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Study of Genitourinary malformations in perinatal autopsies

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Abstract

Introduction: Congenital malformations remain a common cause of perinatal deaths and even though ultrasonography can give fairly accurate diagnosis, perinatal autopsy is essential to confirm the diagnosis and look for associated malformations.

Aim: To emphasize the importance of perinatal autopsy in diagnosing Genitourinary malformations.

Study Design: Retrospective analysis of cases with fetal genitourinary malformations was done. All fetuses were examined with external and internal examination and histopathological examination.

Materials and Material: Present study comprises of 200 cases of perinatal autopsies out of which 17cases of genitourinary malformations were studied.

Results: A total of 17 cases with Genitourinary malformations were studied. Most of them were renal malformations. Of all, 8 were cystic diseases of kidney, 3 cases of bilateral renal agenesis and 2 were unilateral, 1 case of urethral stenosis and 3 cases of extrophy of bladder were found. Among associated syndromes multicystic dysplasia found in Meckel gruber, Majawasky and Potters syndrome, whereas OEIS complex showed Extrophy of bladder. In Edward's syndrome bilateral polycystic kidneys were found.

Conclusion: Even though the prenatal ultrasonography reasonably predicts the malformations, fetal autopsy is essential to look for additional malformations.

Keywords: Congenital malformations, Perinatal, Autopsy, Genitourinary.

Introduction

Congenital malformations are the most common cause of perinatal deaths in developing countries like India accounting for 10-15%.(1) The recurrence risk of these disorders varies from negligibly low to 25 to 50% depending on the genetic component in the etiology of the disorder.(2) The renal anomalies can also be a part of congenital syndromes involving multiple organs, and identification of these abnormalities may significantly change the recurrence risk in future pregnancies.(2) The objective of the present study was to review our cases with fetal genitourinary malformations, to assess the importance of fetal autopsy and histopathology.

Materials and Method

This study includes, perinatal autopsies done in our institution from March 2014 to March 2016. All fetal autopsies were done by taking written consent from parents. Each fetus was examined according to predetermined protocol which included ultrasound diagnosis, external and internal examination. The autopsy protocol included the removal of thoracic, cervical, abdominal and pelvic organs en bloc and subsequently dissected into organ blocks.(3) The placenta, fetal membranes and umbilical cord were studied in all the cases. Histological sections were taken from lung, liver, genitourinary tract, thymus, brain, placenta and umbilical cord.

Results

A total of 200 autopsies performed from March 2014 to March 2016, out of which 17 cases of Genitourinary malformations were identified. Most of them were renal anomalies. Gestational age of fetuses ranged from 14 weeks to 37 weeks and birth weight ranged from 200 gm to 2,800 gm. Among the 17 cases, 8 were therapeutic terminations, 3 were still births, 4 cases of Intrauterine Deaths and 2 were live born. The most common timing of therapeutic termination encountered in this study was 20 – 24 weeks.

There were 7 associated syndromes found along with renal anomalies, 8 were cystic diseases of kidney, 3 cases of bilateral renal agenesis and 2 were unilateral along with agenesis of uterus, each case of urethral stenosis and exstrophy of bladder were found. Associated syndrome details are given in Table 1, Table 2 is showing Ultrasonography and autopsy findings of renal cystic diseases whereas rest of genitourinary malformations details are shown in Table 3.

Table 1: Showing details of renal malformation cases which are associated with syndromes (n=7)

Associated syndromes	USG findings	Autopsy Findings	
		Gross	Microscopy
Meckel Gruber syndrome	Microcephaly with meningomyelocele, severe oligohydramnios. Unable to visualize chambers of heart and abdomen	Encephalocele, polydactyly in all limbs, protuberant abdomen, B/L inverted foot, B/L wrist flexion. Both kidneys are multicystic	Multicystic dysplastic kidneys
Majewsky syndrome	B/L echogenic enlarged kidneys, B/L short limbs, sub cutaneous edema of scalp and anhydramnios	Hypertelorism, cleft palate, low set ears, polydactyly, syndactyly in all limbs, empty scrotal sac C/s of both kidneys show multiple cysts	Multicystic dysplasia of kidneys
Extra pulmonary sequestration with cystic renal dysplasia	B/L pleural effusion, hydrops fetalis, mass in the left thoracic cavity	Hypoplastic left lung, Hypoplastic left kidney with cystic kidneys	Multicystic dysplasia of kidneys and hypoplastic left lung
OEIS Complex	-	Omphalocele, Exstrophy of bladder, imperforate anus and CTEV	Right kidney-single cyst lined by flat cuboidal epithelium
OEIS complex with absent left kidney	Hydrocephalous with omphalocele	Hydrocephalous, omphalocele, absent lumbar vertebra, kyphoscoliosis, bladder exstrophy, imperforate anus and B/L club foot	Section from bladder shows fibromuscular wall.
Potters syndrome	B/L Multicystic dysplasia of kidneys with anhydramnios	Potters facies, B/L enlarged multicystic kidneys	Multicystic dysplasia
Edward syndrome	B/L polycystic kidney with severe oligohydramnios	Depressed nose, low set ears, macroglossia, teeth present, overriding of fingers, Protruded abdomen, polydactyly in all 4 limbs, Rocker bottom foot, meningoencephalocele, Multicystic kidneys	B/L polycystic kidneys

Table 2: Showing Renal cystic diseases (n=8)

Renal cystic diseases	No. of cases	USG findings	Autopsy findings	
			Gross	Microscopy
Polycystic kidney disease	3	Both the kidneys are enlarged and cystic	Bilateral enlarged cystic kidneys	Multiple cysts of variable sizes lined by cuboidal epithelium adjacent to primitive glomeruli and tubules.
Multicystic Dysplasia	4	Multiple cysts are noted in both the kidneys	Bilateral enlarged cystic kidneys	Cystic dilatation of tubules in cortex and medulla showing dysplastic changes
Hydronephrosis	1	Both the kidneys enlarged and showing dilated pelvic calyces	Distended bladder with bilateral enlarged kidneys	Large cysts compressing adjacent glomeruli and tubules,

Table 3: Showing other Genitourinary malformations (n=8)

USG findings	Autopsy findings		Final impression
	Gross	Microscopy	
B/L hypoplastic/agenesis of kidneys with severe oligohydramnios	Uterus, kidney and bladder not identified	Section from right and left pelvic mass shows normal histology of ovaries	Congenital agenesis of uterus, kidney and bladder
Intra Uterine Death	Left kidney and adrenal not identified	Single umbilical artery identified	Left kidney and adrenal agenesis with single umbilical artery
Not available	Cystic swelling present at the back of neck	Cystic hygroma, section from brain-areas of hemorrhage	Intra cerebral hemorrhage, cystic hygroma with urethral stenosis
Severe oligohydramnios	Low set ears, 3 digits in upper limb, short forearm and Left kidney not identified	Unremarkable	Left Kidney agenesis
Missed abortion with cystic Hygroma	Ascites, cystic swelling in nape of neck, Left kidney and spleen not identified	Cystic swelling shows features of Cystic hygroma	Hypoplastic heart, agenesis of left kidney and spleen, Hydrops fetalis and cystic hygroma
Intra Uterine Death	Both kidneys not identified	Both kidneys not identified	IUD with bilateral kidney agenesis
Bilateral Hydronephrosis with Distended bladder and Ascites(Urinoma)	Protuberant abdomen, wrinkled skin, both kidneys showing dilated calyces, tortuous ureters and distended bladder	Both kidneys showing multiple large cysts with dilated calyces	Bilateral hydronephrosis secondary to bladder outlet obstruction with ascites
Anterior abdominal wall cyst	Cyst present on anterior abdominal wall	Fibromuscular wall	Exstrophy of bladder

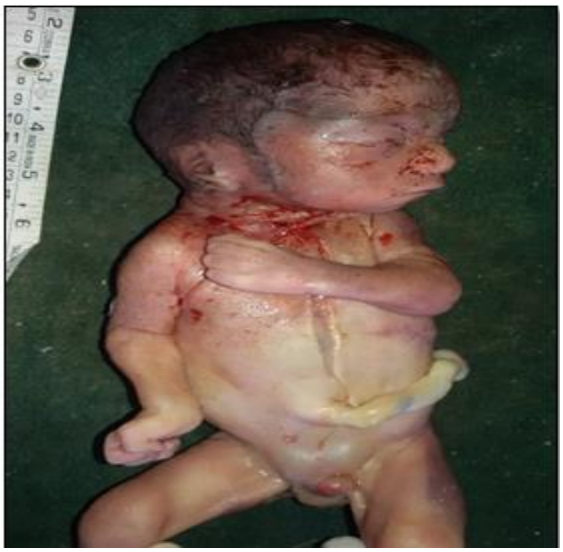

Fig. 1: A case of Potters syndrome showing potter's facies

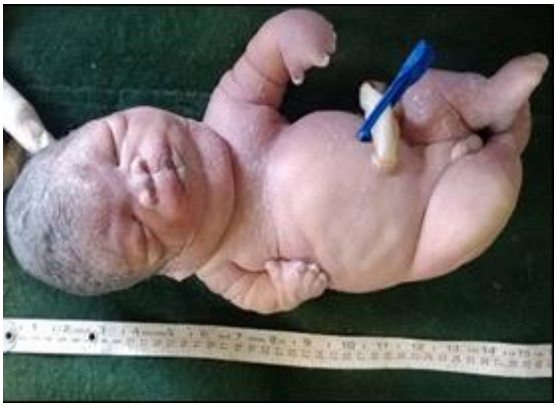

Fig. 2: A case of Majewasky syndrome

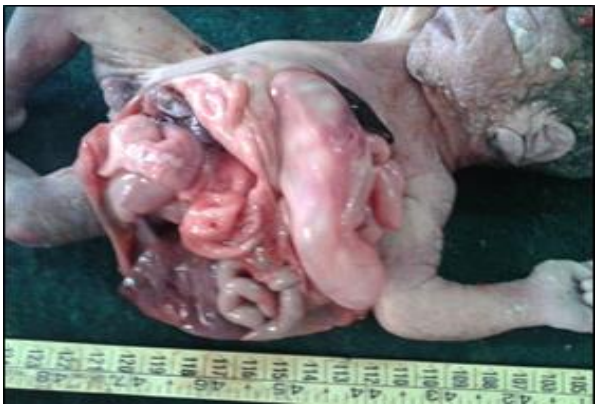

Fig. 3: A case of OEIS Complex

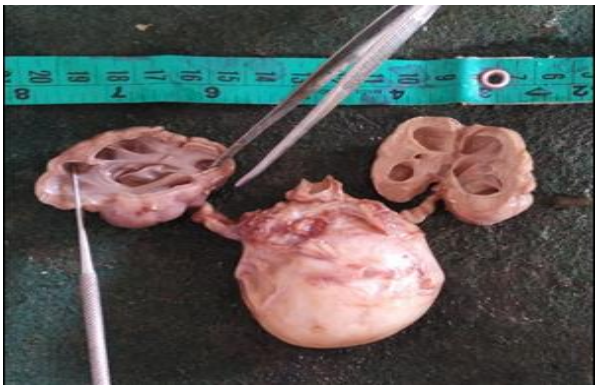

Fig. 4: Gross - showing distended bladder, tortuous ureters and bilateral hydronephrosis

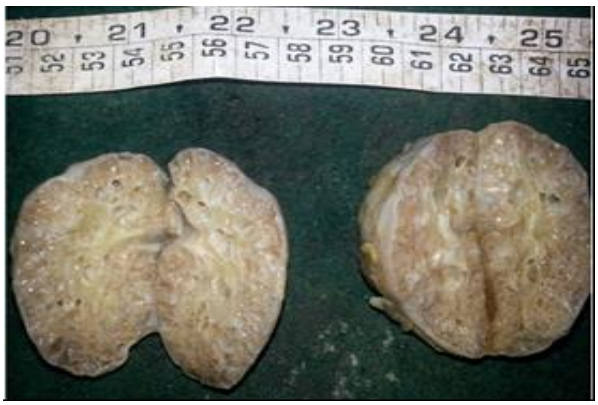

Fig. 5: Gross-Cut section of multicystic kidneys

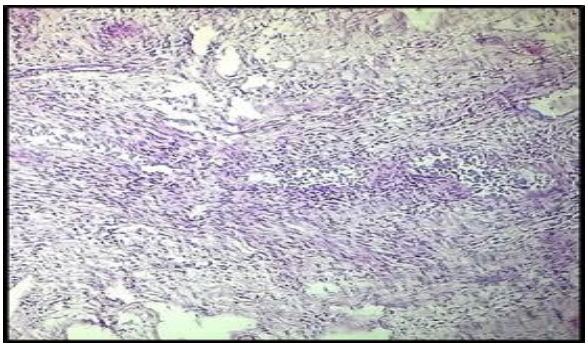

Fig. 6: Microscopy of multicystic dysplasia of kidneys(H & E40x)

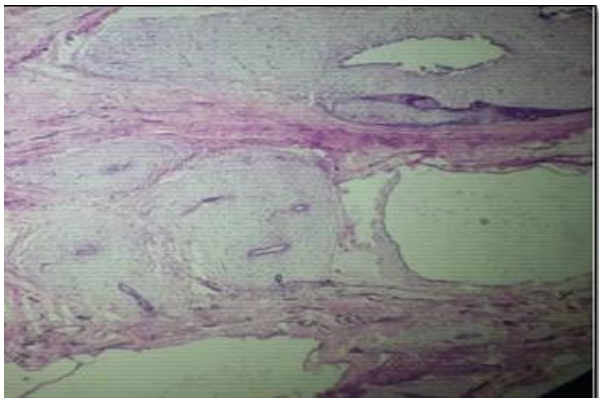

Fig. 7: Concenteric arrangement of mesenchymal tissue in Multicystic dysplastic kidneys (H & E40x)

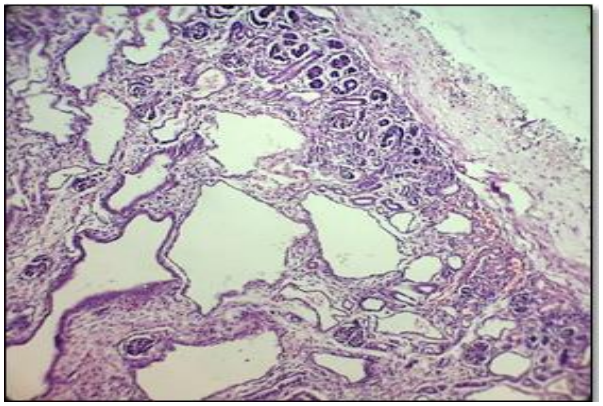

Fig.8: Polycystic kidney showing multiple cysts with normal glomerular structures in cyst wall (H & E 40x)

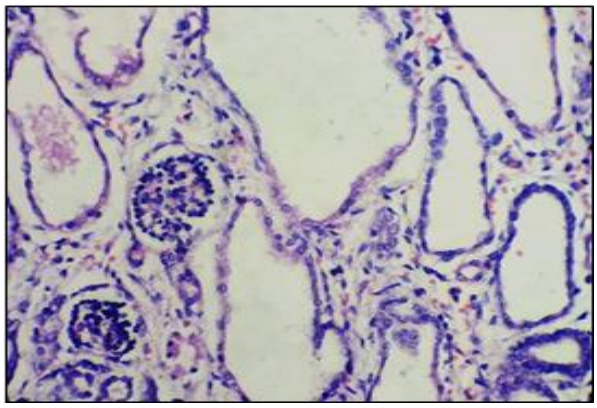

Fig. 9: Polycystic kidney disease showing multiple cysts lined by cuboidal epithelium. (H & E 100x)

Discussion

Fetal autopsy significantly contributes to the diagnosis of intrauterine fetal death and congenital anomalies are the major cause for perinatal death. Urinary tract abnormalities have a profound effect on pregnancy outcome, especially when associated with oligohydramnios.[2] In present study out of 200 cases we found 17 cases of urinary system malformations. The most common mode of death was therapeutic

termination of pregnancy. Most common urinary tract malformation encountered is renal cystic diseases. 4 cases were multicystic dysplastic kidneys, 3 cases of polycystic kidneys and 1 case of hydronephrosis was found. In N Kumari et al study they found 16 cases of cystic diseases out of 21 cases of renal malformations.

Cystic renal dysplasia with obstruction is another form of renal dysplasia. The kidney initially develops normally but later subjected to increased back pressure due to severe urinary tract obstruction in early pregnancy. Most often this process is bilateral and should be suspected by a distended hypertrophied bladder in antenatal ultrasound.[5,6] Detection of dysplastic kidney should warrant a detailed examination of the fetus for other structural anomalies including heart, spine, extremities, face and umbilical cord, because up to 35% of cases may have extra renal anomalies especially with bilateral dysplastic kidney.[8]

Meckel Gruber syndrome, a lethal rare autosomal recessive disorder, characterized by an occipital encephalocele, cystic dysplastic kidneys and polydactyly (constituting classical triad). Associated features that can be present are ductal plate malformation of liver, ambiguous genitalia and hypoplastic lungs. Most of the features were seen in our case. Over 200 cases has been reported so far.[9,10]

OEIS complex, involving omphalocele, exstrophy of the bladder, imperforate anus, and spinal abnormalities/ myelomeningocele, is a rare association with incidence of 1 in 200 000 to 1 in 250 000 births.[11]

In present study two cases of Potters syndrome showed bilateral dysplastic kidneys along with typical potters facies. Potter's syndrome is a rare fatal disorder that occurs in sporadic and autosomal recessive forms with an incidence of 1 in 4000 births.[12] Other characteristic features include premature birth, breech presentation, atypical facial appearance, and limb malformations. Severe respiratory insufficiency leads to a fatal outcome in most infants.

There were 5 cases of renal agenesis out of 17 cases. Renal agenesis seems to result from a failure of the mesonephric duct to give rise to the ureteric bud, with subsequent failure to induce metanephric differentiation. Congenital anomalies of the gastrointestinal (esophageal atresia and tracheoesophageal fistula), cardiovascular (atrial and ventricular septal defects), and central nervous systems (neural tube defects) commonly accompany both unilateral and bilateral renal agenesis. These associations suggest injury occurring between the third and sixth weeks of gestation when separation of the respiratory and enteric components of the foregut, cardiac septation, and neural tube closure are in progress.[13-15]

We found one case of congenital bilateral hydronephrosis, where there was presence of distended bladder and tortuous ureters. Congenital obstruction at the pelviureteral junction is usually due to an intrinsic abnormality of a short segment of the ureteral smooth muscle. The normally spirally arranged muscle bundles are replaced by longitudinal fibers, and fibrous connective tissue is increased to produce an aperistaltic segment.[16]

Table 4: Comparison of Genitourinary malformations with various other authors

Authors	Total no. of autopsies	Total no. of anomalies	With genitourinary malformations
Andola et al[5] (2012)	100	46	9(20.45%)
Potekar et al[17] (2014)	54	35	7(20%)
Naik et al[18] (2015)	46	08	1(25%)
Present study (2016)	200	54	17(31.48%)

In a study of 100 perinatal autopsies done by Andola et al[5] showed 9 cases of renal anomalies constituting 20.45% of total anomalies. Among them majority were polycystic kidney disease followed by renal agenesis cases. This finding is also supported by study done by Potekar et al[17] in which genitourinary anomalies were encountered in 7(20%) out of 35 cases, majority being polycystic kidney diseases and renal agenesis.

As majority of genitourinary malformations are associated with syndromes due to genetic defects, parents of these fetuses need to be counseled regarding incidence of same in subsequent pregnancies. Studies have shown that when the final prenatal diagnosis was made by ultrasound scan, in 27% of cases the information from the autopsy examination led to a refinement of the risk of recurrence, and in 8% this was increased to a one in four risk.[2]

Conclusion

Even though the prenatal ultrasonogram reasonably predicts the malformations, fetal autopsy is essential to look for additional malformations. In our study majority were renal anomalies and among them renal cystic diseases were common which were associated with various syndromes. Thus fetal autopsy helps in identifying cause of fetal loss which will help in genetic counseling of the couple for future pregnancies.

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