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Pathology of renal cystic diseases in children - An autopsy study of 5 cases.

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Abstract

Background: Paediatric renal cystic diseases include variety of hereditary and nonhereditary conditions. Some diseases are part of the group of ciliopathies that include ADPKD, ARPKD, nephronophthisis and glomerular cystic kidney diseases. The present report is based on autopsy findings of infants admitted to our hospital with a clinical diagnosis of cystic kidney disease in order to define the underlying disease.

Material and methods: This observational, retrospective study was conducted on a series of total 5 Paediatric deaths of suspected renal cystic disease. Study was done at our tertiary care centre from January 2015 to December 2020.

Results: In present study report, one case of ARPKD in a 8 months old child (without extrarenal cysts), 3 cases of bilateral cystic renal dysplasia and one case of hydronephrosis in a horseshoe kidney with focal renal dysplasia were found. All were neonates except one. Out of 5 cases, 4 were males and 1 was a case of ambiguous genitalia. All cases clinically presented with difficulty in breathing, requiring mechanical ventilatory support. 4 out of 5 mothers had severe oligohydramnios. Antenatal scan was done in 3 cases and detected bilateral renal cysts.

Conclusion: Bilateral cystic renal disease significantly results in morbidity and mortality. Association with maternal oligohydramnios is important.

Keywords: child, oligohydramnios, renal cystic disease.

Introduction

Renal cysts can be focal or diffuse and unilateral or bilateral. In childhood, most renal cysts are due to hereditary diseases rather than acquired cystic diseases as seen in adults. Inherited cystic diseases are usually

ciliopathies due to a primary ciliary defect (as in polycystic kidney diseases and nephronophthisis). Acquired causes include obstructive cystic dysplasia, dyselectrolytemia, and acquired cysts in renal replacement therapy.[1]

The final diagnosis requires a multispecialty approach, including radiology, pathology, and genetics. Cystic diseases known to affect children are ADPKD, ARPKD, multicystic dysplastic kidney disease, nephronophthisis etc.

It seems possible to differentiate most cases on the basis of history, histological findings in kidney and other organs[2,3] and radiological examination.[4] It is important to establish the exact diagnosis as this helps in genetic counselling. Review of the Indian literature shows only a few reports of this condition.[1,5,6] The present report is based on autopsy findings of infants admitted to our hospital with a clinical diagnosis of cystic kidney disease in order to define the underlying disease and associated anomalies.

Material and methods

This observational, retrospective study was conducted on a series of total 5 Paediatric deaths, at our tertiary care centre during the period from January 2015 to December 2020.

Inclusion criteria

Presence of renal cysts at autopsy, either grossly or microscopically.

Exclusion criteria

i. Those cases where morphological cysts, grossly or microscopically were not seen at autopsy.

ii. Autopsy conducted under Forensic department.

Data collection

In each case, the detailed clinical information such as age of the child, gender, clinical presentation, maternal history, gross and microscopic findings and cause of death were procured from the deceased's records. Consent from the first-degree relatives was taken at the time of autopsy.

Complete confidentiality of the case with respect to identity was maintained at all times. The autopsy protocol followed was that for routine clinicopathological autopsies.

Procedure

In each case, external as well as in-situ examination with dissection and preservation of the visceral organs was done in 10% neutral buffered formalin. A detailed gross examination of all the organs and histopathology was studied and recorded. Paraffin sections then stained with routine Haematoxylin and Eosin.

The autopsy findings were correlated with detailed clinical information and investigation in each case to establish the accurate cause of death. No statistical tests were applied as the study includes a small series Paediatric death.

Results

Out of 5 cases, 4 were males and 1 was a case of ambiguous genitalia. All were neonates except one. All cases clinically presented with difficulty in breathing, requiring mechanical ventilatory support. 4 out of 5 mothers had severe oligohydramnios.

Antenatal scan was done in 3 cases and detected bilateral renal cysts. We found one case of ARPKD in a 6 months old child (without extrarenal cysts), 3 cases of bilateral cystic renal dysplasia and one case of hydronephrosis in a horseshoe kidney with focal renal dysplasia. (Table 1).

Gross images of cases

Figure 1Al Bilateral kidney shows tiny cysts radiating from cortex to medulla.

Figure 1B: Presence of probe shows patency of ductus arteriosus.

Figure C

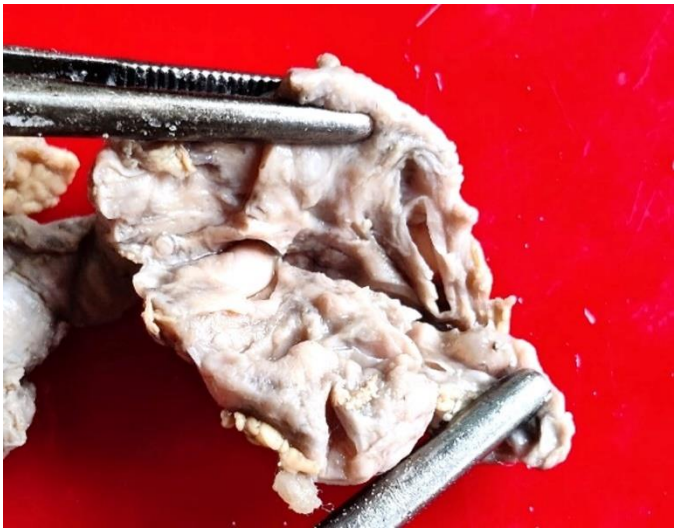

Figure C & D: Bilateral renal dysplasia with hydroureter, thinned off renal parenchyma with variable sized non connecting cysts.

Case 1 summary

A male infant with gestational age of 40 weeks was born to a second gravida mother with one living child, was presented with difficulty in breathing. The infant was born by normal vaginal delivery which was uneventful. Due to respiratory failure, infant was intubated and shifted to NICU immediately after birth. Even after all resuscitative measures infant went into cardiorespiratory arrest and died 3.5 hours after the birth. Severe oligohydramnios and multiple fetal malformations were seen on recent ANC scan. A complete autopsy was performed after an informed consent. Autopsy findings suggestive of bilateral hypoplastic kidney along with hypoplastic lungs. Massive cerebral edema was present with tonsillar herniation and hypoplastic cerebellum. On histopathology, dysplastic tubules surrounded by immature mesenchyme was seen in small focal area in kidney parenchyma, suggestive of renal dysplasia. (Figure 2 and 3).

Case 2 summary

A 4 hours old preterm infant weighing 1.709 kg born to third gravida with two living children, presented with

difficulty in breathing. Infant was born by breech delivery with meconium-stained liquor. Infant had distended abdomen, no anal orifice, no urethral opening and ambiguous genitalia. Infant was intubated with endotracheal tube and meconium suction was done after birth. Bag and mask ventilation was given. Baby went into sudden cardiac arrest and died after 4 hours of birth in spite of optimal resuscitative measures. Recent antenatal scan was suggestive of multicystic dysplastic kidney with severe oligohydramnios. On autopsy, both kidneys were seen attached at lower pole suggestive of horseshoe shaped kidney. Histopathology showed thinned glomerular cortex with occasional dysplastic tubules surrounded by immature mesenchyme. (Figure 2 and 3).

Case 3 summary

A male infant was born to primigravida mother at 35 weeks of gestation. Infant was intubated in view of birth asphyxia and shifted to NICU. In spite of resuscitative efforts, infant died 5 hours after birth. Antenatal scan was suggestive of bilateral enlarged fetal kidneys with multiple cystic lesions with severe maternal oligohydramnios. Autopsy findings were suggestive of bilateral lung hypoplasia with bilateral multicystic renal dysplasia. Histopathology of kidney showed cysts of varying sizes lined by cortical cells, dysplastic tubules surrounded by immature mesenchyme suggestive of renal dysplasia with additional finding of hypoplasia of both lungs. (Figure 5).

Case 4 summary

8 months old male infant presented with increased respiratory activity, strenuous breathing, altered consciousness and 1 episode of vomiting. Infant was apparently alright half an hour before development of above symptoms when food got stuck in the throat. Infant was a known case of patent ductus arteriosus with medical renal disease diagnosed at birth. All the necessary measures were taken to revive the infant from cardiorespiratory arrest but the patient died 2 days after the admission in the hospital. Autopsy findings were suggestive of massive pulmonary edema with broncho pneumonia with congestive heart failure and cystic renal disease in known case of patent ductus arteriosus. Histopathology of kidney was suggestive of autosomal recessive polycystic kidney disease (ARPKD) with multiple funnel shaped cysts from cortex to medulla. (Figure 4).

Case 5 summary

A male infant of 38 weeks of gestational age was born to second gravida mother by normal vaginal delivery. Antenatal scan was suggestive of bladder outlet obstruction with hydroureter and hydronephrosis with bilateral multiple renal cysts and severe oligohydramnios. Infant was immediately intubated after birth and put on mechanical ventilation due to birth asphyxia. In spite of all resuscitative efforts infant was died 3 hrs after the birth. On autopsy, bilateral lung hypoplasia with bilateral renal dysplasia was seen.

External features of Potter's syndrome seen - widely separated eyes, broad nasal bridge, low set ears. Histopathology showed collapsed hypoplastic lung with intra alveolar and intra bronchial haemorrhage.

Kidney showed presence of dysplastic tubules surrounded by mesenchyme and hydronephrotic cyst, compressed renal parenchyma with renal dysplasia.

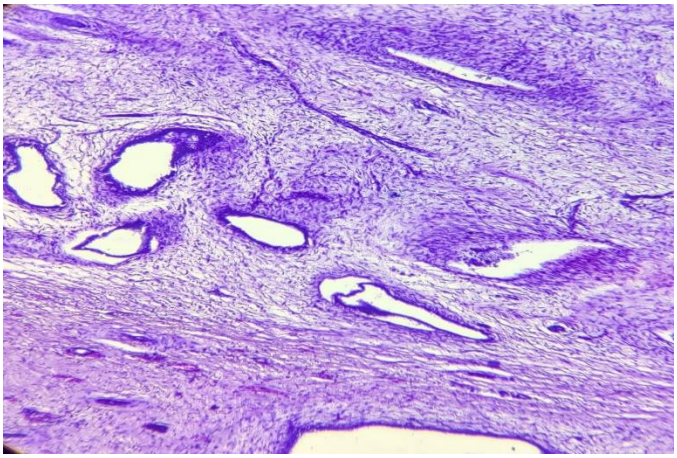

Figure 2: (100X) Shows collarettes of mesenchyme surrounding dysplastic tubules in renal dysplasia.

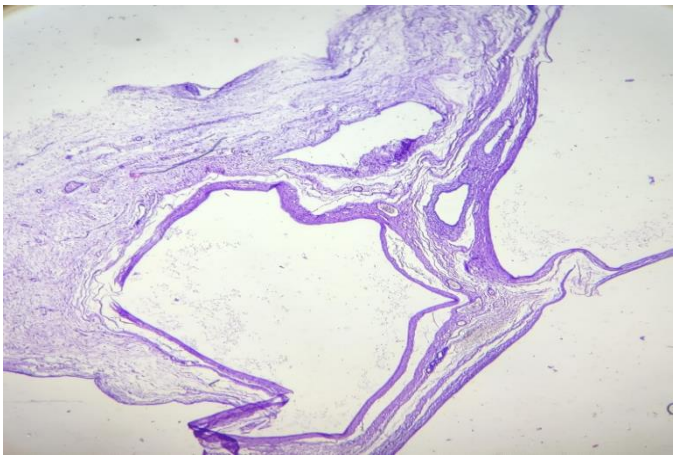

Figure 3: (400X) H&E – Cystically dilated tubule, no functional renal parenchyma.

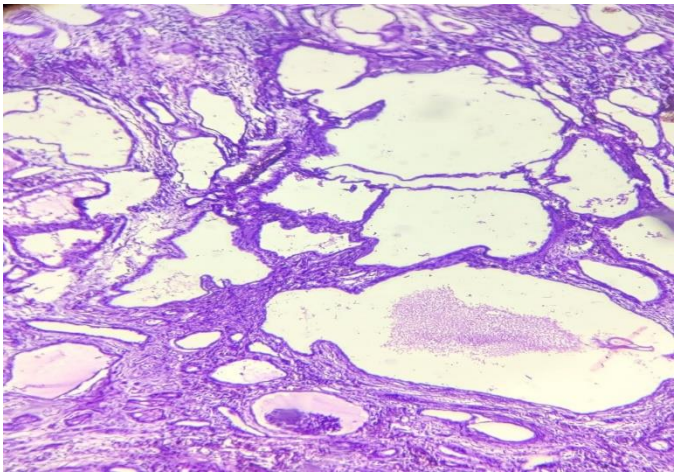

Figure 4: (100x) H&E - Shows dilated tubules at cortex, getting elongated, converging towards the medulla (ARPKD).

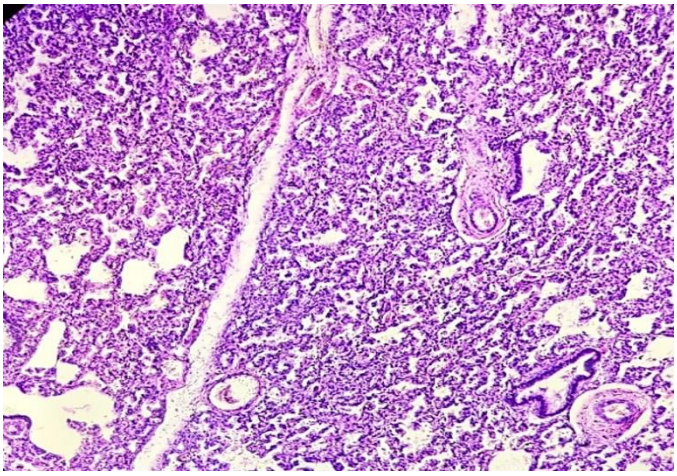

Figure 5: (100x) H&E - shows hypoplastic lung.

Discussion

Presence of bilateral renal enlargement increases the suspicion of polycystic kidney disease in neonates. This may be associated with hypertension during neonatal period.[3] In our study, four cases out of five cases turned out to be renal dysplasia and one was Autosomal recessive polycystic kidney disease (ARPKD).

Congenital hepatic fibrosis often seen with autosomal recessive polycystic kidney was not seen in our case.[2] All cystic diseases in children at autopsy were seen in males suggesting association of cystic renal disease more common in male infants.[7]

Abnormalities of metanephric development with altered structural organization and abnormal nephrotic and ductal differentiation, are known collectively as renal dysplasia[8,9] and are seen in about 2% of Paediatric autopsies.[8-10] The histological hallmarks of dysplasia include primitive tubules surrounded by dense collars of cellular mesenchyme, medullary lobar disorganization and the presence of metaplastic cartilage. (Figure 2 and 3) There is a high prevalence of associated urological abnormalities in patients with cystic renal dysplasia,[11,12] most of which have been reported to be obstructive in nature, emphasizing the role of obstruction in the

pathogenesis of the lesion.[11] There was bladder outlet obstruction in one case.

One patient had horse shoe kidney with renal dysplasia which is rare.[13] The risk of recurrence of renal dysplasia in subsequent pregnancies is greater in cases of renal dysplasia which comprises of unilateral dysplasia, unilateral agenesis and bilateral agenesis and is a part of heritable syndrome.[14] Renal dysplasia was seen in 4 cases in this study; however, no familial pattern was observed. The long-term survival of patients with renal dysplasia depends on the severity of renal affliction and also the presence of abnormalities affecting the contralateral kidney and other systems.[14] We did not come across a case of autosomal dominant polycystic kidney disease.

Autosomal recessive polycystic kidney disease can be diagnosed on the basis of exclusion as no genetic probes are available at the moment for this disease although it has been shown that the mutations leading to autosomal recessive polycystic kidney disease are not allelic with autosomal dominant polycystic kidney disease.[15] Antenatal screening should be made to identify autosomal dominant polycystic kidney disease in family members who may be unaware of their illness. Early identification of cases with autosomal dominant polycystic kidney disease may increase the life span of such individuals. This will help in genetic counselling to such parents. It is also important to differentiate polycystic kidney disease (both autosomal recessive and autosomal dominant) from cases of multicystic dysplasia as the later is a sporadic condition, chances of recurrence of which are minimal.

All the 5 infants in our study had severe renal diseases, incompatible with life, of which, 4 infants died within few hours after birth while 1 infant died at the age of 8 months. The causes of death were multifactorial including prematurity, and its related complications: hypoxia and shock in addition to the life-threatening anomalies.

4 out of 5 mothers had severe oligohydramnios suggesting clear association with oligohydramnios.[16] During lung development, the main physical force experienced by the lungs is stretching induced by breathing movements and lung fluid in the air spaces. Oligohydramnios reduces the intrathoracic cavity size thus disrupting fetal lung growth and leading to pulmonary hypoplasia which causes respiratory distress.

Conclusion

Bilateral cystic renal disease significantly results in morbidity and mortality. Association with maternal oligohydramnios is important and condition needs immediate attention. Detection of cystic disease at autopsy helps in counselling of parents in the present as well as for future pregnancy. Prognosis depends on severity of renal cystic disease and presence of other associated systemic congenital anomalies especially cardiac anomalies.

Table 1: Clinicopathological details of cases

Year	Age	Gender	Oligohydramnios	Type of cystic disease	Associated anomalies	Other pathology	Cause of death
2015	3.5 hours	Male	+	Renal dysplasia	-	-	Bilateral renal dysplasia incompatible with life
2015	4 hours 45 min	Ambiguous genitalia	+	Renal dysplasia	Bilateral hydronephrosis with horseshoe kidney	Perinatal pneumonia with intrapulmonary haemorrhage	Perinatal pneumonia
2016	5 hours	Male	+	Renal dysplasia	Hydroureter and hydronephrosis	Bilateral lung hypoplasia	Bilateral lung hypoplasia
2017	8 months	Male	Not known	ARPKD	Patent ductus arteriosus	CVC Lung, bronchopneumonia with hyaline membrane	Bronchopneumonia with congestive heart failure
2019	3 hrs 15 min	Male	+	Renal dysplasia	-	Bilateral lung hypoplasia	Bilateral lung hypoplasia

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Abbreviations

ADPKD: Autosomal dominant polycystic kidney disease.

ARPKD: Autosomal recessive polycystic kidney disease.