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Diagnosis of Autosomal Dominant Polycystic Kidney Disease in the Uterus and Follow up in a Two-Month Old Infant: A Case Report

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Abstract

Introduction: Polycystic kidney disease (PKD) is classified as a renal cystic disorder that leads to accumulation of cystic lesions in the kidney. This disorder is inherited as both autosomal dominant and recessive. Autosomal dominant polycystic kidney disease (ADPKD), was once thought to be a disease of adults, but is now being reported with increasing frequency in children. The diagnosis is based on clinical, radiologic and genetic evaluation.

Case Report: We present a two-month girl who was admitted to the nephrology ward with fever and discomfort in urination for three days. The prenatal sonography showed a single cyst in both kidneys and in postnatal sonography she had one cyst in the right kidney and two cysts in the left kidney. During the follow-up for kidney cysts, the cysts were increased in size and numbers in both kidneys, which were detected in serial ultrasonography and confirmed by computed tomography. Through the three years follow up; renal function tests remained within the normal limit.

Conclusions: The purpose of this report was prenatal diagnosis of ADPKD by ultrasonography and genetic testing, which may help appropriate management and prompt familial screening.

Keywords: Autosomal Dominant Polycystic Kidney Disease, Prenatal Diagnosis

1. Introduction

Autosomal dominant polycystic kidney disease (ADPKD) is a genetic disease, presented by renal cystic formation, which progresses to end stage chronic renal failure in late life (1, 2). In ADPKD, kidney enlargement develops with age because of progressive cyst formation. In about 50% of patients, renal failure develops because of the growing cysts in number and size over years. This disorder is common in adults with an incidence of 1/500 to 1/1000, regardless of race and gender, geography or ethnicity. Cyst formation occurs in both kidneys and all sites of the nephrons and is more severe in males (3, 4). Manifestation of disease is variable within families due to mutation in intact allele in the epithelial tubular cells, which is responsible for genetic heterogeneity between PKD1 and PKD2. In 85% of ADPKD cases, the disease is developed by defects in the PKD1 gene. Mutation in the PKD1 gene located on chromosome 16 (TRPP1) is responsible for type 1 ADPKD. This gene encodes a transmembrane glycoprotein, polycystin-1(PC1), and in 10 to 15% of cases, the mutation occurs in PKD2 (TRPP2) located on chromosome 4, which encodes polycystin 2 responsible for type 2. Mutation in PKD1 leads to more severe disease in comparison to PKD2 mutation. Autosomal Dominant Polycystic Kidney Disease presents variable clinical features and severity (5, 6). In about 5% of other patients, spontaneous mutation without relation to mentioned genes was reported (7).

No specific criteria were determined for ADPKD diagnosis. Autosomal dominant polycystic kidney disease can occur at any age even in fetuses and neonates. Ultrasonography is used for diagnosis of ADPKD. The potter's disease may be the feature of newborns with ADPKD, who die with pulmonary hypoplasia (8, 9). Antenatal diagnosis is made by ultrasonography, which shows renal enlargement with or without cysts, hyper echoic appearance and increased corticomedullary differentiation. Mutation of PKD1 and PKD2 genes can be identified by prenatal DNA tests. After birth, the disease can present renal enlargement with or without cysts and different degree of renal failure. In the early stages, the disease may present unilateral normal sized kidney but ADPKD is a systemic disorder, which involves multi organ systems (9), and the urinary system leads to end stage renal failure therefore this pa-

tients should be considered for blood-pressure and needs medication (10).

2. Case Report

We describe a two-month old girl, who was admitted to the nephrology ward with fever and discomfort at urination. There was a history of single bilateral renal cyst in prenatal ultrasonography. Postnatal sonography showed a single cyst in the right kidney and two cysts in the left kidney. There was no positive history of PKD in her family. On physical examination she was a well-nourished baby with 4.9 kg of weight and 57 cm of height. Vital signs included temperature of 37 , blood pressure 60/50 mm Hg, pulse rate 80/minute, and respiratory rate of 35/min. Other clinical and laboratory routine examinations were within the normal limit. There was no associated congenital anomaly including hepatic cysts and fibrosis. Lab test results were as follows, hemoglobin (Hb) = 10 g/dL. hematocrit (Hct) = 29.3, Platelet count (plt) = 476/mm^3, white blood count (WBC) = 12300/mm^3 (62% Lymph, 38% PMN), erythrocyte sedimentation rate (ESR) = 64, C-reactive protein (CRP) =62.2 g/L, sodium (Na) =143, potassium (K) = 4.2, calcium (Cl) = 106, HCO_3 = 25, calcium (Ca) = 9.8, blood urea nitrogen (BUN) =15, creatinine (Cr) = 0.5, U/A = normal, U/C: 100/000 colony of *E. coli*, and blood culture was negative. DNA samples from the patient and her healthy family members were investigated by seven markers for linkage analysis. According to the analysis, the D4s423 marker was detected in this family, so the patient was likely to be suffering from ADPKD according to the results. Through the follow up of renal cysts by serial ultrasonography, an elevation in the number and size of cysts was detected in both kidneys, which was confirmed by computed tomography. When the patient was three years old, renal function tests including BUN and creatinine level and other laboratory tests were within normal limits. Detection of renal damage was followed by Cystatin C level as biomarker of renal function, which was normal during three-year follow up.

3. Discussion

Autosomal-Dominant polycystic kidney disease (ADPKD) is one the most important genetic disorders in kidneys, involving both genders with frequency of 1 in 500 to 1 in 1000 individuals (11). The disease is characterized by progressive cyst formation, hypertension, hematuria, proteinuria, concentrating defect, nephrolithiasis, urinary tract infection, end stage renal disease and renal cancer (12). Extra renal clinical presentation including cyst formation in other organs such as liver, pancreas, genital tract, thyroid, spleen, brain and cardiovascular abnormality coronary artery aneurysms, mitral valve prolapse, aortic root dilation, dissection of the thoracic aorta, aneurysm formation in the abdominal aorta, vascular ectasia, and abnormal function of the microvascular bed have been reported (13-16). Although the cyst formation begins in the uterus, about 50% of patients remain asymptomatic lifetime. The ADPKD is responsible for 5 to 10% of end stage renal disease in adults but in affected pediatrics the occurrence of ESRD is rare.

Autosomal dominant polycystic kidney disease should be considered as an adult disease, but rarely occurs during childhood and infancy, which may be diagnosed in the uterus. In congenital ADPKD, variable clinicopathologic cystic changes occur in renal tubules leading to renal failure. A wide clinical spectrum was reported in ADPKD during childhood and infancy including asymptomatic patients to end stage renal disease (14). Mutation in PKD1 gene accounts for about 85% of ADPKD whereas 10-15% of ADPKD mutations map to the PKD2. In the presence of PKD1 gene, clinical presentation of disease may be found in the uterus. Several factors may affect rate of progression, severity and outcome of the disease. On the basis of previous published studies independent factors associated with poor outcome include: the PKD1 gene, young age at presentation, male gender, hypertension, left ventricular hypertrophy, hepatic cysts in females, multiple pregnancies, gross hematuria, urinary tract infection (UTI) in males and size of kidneys; the factors with no relationship with ESRD are gender of parents, mitral valve prolapse, intracranial aneurysms, hepatic cysts in males and urinary tract infections in females (17).

Some previous case reports revealed higher risk of mortality and renal complication in children with fetal and infantile diagnosed ADPKD (18, 19), but according to other studies over 90% of children with confirmed ADPKD before 18 months of age maintained preserved renal function well into childhood (20).

Joseph Tomas et al. presented a fetus with ADPKD, which was diagnosed in the uterus via sonography and died two months after birth (15).

Namrata et al. reported two prenatal cases with different features and outcomes (21).

For two of four prenatal diagnosed patients in a family, termination of pregnancy was done after detection of enlarged echogenic cysts in the uterus, which was confirmed with DNA analysis for PKD1, in one fetus high risk PKD1 allele was found and one fetus remi unaffected (22).

Burn et al. demonstrated moderately enlarged hyper echogenic kidneys with increased corticomedullary as the major presentation of ADPKD (23).

In the study of Shamshirsaz, 199 patients were diag-

nosed with ADPKD. Renal function was maintained within the normal range in more than 90% of patients till childhood (20).

Our case presented complications in the uterus, which was confirmed by DNA analysis as ADPKD and in agreement with the study of Shamshirsaz her renal function tests remained within normal limit despite development of cysts after three months of follow up.

3.1. Conclusion

In conclusion ADPKD was confirmed by the presence of enlarged kidneys containing large cysts in both kidneys in a person with a history of PKD in first-degree relatives. The diagnosis could be approved by ultrasonography. Occurrence of renal enlargement with or without cysts in prenatal ultrasonography, especially in the presence of family history of ADPKD, can suggest the diagnosis of this disease. Because screening of ADPKD by renal ultrasonography may be normal in $\leq$ 20% by 20 years of age and $<$ 5% by 30 years of age, prenatal diagnosis by identifying mutations in the PKD1 or PKD2 genes in families with affected members is suggested.

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References

1. Porter CC, Avner DE. Autosomal Recessive Polycystic Kidney Disease. Philadelphia. US: Saunders; 2011.
2. Terfik EC, Brosnohan GMF. Autosomal Recessive Polycystic Kidney Disease. Philadelphia. US: Lippincott Williams Wilkins; 2007.
3. Ravine D, Walker RG, Gibson RN, Forrest SM, Richards RI, Friend K, et al. Phenotype and genotype heterogeneity in autosomal dominant polycystic kidney disease. *Lancet.* 1992;**340**(8831):1330–3. [PubMed: 1360045].
4. William E, Sweeney J, Ellis DA. Polycystic Kidney Disease, Autosomal Recessive Initial Posting. 2001
5. Daoust MC, Reynolds DM, Bichet DG, Somlo S. Evidence for a third genetic locus for autosomal dominant polycystic kidney disease. *Genomics.* 1995;**25**(3):733–6. [PubMed: 7759112].
6. McConnell RS, Rubinsztein DC, Fannin TF, McKinstry CS, Kelly B, Bailey IC, et al. Autosomal dominant polycystic kidney disease unlinked to the PKD1 and PKD2 loci presenting as familial cerebral aneurysm. *J Med Genet.* 2001;**38**(4):238–40. [PubMed: 11368027].
7. Ong AC, Harris PC. Molecular pathogenesis of ADPKD: the polycystin complex gets complex. *Kidney Int.* 2005;**67**(4):1234–47. doi: 10.1111/j.1523-1755.2005.00201.x. [PubMed: 15780076].
8. Elhassan E, Masoumi A, Schrier RW. Progress on Autosomal Dominant Polycystic Kidney Disease. *Arab J Nephro Transplant.* 2009;**2**(2):27–44.
9. Zhao X, Paterson AD, Zahirieh A, He N, Wang K, Pei Y. Molecular diagnostics in autosomal dominant polycystic kidney disease: utility and limitations. *Clin J Am Soc Nephrol.* 2008;**3**(1):146–52. doi: 10.2215/CJN.03430807. [PubMed: 18077784].
10. Schrier RW, Abebe KZ, Perrone RD, Torres VE, Braun WE, Steinman TI, et al. Blood pressure in early autosomal dominant polycystic kidney disease. *N Engl J Med.* 2014;**371**(24):2255–66. doi: 10.1056/NEJMoa1402685. [PubMed: 25399733].
11. Iglesias CG, Torres VE, Offord KP, Holley KE, Beard CM, Kurland LT. Epidemiology of adult polycystic kidney disease, Olmsted County, Minnesota: 1935-1980. *Am J Kidney Dis.* 1983;**2**(6):630–9. [PubMed: 6846334].
12. Vijay A, Vijay AR, Preethy P. Autosomal Dominant Polycystic Kidney Disease: A Comprehensive Review. *Int J Nephrol Urol.* 2010;**2**(1):172–92.
13. Lonergan GJ, Rice RR, Suarez ES. Autosomal recessive polycystic kidney disease: radiologic-pathologic correlation. *Radiographics.* 2000;**20**(3):837–55. doi: 10.1148/radiographics.20.3.g00ma20837. [PubMed: 10835131].
14. Kumar S, Bhat RV, Bhatt BV. Autosomal recessive polycystic kidney disease with congenital hepatic fibrosis and encephalocele. *Indian Pediatr.* 2001;**38**(3):292–4. [PubMed: 11255310].
15. Thomas J, Manjunath AP, Rai L, Kudva R. Autosomal recessive polycystic kidney disease diagnosed in fetus. *Indian J Urol.* 2007;**23**(3):328–9. doi: 10.4103/0970-1591.33738. [PubMed: 19718344].
16. Ratnam S, Nauli SM. Hypertension in Autosomal Dominant Polycystic Kidney Disease: A Clinical and Basic Science Perspective. *Int J Nephrol Urol.* 2010;**2**(2):294–308. [PubMed: 25364490].
17. Gabow PA, Johnson AM, Kaehny WD, Kimberling WJ, Lezotte DC, Duley IT, et al. Factors affecting the progression of renal disease in autosomal-dominant polycystic kidney disease. *Kidney Int.* 1992;**41**(5):1311–9. [PubMed: 1614046].
18. Michaud J, Russo P, Grignon A, Dallaire L, Bichet D, Rosenblatt D, et al. Autosomal dominant polycystic kidney disease in the fetus. *Am J Med Genet.* 1994;**51**(3):240–6. doi: 10.1002/ajmg.1320510314. [PubMed: 8074152].
19. Hyland VJ, Suthers GK, Friend K, MacKinnon RN, Callen DF, Breuning MH, et al. Probe, VK5B, is located in the same interval as the autosomal dominant adult polycystic kidney disease locus, PKD1. *Hum Genet.* 1990;**84**(3):286–8. [PubMed: 1968038].
20. Shamshirsaz AA, Reza Bekheirnia M, Kamgar M, Johnson AM, McFann K, Cadnapaphornchai M, et al. Autosomal-dominant polycystic kidney disease in infancy and childhood: progression and outcome. *Kidney Int.* 2005;**68**(5):2218–24. doi: 10.1111/j.1523-1755.2005.00678.x. [PubMed: 16221221].
21. Namrata Pradhan M, Singh N, Yadav S. Dilemma of Fetal Autosomal Dominant Polycystic Kidney Disease, a Disease Rare to Present in Fetal Life !. *JMPCR.* 2015;**5**(5):1–7.
22. MacDermot KD, Saggar-Malik AK, Economides DL, Jeffery S. Prenatal diagnosis of autosomal dominant polycystic kidney disease (PKD1) presenting in utero and prognosis for very early onset disease. *J Med Genet.* 1998;**35**(1):13–6. [PubMed: 9475088].
23. Brun M, Maugey-Laulom B, Eurin D, Didier F, Avni EF. Prenatal sonographic patterns in autosomal dominant polycystic kidney disease: a multicenter study. *Ultrasound Obstet Gynecol.* 2004;**24**(1):55–61. doi: 10.1002/uog.1098. [PubMed: 15229917].