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CASE REPORT

Polycystic kidney disease: case report and literature review

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INTRODUCTION

Polycystic kidney diseases (PKD) are a group of serious pathologies that may lead to renal failure[1].

In the polycystic kidney, cysts are functional portions of nephrons that become progressively dilated, possibly culminating with obstruction of adjacent tubules. For this PKD form, two distinct etiological entities are recognized, according to pattern of inheritance, cyst morphology and clinical, radiological and laboratory aspects. These entities are known as autosomal recessive polycystic kidney disease (ARPDK) and autosomal dominant polycystic kidney disease (ADPKD)[2].

Mutation analysis is essential to understand action mechanisms involved in the disease[3].

CLINICAL CASE

L. A. G. S., a 22-year-old pregnant indigenous female, G3 P2 A0, from Triunfo community, city of Uiramutã in the state of Roraima, was admitted to the emergency unit of the Maternal and Child Hospital Nossa Senhora de Nazaré without prenatal records. She was in the expulsive phase of labor, which started in her village, with inaudible fetal heartbeat (FHB).

Already in the delivery room, patient presented difficulty in fetus extraction, with head and upper limbs expelled but torso and abdomen retained in the vaginal canal. She was urgently transferred to the operating room, anesthetized and the fetus was removed vaginally. Fetus was male, weighed 3.025g and had visible malformations with significant abdominal increase, gonadal agenesis and congenital malformed feet.

Amniotic fluid was fetid and the mother presented hyperthermia. Echography revealed multiple rounded anechoic images of cystic content, smooth surface and various sizes located bilaterally. The kidneys were deformed and increased in volume, suggesting giant bilateral polycystic kidney.

Development

The genetic inheritance pattern of ARPDK is autosomal recessive, parents are not affected and there is a 25% risk of disease development in each pregnancy. Fetal ultrasound examination performed from week 30 of pregnancy onward may show kidneys with increased echogenicity, associated with small or non-visualized bladder in severe cases, and oligohydramnios.

These findings are not pathognomonic of ARPDK and may also occur in ADPKD and Meckel syndrome. Increases in alpha-fetoprotein and/or trehalase concentrations in the amniotic fluid can be used as adjunct but not specific markers for ARPDK[2].

ARPDK is characterized by the bilateral occurrence of renal cysts in neonates, infants, children and, occasionally, in adults. The presence of palpable kidneys at birth is common but also may occur later, with disease progression[2].

ARPDK associates with congenital hepatic fibrosis and portal hypertension, with bile ducts proliferation and, occasionally, with pancreatic fibrosis, and may present with systemic arterial hypertension (SAH) and evolve into progressive renal insufficiency.

The kidneys present typical radiological and histological characteristics, namely increased size due to dilation of collecting tubules, and increased echogenicity on ultrasound examination. The cysts tend to grow to sizes smaller than two centimeters in diameter[2].

ADPKD is the most frequent congenital kidney disease, affecting one in 400 to 1,000 births[1]. It is an important cause of chronic renal failure (CRF) in adults, generally manifested in

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30 to 40-year-old individuals, and rarely affects children and eventually newborns[2].

ADPDK is an autosomal dominant disease, which means that the patient offspring has a 50% chance of inheriting the mutated allele. Almost 100% of individuals who inherit the mutated allele develop the disease[2].

ADPKD is usually caused by genetic mutations in the PKD1 locus, which is located on chromosome 16 short arm. However, in approximately 4% of the affected families the disease is related to yet unknown mutations, probably located elsewhere in the genome[2].Evidences suggest the functional interaction of polycystin-1 and polycystin-2 proteins in extracellular adhesion signaling and ion transport, associated with Ca^{++} transmembrane flux regulation[3].

ADPKD is characterized by cystic dilation of renal collecting ducts invariably associated with liver abnormalities, such as bile ducts dysgenesis and periportal fibrosis. The disease can be diagnosed on the fetus during gestation, through ultrasound examination. It presents with oligohydramnios and pulmonary hypoplasia, which are secondary to decreased urinary production. Respiratory failure is a major cause of perinatal morbidity and mortality. About 30% of affected newborns die shortly after birth, while approximately 50% of those who survive the neonatal period progress to chronic renal failure in the first decade of life[4].

The clinical manifestations of ADPKD are hypertension, which requires treatment in over 70% of cases, nephrolithiasis, renal failure, portal hypertension, gastrointestinal bleeding, rupture of esophageal varices, thrombocytopenia, splenomegaly and cholangitis and icterus[4].

Genetic counseling and clinical investigation are fundamental for these family groups. ADPKD is manifested mainly by hematuria, back pain and SAH. Kidneys are increased and contain numerous cysts of various sizes, but usually large, which gives the organ a lobed appearance[1].

Several comorbid conditions may be related to ADPKD, such as direct involvement of other organs, connective tissue abnormalities, cardiac disease, intracranial aneurysm, diverticular disease and even vena cava thrombosis due to extrinsic compression by the renal cysts. Inferior vena cava thrombosis due to intrahepatic cysts in ADPDK patients has also been reported[1].

Intracranial aneurysms are the most serious extra-renal ADPKD manifestation, although they are present in only 5% of patients. Rupture of aneurysms typically occurs when they reach more than 10 mm[1].

The major cause of mortality in PKD patients is cardiovascular disease, which has hypertension as its main determinant[1].

Current ADPKD treatment is based on the symptomatic management of disease sequelae, including control of hypertension.Survival rates increased significantly due to the improvement of neonatal care and antihypertensive therapies.

Angiotensin-converting enzyme inhibitor, angiotensin II receptor blockers, diuretics, calcium channel blockers and cholesterol-lowering agents are used to reduce progression to chronic renal failure. Renal failure is treated with dialysis or kidney transplant[4].

Comorbidities caused by ADPKD, such as hypertension, proteinuria, left ventricular hypertrophy and other extra-renal complications including cysts in other organs causing mass effects (vena cava compression, obstructive icterus) are also noteworthy. Punctures to reduce cyst volume are recommended in these cases[1].

Nevertheless, several drugs are under tests in pre-clinical and clinical trials. Targets of such drugs are abnormal cellular signaling cascades that lead to unregulated cellular proliferation, dedifferentiation, apoptosis, and liquid secretion. Promising drugs include: vasopressin V2 receptors antagonists, such as tolvaptan, that reduce cystic volume, preventing disease progression; octreotide, which inhibits cAMP production and cystic formation, also acting in hepatic cysts; rapamycin and sirolimus, which are immunosuppressive drugs that inhibit mTOR and reduce cell and cystic growth; etanercept, a TNF-α inhibitor; pioglitazone, which seems to act in the Wnt/β-catenin pathway and Roscovitine, a cyclin-dependent kinase (cdk) inhibitor which effectively inhibits cystic growth through blockage of the cell cycle progression. Roscovitine intermittent administration produces even longer lasting anti-cystic effects[1].

Recent studies have been suggesting new classes of ADPKD therapeutic agents, such as lysophosphatidic acid (LPA) receptors antagonists and PPAR-γ agonists. These drugs act by blocking the synthesis of CFTR (cystic fibrosis transmembrane conductance regulator) protein, thus preventing Cl^- ion secretion into renal and bile cyst fluid and cyst growth[1].

Prognosis varies with the severity of renal disease. Children with more than 90% affected ducts may not survive the neonatal period, due to association with pulmonary hypoplasia in 30% of affected neonates[4].

CONCLUSION

The ADPKD is a complex disease that arises from various alterations in cell signaling pathways. The natural course of the disease includes cystic growth, formation of new cysts and deterioration of renal function[1].

Early diagnosis, through tests such as ultrasonography, is fundamentally important. Attention should be paid to symptoms such as pain, hematuria and cystic infection, which may occasionally appear in patients with the disease.

The control of comorbidities, including hypertension, proteinuria, aneurysms and left ventricular hypertrophy is an essential part of the treatment. The main therapeutic goal is to reduce morbidity and mortality and control comorbidities. Therapeutics is based on the use of effective drugs to reduce cystic growth and preserve kidney function[1].

Prognosis varies with the severity of renal disease. Most of the children who survive the neonatal period evolve to terminal renal failure[4]. The early diagnosis and appropriate

clinical monitoring may minimize and/or delay the onset of complications, especially SAH, which appropriate clinical management may delay renal function loss[2].

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