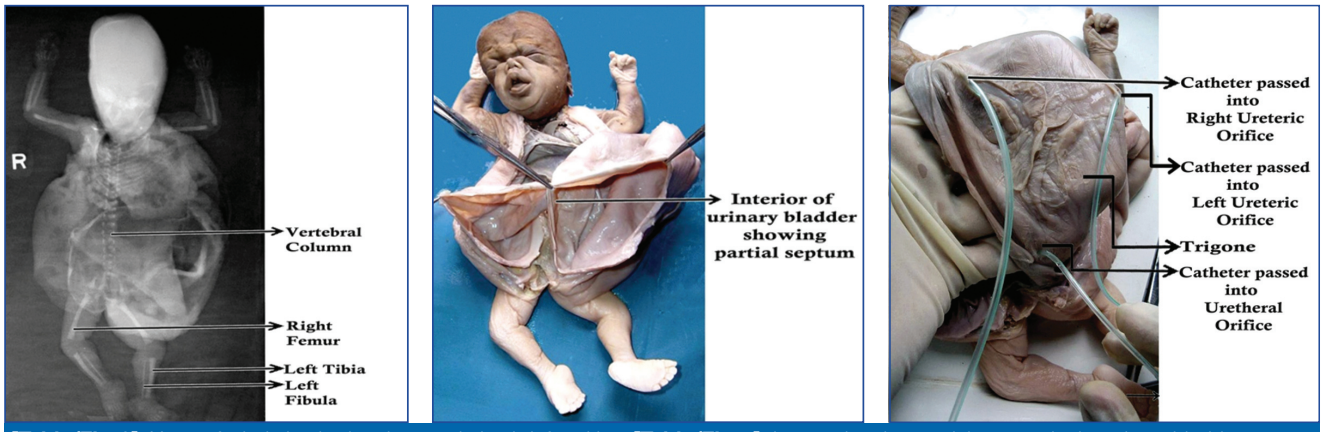
Per abdominal examination revealed 32 weeks of gestation. Foetal heart sounds were present. Ultrasonography, revealed a single viable foetus with vertex presentation of gestational age 22 weeks. Foetal head was deformed. There was a well circumscribed cystic mass in the foetal abdomen. Other investigations were within normal limits. Abortion was induced and a single dead foetus weighing 2.4 Kg was delivered. Placenta expelled out in toto. The dead foetus was sent to Anatomy Department, for further evaluations after obtaining patient consent.

Autopsy Findings

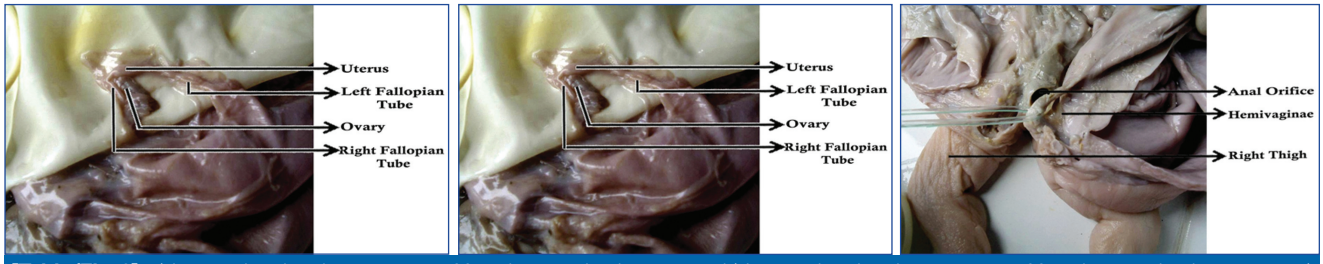
Gross examination: Foetus weighed 2.4 Kg. It had Potter's facies consisting of ocular hypertelorism, low set ears, receding chin and flattening of the nose. The abdomen was distended with deficient development of abdominal muscles. External genitalia, urethral and vaginal orifice were absent. The lower extremities showed talipes equinovarus [Table/Fig-1]. Anal orifice was present [Table/Fig-2]. On radiological examination, X-ray revealed no skeletal abnormalities [Table/Fig-3]. On opening the abdomen, urinary bladder was grossly enlarged occupying the entire abdominal cavity. On cut section, the bladder cavity was abnormally dilated. It had partial septum and filled with straw-colored fluid [Table/Fig-4]. Both inner and outer surfaces of the bladder wall were smooth. No tumour was identified. The urethral orifice in the bladder and both the ureteric orifices were patent [Table/Fig-5]. Adrenals were normal. Both kidneys were normal in anatomical location but slightly increased in size and both the ureters were dilated. Bilateral fallopian tubes and ovaries



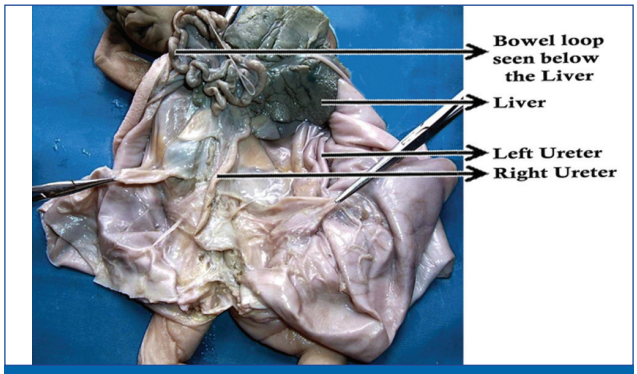
[Table/Fig-1]: Image showing various other associated congenital anomalies. **[Table/Fig-2]:** Image showing presence of anal opening.



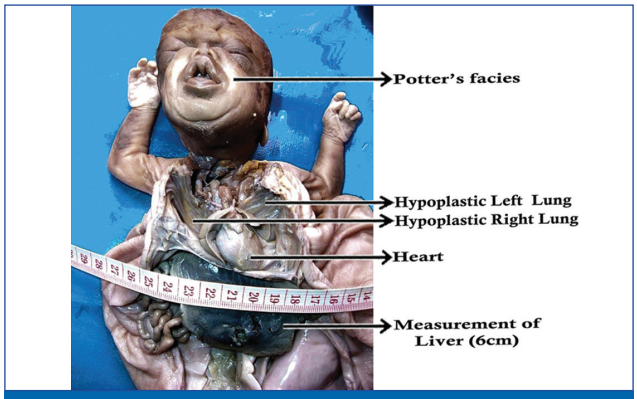
[Table/Fig-3]: X-ray of whole body showing no skeletal deformities. **[Table/Fig-4]:** Image showing partial septum in the urinary bladder. **[Table/Fig-5]:** Image showing the probed catheters into the ureteric orifice bilaterally and internal urethral orifice. (left to right)



[Table/Fig-6]: a) Image showing the presence of female reproductive organs; b) Image showing the presence of female reproductive organs; c) Image showing the presence of hemivaginae. (left to right)



[Table/Fig-7]: Image showing the presence of bowel loops beneath the liver on right side.



[Table/Fig-8]: Image showing the presence of hypoplastic lungs on both sides, heart and measurement of liver.

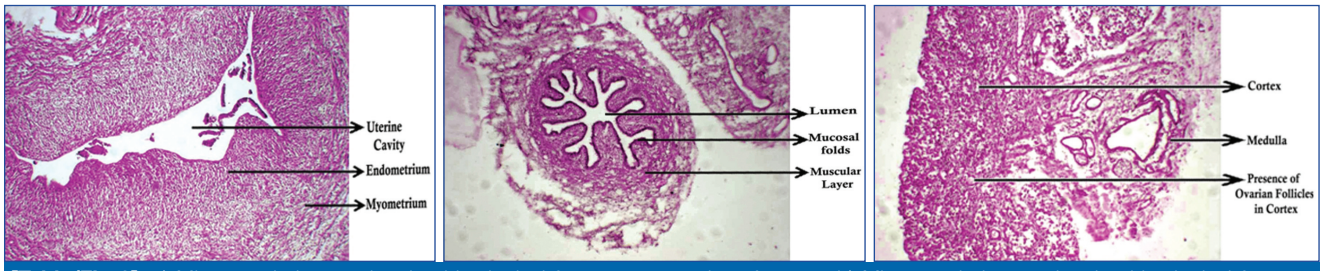
were seen. Uterus didelphys with two hemivaginae were identified entering into the urinary bladder in the posterior aspect [Table/Fig-6a-c]. Gut was malrotated and bowel loops were on right side below the liver [Table/Fig-7]. The lungs were hypoplastic. Heart was normal and no cardiac anomalies were found [Table/Fig-8].

Histopathological examination: Tissues from the suspected uterus, fallopian tubes and ovary on both the sides were subjected to histopathological examination. Histology confirmed the identity of the respective organs and its bilateral presence [Table/Fig-9a-c].

On the basis of gross examination, autopsy findings and histopathological examination the final diagnosis of foetus as Prune-Belly Syndrome (PBS) in a female foetus was made.

DISCUSSION

The PBS was first appreciated by Frohlich in 1839 and the name PBS was given by Osler in 1901 due to wrinkling skin of abdomen like a Prune associated with two other characteristic features like bilateral cryptorchidism and an anomalous urinary tract or the Eagle-Barrett syndrome, triad syndrome is a rare congenital anomaly of unknown etiology, with the incidence of 1 in 29,000 to 50000 births. By definition, the PBS can occur in its full form only in males. Rarely, in the absence of cryptorchidism the condition can be present in females also [1]. Such infants are either stillborn or die within the first few weeks



[Table/Fig-9]: a) Microscopic image showing histological features suggestive of uterus; b) Microscopic image showing histological features suggestive of fallopian tube; c) Microscopic image showing histological features suggestive of ovary. (left to right)

of life due to combination of associated anomalies [2]. This case is a female foetus with PBS and reported for its rarity.

The etiology of PBS is not known, however some of the studies reveal the possibility of genetic inheritance [3]. PBS has been reported to occur in association with trisomy 18, trisomy 21 (Down syndrome) and a mutation in the CHRM3 gene [4].

HNF1β is a transcription factor which is expressed in numerous tissues like kidney, prostate, mesonephric duct derivatives, pancreas, gut and liver that regulates for normal mesodermal and endodermal development. Current report indicates chromosome 17q12 microdeletions encompassing the *HNF1β* gene results in PBS [5,6]. Any alteration in *HNF1β* gene expression disturbs normal intermediate mesoderm differentiation, resulting in the urinary tract maldevelopment as reported in PBS [7,8].

In the literature the incidence of PBS associated clubfoot is 45%, pulmonary hypoplasia 27%, Potter facies 27%, imperforate anus 27%, and arthrogryposis (18%) [2]. There are associated malformations of the cardiopulmonary, gastrointestinal, and orthopaedic systems in about 75% of PBS [9].

Embryological Explanation

Three theories have been postulated to explain the anomalies that are associated with PBS. The three theories include (i) Early ureterourethral obstruction; (ii) Mesodermal arrest theory; (iii) Defect in the yolk sac [1].

The mesodermal arrest theory which depicts the lateral plate mesoderm defect results in the abnormal development of the derivatives of the first lumbar myotome leading to abdominal wall deficiency and urinary tract abnormalities around 6 to 10 weeks of gestation [10].

An alternate theory, the urethral obstruction malformation complex, leads to massive distension of the bladder and ureters which in turn results in pressure atrophy of the abdominal wall muscles. The basic defects that lead to duplication of the lower urinary tract are unknown [11]. Septations may be complete or incomplete. Incomplete septum leading to duplication of bladder which communicates anteriorly or distally, depending on the direction and depth the septum protrudes into the bladder. No overt clinical findings are observed in an incomplete septum of bladder [12].

Duplication of uterus results from lack of fusion of the paramesonephric ducts throughout their normal line of fusion. Its extreme form where uterus is entirely double is uterus didelphys. Around 5th month vaginal outgrowth is fully canalised. Failure of fusion of sinovaginal bulbs results in bilateral hemivaginae (double vagina). The lumen of vagina remains separated from urogenital sinus by a thin tissue plate called hymen. It usually develops a small opening during perinatal life.

During third week of development, mesenchymal cells originating in the region of primitive streak migrate around the cloacal membrane form cloacal folds. Cranially, these folds form genital tubercle that develops into clitoris. Caudally, these folds divide into urethral fold and anal fold and urethral folds are surrounded by genital swellings which later form the labia majora. Urethral folds develop into labia minora. Estrogens stimulate the development of external genitalia in female [13]. Failure of migration of mesenchymal cells in the primitive streak around cloacal membrane might have resulted in external genital aplasia.

There is no known prevention but the routine use of screening should be done for foetal anomalies. Intrauterine surgery can be performed to prevent the development of PBS if urinary obstruction is diagnosed antenatally [14]. Thus, with the current review it is most apparent that mutations in *HNF1β* gene resulted in mesodermal defect or uterourethral obstruction or spontaneous mesodermal defect may result in this peculiar condition called PBS.

CONCLUSION

Our findings brought us to a conclusion that the foetus was born as a female equivalent of the PBS, which was associated with external genital aplasia. The occurence of the PBS in females is rare. Only a few cases of PBS in female foetuses have been discussed in detail so far. In stillborn babies with obvious congenital anomalies autopsy evaluation should never be missed. This helps us to confirm and reveal other associated anomalies, as well as to understand the embryogenesis of their formation. This case has been reported to contribute some to the existing knowledge about PBS.

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