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Case Report

Autosomal recessive polycystic kidney disease (ARPKD) in fetus: Autopsy based approach

Lipika Behera[1], Shilpa Padhi[1], Swetambari Acharya[1], Shushruta Mohanty[1,*]

[1] *Dept. of Pathology, M.K.C.G Medical College, Berhampur, Odisha, India*

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ABSTRACT

Polycystic kidney disease is a rare developmental anomaly inherited as Autosomal dominant or recessive. Autosomal recessive polycystic kidney disease (ARPKD) is an intractable cystic renal disease that results in chronic renal failure. It has a profound effect on growing fetus and result in serious implications if pregnancy is continued in the long run after being detected on sonography. Although prenatal imaging studies and clinical findings are suggestive of ARPKD it can be accurately diagnosed by histopathology if an autopsy is performed in cases of infant death. In this article we here in present the features of ARPKD diagnosed antenatally by USG in a 22 yr female, and was confirmed further by fetal autopsy.

1. Introduction

Autosomal recessive PKD (ARPKD) is the most common heritable cystic renal disease, occurring in infancy that is characterised by accumulation of fluid filled cysts in the kidney along with developmental failure of biliary collection system that results in bile duct dysgenesis and periportal fibrosis. This entity is uncommon with incidence ranging from one in 6000 to 40,000 live births.[1,2] Death reported in these neonates is around 30% during or shortly after birth and is mostly due to respiratory insufficiency subsequent to oligohydramnios.[3] So correct and timely diagnosis of PKD is important so that proper counselling and appropriate management can be rendered both from obstetrics as well as from paediatric point of view.

2. Case Report

A 22-year female patient presented at 15 weeks for a routine antenatal check up. She was G4-P1-A2. Prior to current pregnancy she had two abortions due to some anomaly in fetus detected in sonography as informed by her, reports of which were not present. No further investigations were done to rule out the cause of previous abortions. Having a bad obstetric history in the past compelled her to seek medical attention in current pregnancy. USG revealed a single live fetus with longitudinal lie and cephalic presentation. FHR-153beats/min. Period of gestation estimated was 19wks 3 days. Liquor volume was grossly reduced with severe oligohydamnios. Placenta was anterior and not low lying. On Biophysical Profile fetal movements, tone and breathing were normal. Bilateral enlarged kidneys with increased echogenecity, multiple tiny cysts were noted in bilateral kidneys. No other congenital anomalies were noted and fetal liver was normal. Umblical cord showed presence of three vessels with blood flow being intact. On evaluation there was no history of consanguinity amongst parents nor there was any family history of any renal disease. After counselling the parents, about the outcome of this pregnancy, and taking their consent the pregnancy was terminated. A male fetus was delivered that was sent to our dept for hisopathological analysis. **Anthropometry**:

* *Corresponding author*.
E-mail address: sushruta.mohanty@gmail.com (S. Mohanty).

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Weight of the fetus was 400g.CRL-18 cms, CHL-33.5 cms, HC-16 cms, C-18 cm, foot length was 3 cms. **External examination**: Both upper and lower limbs were normal with no amniotic bands. Ear cartilage, hair and nails were well-developed. Fetus had no cranio facial anomalies. No signs of IUGR were seen. **Internal examination**: was done following virchows technique and by giving a modified Y shaped incision starting from below the ears to symphysis pubis encircling umbilicus to the left side. Both thorax and abdomen were opened. Grossly liver and intestines were normal in appearance. Kidneys b/l were enlarged, rt side measured 4x2x1 cm while left kidney measured 5x3x2 cms left sided kidney showed surface lobulations. Both the kidneys due to presence of cysts showed poor corticomedullary differentiation. Microscopically kidneys showed numerous cysts lined by a single layer of flattened to low cuboidal epithelial cells with thick peritubular mesenchyme. Glomeruli appeared normal. Liver showed normal histology. Gross and microscopy features were in favour of ARPKD. Other organs submitted for HP study appeared normal both grossly as well as microscopically.

Fig. 1: Gross of fetus showing intraabdominal enlarged polycstic kidneys

3. Discussion

ARPKD is the most common heritable cystic renal disease occurring in infancy, with mutations of a single localized gene in an area in Chromosome 6 (PHKD1).[2] PHKD1 gene is expressed at high levels in fetal and adult kidneys and at lower levels in the liver and this corresponds to the principal sites of the disease. The characteristic pathologic changes occur in the kidneys and the liver with a reciprocal relationship between the degree of renal and

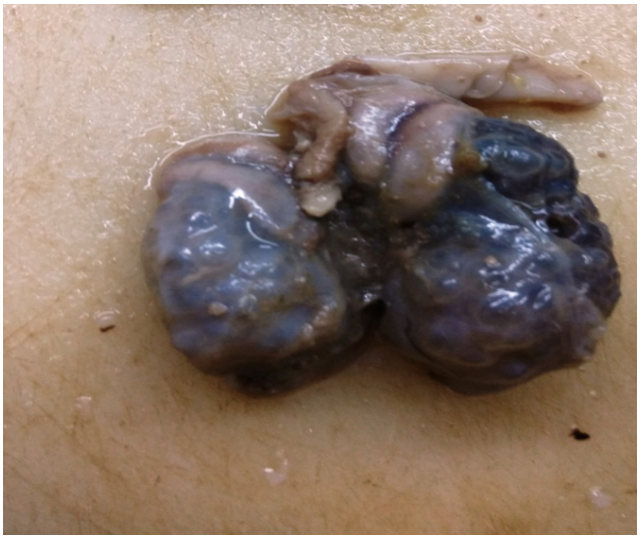

Fig. 2: Gross Pic of b/l enlarged kidneys with surface lobulations

hepatic involvement.

The hallmark manifestation in the liver is normal echogenecity on sonography, congenital hepatic fibrosis with varying degrees of biliary ectasia and periportal fibrosis. Hepatic fibrosis is considered as essential diagnostic criterion for autosomal recessive disease.[4] Signs of portal hypertension, cholangitis or bile duct dysgenesis favors more towards ARPKD. In our case the liver appeared normal both grossly and histologically.

Pathologically kidneys in ARPKD usually shows subcapsular cysts less than 3 mm in diameter, representing ectasia of the collecting tubules.[5] In the cross-section, these dilated tubules can be seen in a radial arrangement extending from the calyx to the capsule. There is epithelial hyperplasia along the collecting ducts and these hyperplastic cells undergo a functional change from resorption to secretion. The combination of epithelial hyperplasia and fluid secretion results in ductal ectasia. Histological examination of biopsies reveals cystic dilatation, primarily limited to the collecting tubules, with flattening of the epithelium. In our case microscopically kidneys showed multiple dialated cystic stuctures involving cortex and medulla with no distict corticomedullary differentiation. The cytic structures are lined by cuboidal to flat epithelium lining thus favouring diagnosis of ARPKD.

Prenatal diagnosis using fetal sonography is unreliable in early pregnancy. The diagnostic features of ARPKD in USG are usually evident in late second trimester mostly during 17wks by usage of high resolution ultrasound techniques[6] and results (i) Enlarged kidneys due to presence of microcysts with increased homogenous echogenecity (ii) absence of corticomedullary differentiation and (iii) difficulty in identifying fetal blader.[7] The increased echogenicity in the kidneys is due to the return of the

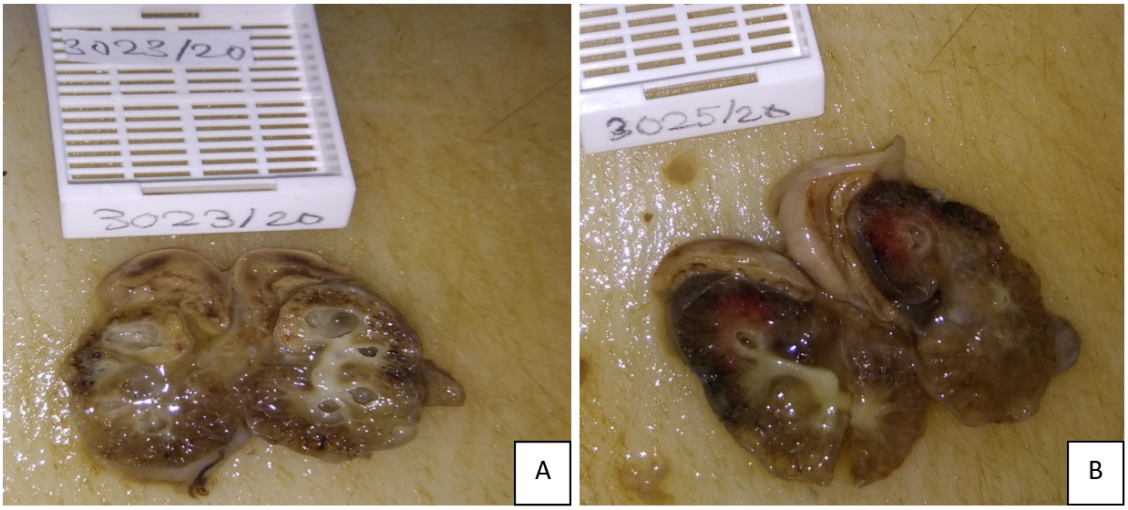

Fig. 3: (**A**) Cut section of rt kidney measuring 4x2x1; (**B**): Left kidney measuring 5x3x2 both the kidneys show numerous cystic spaces with no corticomedullary differentiation

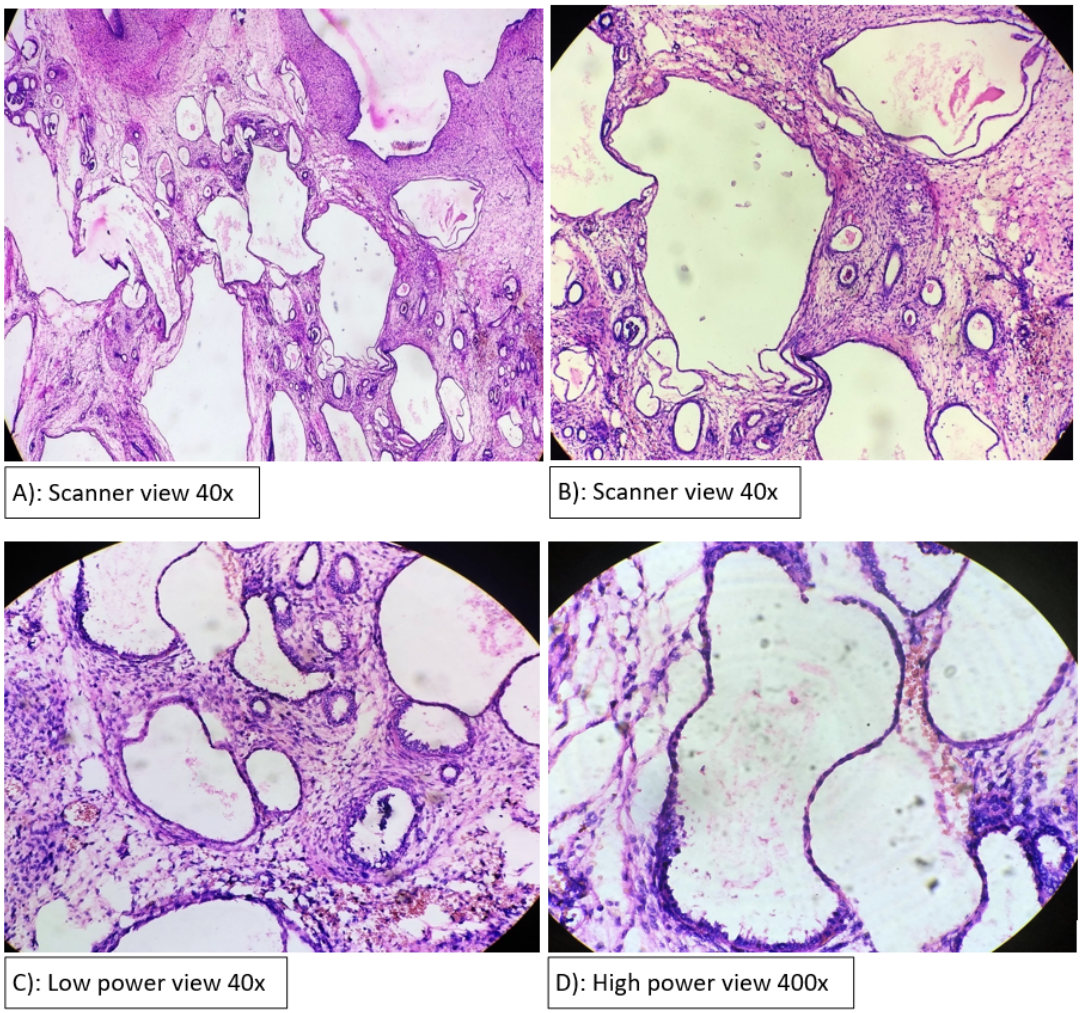

Fig. 4: A-D): Microsetion shows numerous cysts lined with cuboidal to flattened lining epithelium [some right angle to cortical surface], no cotico medullary differentiation seen

sound waves from the enormous number of interfaces created by tightly compacted collecting ducts. However one should keep in mind that it is not the enlarged echogenic kidneys in the fetus that is only diagnostic of PKD as there are other disorders like meckel Gruber syndrome, renal dysplasia, congenital nephritic syndrome in which increased echogenicity seen in USG, however these abnormalities return to normal soon after birth. On the contrary, in dominant polycystic variant fetus shows presence of macrocyst with normal amniotic fluid.

The prognosis of ARPKD is very grim. Childrens born with this entity develops renal failure before they reach adulthood. Severity increases if ARPKD detected in antenatal USG around 24wks of gestation. Death finally ensues due to uremia or respiratory failure.- → leading to oligohydramnios and pulmonary hypoplasia. So as the pregnancy advances the risk related to this entity also increases.

4. Conclusion

There are no studies reporting the problem statement of PKD. There has been a decline in autopsy rate and studies conducted today. Our case report highlights the importance of doing autopsy by which one can confirm sonographic and clinical findings or can negate the diagnosis of ARPKD. Couple should be advised to go for chromosome analysis study and genetic conselling so as to reduce the risk of such anomalies in future pregnancy. Evaluation of polyductin /fibrocystin protein in affected fetuses are other important diagnostic tools.

5. Source of Funding

None.

6. Conflict of Interest

None.

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Author biography

Lipika Behera, Assistant Professor

Shilpa Padhi, Tutor

Swetambari Acharya, Postgraduate

Shushruta Mohanty, Assistant Professor

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