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Original scientific paper

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Review

Case report

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Betimi i Hipokratit

Në çastin kur po hy në radhët e anëtarëve të profesionit mjekësor premtoj solemnisht se jetën time do ta vë në shërbim të humanitetit. Ndaj mësuesve do ta ruaj mirënjohjen dhe respektin e duhur. Profesionin tim do ta ushtroj me ndërgjegje e me dinjitet. Shëndeti i pacientit tim do të jetë brenga ime më e madhe. Do t'i respektoj e do t'i ruaj fshehtësitë e atij që do të më rrëfehet. Do ta ruaj me të gjitha forcat e mia nderin e traditës fisnike të profesionit të mjekësisë.

Kolegët e mi do t'i konsideroj si vëllezër të mi.

Në ushtrimin e profesionit ndaj të sëmurit tek unë nuk do të ndikojë përkatësia e besimit, e nacionalitetit, e racës, e politikës, apo përkatësia klasore. Që nga fillimi do ta ruaj jetën e njeriut në mënyrë apsolute. As në kushtet e kërcënimit nuk do të lejoj të keqpërdoren njohuritë e mia mjekësore që do të ishin në kundërshtim me ligjet e humanitetit. Këtë premtim po e jap në mënyrë solemne e të lirë, duke u mbështetur në nderin tim personal.

The Oath of Hippocrates

Upon having conferred on me the high calling of physician and entering medical practice, I do solemnly pledge myself to consecrate my life to the service of humanity. I will give my teachers the respect and gratitude which is their due. I will practice my profession with conscience and dignity. The health of my patient will be my first consideration. I will respect the secrets which are confided in me, even after the patient has died. I will maintain by all the means in my power, the honor and the noble traditions of the medical profession.

My colleagues will be my brothers.

I will not permit considerations of religion, nationality, race, party politics or social standing to intervene between my duty and my patient. I will maintain the utmost respect for human life from its beginning even under threat and I will not use my medical knowledge contrary to the laws of humanity. I make these promises solemnly, freely and upon my honor

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THE ROLE OF THE EARLY DIAGNOSIS OF AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE IN FETUSES- CASE STUDY

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ABSTRACT

Introduction:The autosomal recessive polycystic kidney disease (ARPKD) is a rare disorder that is present in 1:20,000 babies. A fetal death may occur due to a severe oligohydramnios, or neonatal death caused by pulmonary insufficiency. The aimof the case study presentation is to point out the importance of the ultrasound diagnosis as early as possible in the pregnancy, so that the right decision is made by the parents and by the gynecologist. Methods: The methods used in this case include ultrasound, invasive diagnosis- amniocentesis and chorionic villus sampling, cytopathologic analysis and PCR amplification and sequencing of PKHD1 gene in the parents' blood, amniotic fluid and chorionic villi. Results:The patient is 29 years old women, fourth pregnancy, previous two labors on time with caesarean section, both of the babies died in the neonatal period and are subject to post-mortem examination. The findings from the post-mortem examination shown a suspicion for autosomal recessive polycystic kidney disease (ARPKD). After the second result of the post-mortem examination, the parents were examined for having a mutation in the PKHD1 gene and it was confirmed that both of them are having this mutation. The third pregnancy ended with an induced abortion because the amniocentesis confirmed a fetus having a homozygote for ARPKD. In the fourth pregnancy a chorionic villus sampling was performed and a fetus was found with a heterozygote for ARPKD and the pregnancy was successful with a viability of the fetus. Conclusion:The timely intervention of gynecologist can prevent unfavorable effects- Caesarean section of matured fetuses that then usually exist in the first two months, because dialysis is the only therapy, temporarily until kidney transplantation takes place. This leads to emotional and medical consequences suffered by the parents.

CASE STUDY

INTRODUCTION: The isolated presence of big hyperechogenic kidneys with reduced or absent amniotic fluid in the pregnancy can suggest polycystic disease of the fetus. The timely prenatal diagnosis is important ,because this state can have serious implications if the pregnancy continues. Thus having into consideration the lethal outcome when the fetus is a homozygote for mutation and evaluation and genetic counseling of the parents is necessary. More precisely, in this case the outcomes of the fetuses are shown, with the parents, carriers of heterozygotes for mutation of genes for autosomal polycystic kidney disease with an incidence 1 of 20000 newborns.

AIM: The timely prenatal diagnosis with the use of ultrasound, prenatal diagnosis for the presence of mutations of the gene PKHD1 in the both parents and genetic counseling is the only way to prevent the unfavorable outcome of newborns that are homozygotes, carriers of the mutation for PKHD1. The aim of the case study presentation is to point out the importance of the ultrasound diagnostics in the early stage of the pregnancy so that the parents and the gynecologist can make the right decision.

METHODS: The methods used in this case include ultrasound, invasive diagnosis- amniocentesis and chorionic villus sampling, cytopathologic analysis and PCR amplification and sequencing of PKHD1 gene in the

parents' blood, amniotic fluid and chorionic villi.

RESULTS: The patient is 29, fourth pregnancy, previous two labors with Caesarean section due to reduced amniotic fluid with a development of fetal distress in term. The first pregnancy resulted in a girl, 3620 grams, the second with a living male, 3500 grams, born on time and the second pregnancy with urgent Caesarean sections due to fetal distress with oligohydramnios with an Apgar score equal or higher than 7. Both newborn children died in the neonatal period and subject to post-mortem examination. The post-mortem examination show autosomal recessive polycystic kidney disease (ARPKD):»Ren polycysticus,Portal fibrosis at cystis haepaticae,Hypoplasio pulmonum». Even though after the results of the first post-mortem examination were obtained the recommendation of the pathologists was APRKD examination to be done, it was not performed. After the second post-mortem examination has been made, the parents were examined for being carriers of mutation for polycystic disease and the following results were obtained: mother, carrier s. 2414C>T in the exon 24 and s.9530 T>C in the exon 58 (mutation in the PKHD1 gene). In the course of the third pregnancy amniocentesis was performed in the 17th gestation week and it was determined that the fetus has a presence of mutation in the PKHD1 gene- inherited the two mutations from the two parents, i.e. that it has a genotype related with ARPKD, due to which the pregnancy was terminated with an induced abortion- with a finding of medullary kidney disease. Chorionic villus sampling was performed in the fourth pregnancy and it was determined that the fetus is a heterozygote of ARPKD (mutation inherited from the father). The pregnancy is with normal ultrasound findings and successfully terminated on time with a third Caesarean section, with eutrophic male baby.

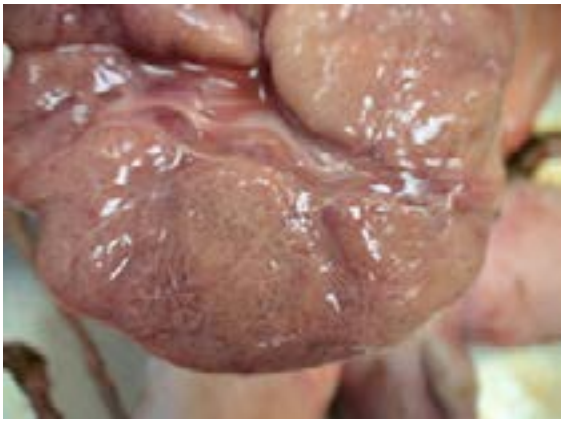
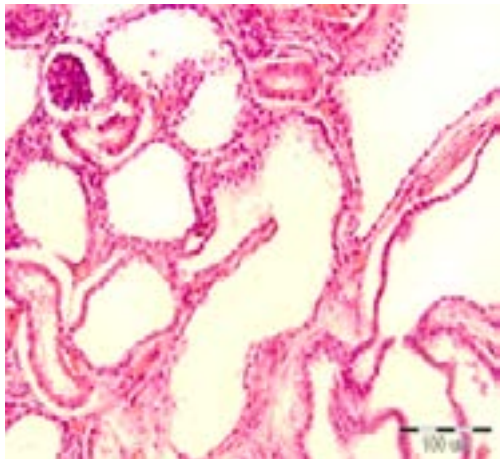
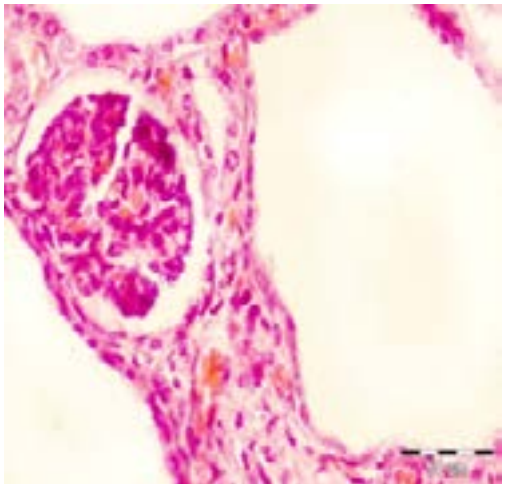
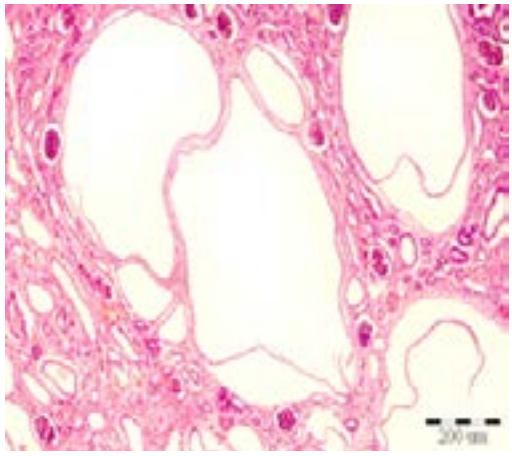


Image 1. Post-mortem examination finding. Iamge -macroscopic

2. Hystopathological finding







DISCUSSION: The autosomal recessive polycystic kidney disease (ARPKD) is a rare disorder that appears in 1:20,000 infants. A fetal death may occur due to a severe oligohydramnios, or neonatal death caused by pulmonary insufficiency. (1) The renal pathology in ARPKD is characterized by non-obstructive dilatation or extension of the collecting tubules in the renal medulla that results in microcysts with a diameter up to 2 mm.

In severe cases the cysts may expand in the cortex. The external renal cortex remains normal because this disease does not have tubules. The severity of the kidney disease is proportional to the percent of nephrons affected by cysts and is correlated with the seriousness of mutations of PHKD1. (2) Furthermore, all affected individuals have a certain degree of engagement of the liver with biliary dysgenesis and hepatic fibrosis. The survival of the persons with ARPKD depends on the subtype: perinatal (hours), neonatal (months), infantile (up to 10 years) and junior (decades). The involvement of the kidney is more common in cases with perinatal presentation, while the inclusion of the liver is more common for the later diagnosis of ARPKD.There are a numerous cases stated in the literature where a large part of ARPKD with postnatal diagnosis, after the death of the neonate as it happened in the first and second pregnancy of our patient. In one case study of Joseph Thomas and collaborators including a 27-year old patient, primigravida, the pregnancy was normal until the 24th gestation week, but, after the second trimester, after a series of ultrasonic examinations have been performed, bilateral symmetrically increased and hyperechogenic kidneys have been noticed, absence of urinary bladder and amniotic fluid index 9. In the 28th gestation week the same finding was confirmed with an ultrasound, with additional oligohydramnios and fetal acid. The patient started with early labor which ended with a difficult spontaneous labor due to big fetal kidneys. A finding of the autopsy showed the presence of ARPKD. (3) Unlike our case, the disease from the first pregnancy was not excluded, apart from the advice given by the pathologists and obstetricians. In a lot of cases in the world ARPKD is detected in the prenatal period or right after the death of the first newborn with ARPKD. The ultrasound diagnosis of APRKD is highly pathognomonic when there are significantly increased echogenic kidneys on both sides, small or absent urinary bladder and oligohydramnios; but, nevertheless, the precise prenatal diagnosis cannot be made certain just with an ultrasonic examination. (4) In one case presented by Dayananda Kumar Rajanna, a 26-year old patient with a second pregnancy, the first normal in the 24-26 gestation week a fetal antenatal diagnosis was determined for autosomal recessive polycystic disease with a severe oligohydramnios, and under aseptic conditions, the pregnancy was terminated with an induced early birth. The autopsy finding shows ARPKD. (5) The ARPKD is not related with an increased frequency of abnormal karyotype because the chromosome studies are not useful in determining the diagnosis, but can be of use for excluding other disorders in the differential diagnosis related to abnormal karyotype. Additionally, an amniocentesis or chorionic villus sampling can be performed so the molecular diagnostic tests may be run of fetal DNA, that sometimes can confirm the ARPKD diagnosis. The prenatal diagnosis is possible with the use of analysis of haplotypes or analysis of a direct mutation of the gene PKHD1. PKHD1 is a big gene expanding via the genome segment of 500 kilobases of the chromosome number 12. Direct analyses of the mutation have been declared to discover 85 percent of the cases. (6) Therefore, in our case, after the second post-mortem examination finding the parents have been examined for being carriers of mutation in the PKHD1 gene, where it was confirmed that the both of them are carriers of this mutation. In the third pregnancy an amniocentesis was performed in the 17th gestation week and it was determined that the fetus has a mutation of the gene inherited by the both parents due to which the pregnancy was terminated. In the fourth pregnancy prenatal diagnosis was also performed, chorionic villus sampling was performed and it was determined that the fetus is a heterozygote for ARPKD (mutation inherited only from the father) and the pregnancy was successfully terminated until the term set with a eutrophic male baby.

CONCLUSION: The methods of molecular diagnosis should be used in early pregnancy, but this disease is usually ultrasonically detected in the second trimester and has an incidence of 1 of 20000 newborns. Even though it is characteristic the ultrasound to show increased homogenic (mycrocystic) hyperechogenic kidneys of the fetus with oligohydramnios associated with pulmonary hypoplasia, so called club foot and Potters' face, nevertheless, this disorder is characterized by a spectrum of ultrasonic findings. The timely intervention of the gynecologist can prevent unfavorable effects- Caesarean section of babies ready to be delivered that afterwards usually live in the first two months because the only therapy is dialysis to a kidney transplantation. This can cause emotional and medical consequences suffered by the parents.

REFERENCES

1. Wilson PD. Polycystic kidney disease. N Engl J Med 2004; 350:151
2. Denamur E, Delezoide AL, Alberti C, et al. Genotype-phenotype correlations in fetuses and neonates with

autosomal recessive polycystic kidney disease. Kidney Int 2010; 77:350

3. Joseph Thomas, A. P. Manjunath, Lavanya Rai, and Ranjini Kudva.Autosomal recessive polycystic kidney disease diagnosed in fetus. Urol. 2007 Jul-Sep; 23(3): 328–329
4. Tsatsaris V, Gagnadoux MF, Aubry MC, et al. Prenatal diagnosis of bilateral isolated fetal hyperechogenic kidneys. Is it possible to predict long term outcome? BJOG 2002; 109:1388
5. Dayananda Kumar Rajanna, Anjani Reddy,1 Naren Satya Srinivas, and Ankur Aneja.Autosomal Recessive Polycystic Kidney Disease: Antenatal Diagnosis and Histopathological Correlation J Clin Imaging Sci. 2013; 3: 13.Published online 2013 Mar 29. doi: 10.4103/2156-7514.109733
6. Dayananda Kumar Rajanna, Anjani Reddy,1 Naren Satya Srinivas, and Ankur Aneja.Autosomal Recessive Polycystic Kidney Disease: Antenatal Diagnosis and Histopathological Correlation J Clin Imaging Sci. 2013; 3: 13.Published online 2013 Mar 29. doi: 10.4103/2156-7514.109733

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АПСТРАКТ

Вовед: Автозомно рецесивна полицистична болест на бубрезите (ARPKD) е ретко нарушување, кое се јавува кај 1: 20,000 живородени деца. Може да настане фетална смрт поради тежок олигохидрамнион, или неонатална смрт поради белодробна инсуфициенција.Целта на презентацијата на случајот е да се поентира важноста на ултразвучна дијагностика што е можно порано во бременоста,за правилна одлука на родителите и гинекологот.Методи:Во овој случај се користени како методи-ултразвук,инвазивна дијагностика-амниоцентеза и хорионбиопсија, хситопатолошка анализа и PCR амплификација и секвенционирање на PKHD1 ген во крв од родители, плодова вода и хорионски ресички.Резултати:Пациенткана 29 годишнавозраст, четвртабременост, пр етходнидветерминскипородувањасоЦарскирез при што обете новородени се починати во неонатален период и дадени на обдукција. Добиен обдукционен наод во прилог на автозомна рецесивна полицистична бубрежна болест(ARPKD).По вториот обдукционен наод, родителите се испитувани за носителство на мутација во PKHD1 генот, каде што потврдено е дека двајцата се носители на ова мутација.Третата бременост завршено со индуциран абортус бидејќи на амниоцентеза потврден фетус кој хомозигот за ARPKD. Во четвртата бременост направена хорионбиопсија и утврден фетус кој е хетерозигот за ARPKD и бременоста успешно е завршена со вијабилен плод.Заклучок:Навремената интервенција на гинекологот може да превенира неповолни ефекти-царски рез кај плодови во термин кои потоа егзитираат најчесто во првите два месеци од животот, бидејќи единствена терапија е дијализа, привремено до трансплантација на бубрег. Ова доведува до емотивни и медицински последици кај родителите.