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Case Series

Congenital urogenital anomalies detected in foetal autopsies: a case series

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ABSTRACT

Foetal anomalies are congenital defects that can affect multiple organ systems, including the urogenital system. Congenital anomalies of the kidney and urinary tract (CAKUT) are a significant subset of these disorders, often leading to severe complications that impact foetal viability and affect postnatal outcomes. Early prenatal detection through imaging and genetic testing plays a crucial role in managing these conditions. Despite advances, foetal autopsy remains the gold standard for confirming diagnoses, identifying other associated anomalies, and understanding the embryological developmental basis of these defects. This autopsy series was conducted at the department of pathology, Sri Ramachandra institute of higher education and research, to analyse urogenital anomalies detected in foetal autopsies over a four-year period (January 2020-January 2024). Out of 352 foetal autopsies, 19 cases exhibited urogenital anomalies. We present a detailed analysis of five representative cases, which include unilateral renal agenesis associated with pentalogy of Cantrell, autosomal recessive polycystic kidney disease (ARPKD), Pearson syndrome with renal involvement, foetal megacystis, and bilateral renal agenesis with oligohydramnios (Potter syndrome). Each case highlights the complexity of urogenital malformations, their systemic implications, and the necessity for genetic counselling. These findings reinforce the importance of foetal autopsy in validating prenatal imaging and genetic results. Autopsy data provide valuable insights into the anatomical and pathological characteristics of these anomalies, aiding in the accurate classification of congenital disorders. Additionally, this series emphasises the role of genetic counselling in assisting parents with recurrence risk assessment and future planning. By integrating prenatal diagnostic techniques with post-mortem findings, this series emphasises the need for a multidisciplinary approach in managing congenital urogenital anomalies, thereby improving diagnostic accuracy, management, and family support strategies.

Keywords: Congenital anomalies of the kidney and urinary tract, Renal agenesis, Autosomal recessive polycystic kidney disease, Pearson syndrome, Genetic counselling, Fetal megacytis

INTRODUCTION

Foetal anomalies are defects in the normal development of a foetus, which could affect multiple organ systems such as the brain, heart, urogenital system and so on. At times, these anomalies may not be restricted to a single organ or organ system and could potentially affect multiple organs. If felt undetected, these anomalies may severely impair the quality of life of the foetus and could also result in life-limiting complications.

The ureteral bud (UB) and metanephric mesenchyme

(MM) are the embryogenic structures that are responsible for kidney formation. The MM gives rise to nephrons, whereas the UB gives rise to collecting ducts, ureters, and the bladder. Kidneys take their final shape due to mutual interplay of UD and MM. Kidneys ascend during their formation to occupy retroperitoneal lumbar region.[1,2]

CAKUT, including the kidney, ureters, bladder, and urethra are embryonic urinary system disorders that cause problems during development.[3] Based on hospital registries, the prevalence of CAKUT is estimated to be 4-60 per 10,000 births, with variations in diagnosis methods and ethnic and country variances between studies.[4,5]

Urogenital anomalies, though not life-threatening in most, could be life-threatening in a few. According to studies, 1% of all pregnancies have abnormalities, with 20-30% of those affecting the genitourinary system (GUS).[6] Prenatal testing can help pick up these anomalies in the early antenatal period, which will thereon influence the progression of pregnancy. The role of prenatal testing is important not only to identify the anomaly, to also counsel the parents and decide on the further progression of pregnancy.

With the advent of newer methods in prenatal diagnoses of anomalies, the requirement for reliance on foetal autopsies has come down. Despite this, foetal autopsies are still the gold standard method of confirming the diagnosis. The information obtained from the foetal autopsy can help identify the anatomical basis of the defect, associated conditions, and their causes including genetic and environmental triggers.

We present a series of congenital urogenital anomalies that were confirmed by foetal autopsies. These cases were examined in detail to highlight the role of post-mortem studies in improving antenatal diagnosis and future clinical management.

CASE SERIES

This study was carried out retrospectively with the department of pathology at Sri Ramachandra institute of higher education and research, to study the urogenital anomalies detected in foetal autopsies over the last 4 years (January 2020-January 24). Approval from the institutional ethics committee was obtained (IEC number-CSP-III/24/ APR/04/133). A total of 352 foetal autopsies were carried out over the 4 years period of which 19 presented with urogenital anomalies. In this paper, we aim to discuss 6 cases in detail.

Case 1

A 24-year-old female married non-consanguineously, with a live healthy baby boy came to the hospital for her second pregnancy complicated by the risk of Rh iso-immunization. At 17 weeks+6 days of gestation decision to terminate the pregnancy was taken following abnormal findings on prenatal imaging, raising concerns for major urogenital anomalies associated with multiple system abnormalities.

Following termination, a foetal autopsy was performed to confirm the diagnosis and give further insight into the observed abnormalities.

Autopsy findings

Gestational age was 17 weeks+6 days, sex-female, weight of the fetus was 116 gm.

Gross appearance

Urogenital system: The left renal fossa was noted to be empty, absent left kidney with the right kidney showing growth consistent with gestational age.

Cardiovascular system: IVC dilated in the left side of the diaphragm with the heart and aorta pushed to the right side of it.

Gastrointestinal: Stomach, intestines, liver and intestines pushed to the right side.

Central nervous system: Increased anterior to posterior head shape, with occipital enlargement and occipital omphalocoele.

Head: Increased extra caudal distance with broad nasal bridge, stubby nose, retrognathia noted.

Microscopy: Unremarkable microscopic findings

Diagnosis: The above-mentioned findings are consistent with the Pentalogy of Cantrell. This is characterized by cardiac anomalies, omphalocoele, sternal cleft (though not often), diaphragm defects and abdominal wall defects

Arhinia with renal agenesis: Empty renal fossa, dilated IVC and heart pushed to the opposite side, occipital defect, facial features- Meckel-Gruber syndrome.

Case 2

A 25-year-old female married non-consanguineously with one previous live birth and a first-trimester miscarriage before that. Her foetus was diagnosed to have bilateral polycystic kidneys on USG screening done at 20 weeks for screening of anomalies.

Despite counselling against foetal complications, she decided to continue her pregnancy. At 30 weeks of gestation, she presented to the hospital with labour pains. She delivered vaginally and child was non-responsive, despite resuscitation measures and was declared a stillbirth. The body of the foetus was sent for autopsy.

Autopsy findings

Gestational age was 29 weeks +4 days, sex-female and weight of the fetus was 1300 gm.

Gross appearance

Urogenital system: The right kidney weighs 36 grams and measures 7.2×6×1.5 cm and the left kidney weighs 34 grams and measures 6.5×4.5×1.5 cm with the external surface of both kidneys appearing bosselated, showing multiple cysts ranging from 0.3-0.5 cm. The cut section revealed multiple cystic spaces extensively replacing the renal parenchyma. Cystic spaces measure 0.5-0.6 cm.

All other systems appear normal

Microscopy: B/L kidneys show cystically dilated spaces lined with flattened cuboidal epithelium filled with eosinophilic acellular material

Diagnosis: The findings of the autopsy were consistent with polycystic kidney disease. Genetic testing done via amniocentesis revealed ARPKD. Correlating the two, the autopsy findings are consistent with genetic testing findings. The couple should be advised to undergo genetic counselling.

Case 3

A 30-year-old consanguineously married female, about 23 weeks pregnant with one live baby and two previous miscarriages, was advised for termination as her fetus was found to have CAML on genetic testing with the kidneys seen as echogenic masses on ultrasound.

The exome sequencing suggested the baby to have Pearson syndrome.

Autopsy findings

Gestational age was 23 weeks + 6 days, sex-male and weight of the foetus was 561 gm.

Gross appearance

Urogenital system: Both kidneys show dilated tubules with hyaline eosinophilic infiltrative material.

Other systems: Appear Normal, development corresponds to the gestational age.

Microscopy: B/L kidneys show dilated tubules with hyaline eosinophilic infiltrative material.

Diagnosis: The findings of this autopsy are consistent with Pearson syndrome, as suggested by the exome sequencing study.

Case 4

A female with a healthy live child, one previous abortion, pregnant at 13 weeks was advised to undergo abortion based on ultrasound findings of foetal megacystitis.

She was advised to undergo genetic testing to identify other genetic anomalies.

Autopsy findings

Gestational age was 13 weeks + 4 days, sex-male and weight of the foetus was 55 gm.

Gross appearance

Urogenital system: Both kidneys weigh 3 grams each, urethra, testes and external genitalia appear normal.

The bladder appears to be grossly distended measuring 1.8×1×1 cm.

Other systems: Appear normal.

Microscopic findings: Corresponds to normal development.

Diagnosis: Foetal megacystitis-gross distension of the bladder, occasionally corrects by the end of the second trimester most often does not.

Once born, the child is prone to recurrent infections of the renal system and longevity could become affected.

Megacystitis can also be associated with other syndromes. The couple should be advised to undergo genetic testing.

Case 5

A female aged about 24 years, primigravida at about 15 weeks of gestation was advised to undergo abortion as her foetus was identified to have agenesis of both the kidneys associated with oligohydramnios.

She underwent MTP following medical advice and was advised to undergo genetic testing to detect other abnormalities.

Autopsy findings

Gestational age was 15 weeks + 6 days, sex-unidentified and weight of the fetus was 54 gm.

Gross appearance

Urogenital system: Both kidneys cannot be visualized. The rest of the urogenital system and the external genitalia could not be identified.

Other systems: Appear normal.

Microscopic appearance: Unremarkable, findings consistent with gestational age.

Diagnosis: Bilateral renal agenesis with oligohydramnios, autopsy findings consistent with ultrasound. Advised to undergo genetic testing.

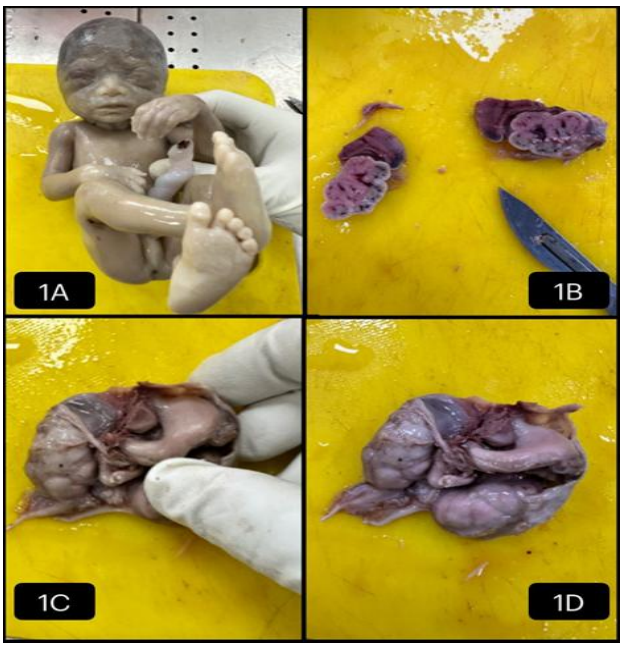

Figure 1 (A-D): A-Presents a male fetus with severed umbilical cord brought in for autopsy. B-Cut surface of kidney showing multiple dilated cystic spaces. C and D-external surface of kidney revealing malformations.

DISCUSSION

The following paragraph aims to highlight the distinct renal anomalies found in this series, the complexity of congenital urogenital anomalies and their often interconnected systemic and genetic conditions. Each case highlights the role of autopsy in corroborating prenatal findings, gathering further information, and emphasizing on the role of genetic counselling.

Case 1: Renal agenesis and pentalogy of Cantrell

In case 1, a diagnosis of unilateral renal agenesis was confirmed, an anomaly caused by the failure of ureteric bud induction and MM differentiation.[7,8] While unilateral renal agenesis might allow continuing life with a single functional kidney, the presence of systemic abnormalities in this case, specifically features associated with the pentalogy of Cantrell, suggests a complex multisystem developmental anomaly. Renal agenesis can occur with other congenital anomalies, often pointing to syndromic or genetic etiologies such as Meckel-Gruber syndrome, which involves renal and facial anomalies among other abnormalities.[9] The information from autopsy findings reinforces the role of renal agenesis as a marker for possible multisystem involvement, which can guide genetic testing and further evaluation in similar cases.

Case 2: ARPKD

Case 2 showcased bilateral polycystic kidneys, aligning with features of ARPKD confirmed by genetic testing. ARPKD is associated with cystic changes in the renal collecting ducts, leading to severe renal dysfunction and commonly to perinatal or neonatal mortality due to pulmonary hypoplasia resulting from oligohydramnios.[10] The extensive cystic involvement of the renal parenchyma observed in this case is characteristic of ARPKD and highlights the critical need for genetic counselling given its autosomal recessive inheritance pattern and a 25% recurrence risk in future pregnancies.[11]

Case 3: Pearson syndrome with renal anomalies

In case 3, Pearson syndrome, a mitochondrial disorder, was associated with renal anomalies characterized by dilated renal tubules containing eosinophilic material. Although Pearson syndrome primarily impacts haematological and pancreatic function, renal anomalies such as nephronophthisis can also be seen in mitochondrial disorders.[12] The autopsy findings in this case, along with genetic testing results, underscore the importance of considering systemic mitochondrial disorders when evaluating renal anomalies. Recognizing this connection allows for early parental counselling, as Pearson syndrome has a poor prognosis and genetic origins that could inform future family planning.

Case 4: Fetal megacystis

This case presented fetal megacystis, an anomaly characterized by a grossly distended bladder, often due to urethral obstruction or neuromuscular dysfunction of the bladder.[13] Although fetal megacystis may resolve spontaneously, persistent cases can lead to complications, including oligohydramnios and pulmonary hypoplasia. While other organs appeared normal in this case, megacystis can sometimes be associated with chromosomal or genetic anomalies, thus genetic testing was advised to evaluate potential syndromic links.[14] Fetal megacystis, identified early in pregnancy, necessitates monitoring for spontaneous resolution and further testing if abnormalities persist.

Case 5: Bilateral renal agenesis with oligohydramnios

In case 5, bilateral renal agenesis, or Potter syndrome, was diagnosed, as an anomaly that results in severe oligohydramnios and subsequent pulmonary hypoplasia, typically incompatible with life.[15] The absence of both kidneys reflects the failure of the ureteric buds to develop, halting nephrogenesis. While generally sporadic, familial cases have been noted, especially in populations with

higher rates of consanguinity, underscoring the importance of genetic counseling.[16] This case emphasises the need for prenatal detection and genetic evaluation, given the poor prognosis associated with bilateral renal agenesis.

CONCLUSION

The findings from these 5 cases showcase the range of congenital renal anomalies and their association with systemic abnormalities, underscoring the value of fetal autopsy in confirming diagnoses and revealing additional anatomical data. The diversity of anomalies encountered in this case series also emphasizes the need for comprehensive prenatal imaging, genetic testing, and family counselling to anticipate potential outcomes and recurrence risks. The data from fetal autopsies not only aid in providing closure for families but also contribute valuable information for advancing prenatal diagnostic approaches and understanding the developmental origins of congenital renal and systemic anomalies.

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