Original Article

Autosomal Recessive Polycystic Kidney Disease in a Child Complicated by Autoimmune Hemolytic Anemia: A Case Report

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Received: 9/3/2022; Accepted: 17/5/2022; Published online: 2/8/2022

Abstract:
Autosomal recessive polycystic kidney disease (ARPKD) is a rare genetic disorder that presents as an isolated polycystic renal disease in childhood, or associated with congenital hepatic fibrosis and/or Caroli disease. The spectrum of complications of ARPKD include end stage kidney disease, systemic hypertension and liver disease. Anemia in ARPKD is commonly due to be reduced erythropoietin or iron deficiency. We present a 2-year old male patient with ARPKD who presented to the emergency room by striking pallor and dark urine. Initial lab work revealed Hemoglobin level 2g/dL. Blood transfusion was challenging due to difficult typing and frequent mismatch. Other labs showed elevated urea and creatinine, positive direct Coomb’s anticoagulant test and positive urine culture. Imaging was consistent with ARPKD. The patient was resuscitated and after stabilization, he received pulsed methylprednisolone at 30 mg/day for 5 days followed by prednisone 2mg/kg/day for 4 weeks that was tapered over 2 months with marked improvement. Herein we report autoimmune hemolytic anemia as another and rare cause for anemia associated with ARPKD.

Level of Evidence of Study: IV (4).

Keywords: Autosomal recessive polycystic kidney disease; autoimmune hemolytic anemia; congenital hepatic fibrosis; hepatosplenomegaly

Abbreviations: ARPKD: Autosomal recessive polycystic kidney disease; ADPKD: Autosomal dominant polycystic kidney disease; PKHD1: polycystic kidney and hepatic disease 1; CKD: chronic kidney disease; EPO: erythropoietin.

Introduction

Cystic kidney diseases are common causes of end stage renal disease in children and adults. They are characterized by the presence of numerous fluid-filled cysts in the renal parenchyma that continue to enlarge throughout a patient’s lifetime (2). The 2 most important cystic diseases are autosomal recessive polycystic kidney disease (ARPKD) and autosomal dominant polycystic kidney disease (ADPKD). ARPKD is a rare inherited hepatorenal cystic disease. It results from mutation in the PKHD1 gene which normally encodes the fibrocystin protein (3). Fibrocystin functions as a key regulator of cell proliferation, apoptosis and polarization. When mutated, it can no longer serve these roles, resulting in cystic changes within the kidney and a range of extrarenal manifestations together constituting ARPKD (4). ARPKD can be diagnosed prenatally by ultrasound which shows enlarged hyperechoic kidneys with multiple microcysts in the renal cortex and medulla. The newborn exhibits a “Potter” phenotype encompassing massive kidney enlargement, pulmonary hypoplasia, contracted limbs with club feet in addition to the characteristic facies. Approximately 80% will develop arterial hypertension during the first month of life which is usually difficult to control (5). Renal disease ranges from a mild tubular concentration defect up to complete renal dysplasia and end stage renal disease.

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ARPKD can present as isolated cystic kidney disease or can be associated with congenital hepatic fibrosis and/or Caroli disease (6). Complications of ARPKD include end stage kidney disease, anemia, resistant hypertension and liver disease. Anemia is a common complication of chronic kidney disease (CKD) and is associated with a poor quality of life, significant morbidity and higher mortality. The mechanisms involved in anemia associated to CKD are diverse and complex but mostly related to erythropoietin and iron. They commonly include a decrease in erythropoietin (EPO) production, iron deficiency and inflammation with high hepcidin levels (7). Autoimmune hemolytic anemia is a rare complication of ADPKD and ARPKD, with a single case reported in 62-year old female patient with ADPKD (8). To our knowledge, it was never reported in patients with ARPKD in the pediatric age group. Herein, we describe a rare case of ARPKD who presented with autoimmune hemolytic anemia.

Case Presentation

A 2-year old male patient presented to the emergency room with severe pallor, dark colored urine, dyspnea and signs of shock. The patient had fever 3 days prior to his admission. There was no history of jaundice, bleeding from any orifice, eye puffiness, lid pain, joint pain or swelling, malar rash, oral ulcers or hair fall. There was past history of blood transfusion at the age of 18 months; however, there is no data available on the indication for blood transfusion at that time. Initial blood work revealed Hemoglobin of 2g/dL, elevated creatinine and urea, positive direct Coomb’s anticoagulant test and urinary tract infection evidenced by urine analysis and culture. Reticulocyte count was normal. Blood was secured after frequent mismatches. Following resuscitation and stabilization of the patient’s condition, complete evaluation was carried out.

![Figure 1](https://cupsj.journals.ekb.eg/)

**Figure 1.** Axial and coronal reformatted images of CT UT showing enlarged, hypoattenuating kidneys with lobulated outline and very faint medullary calcifications as well as enlarged liver with mild diffuse dilatation of the intrahepatic biliary radicals.

The patient’s weight was between the 10th and 25th percentiles and height for age was between the 5th and 10th percentiles. Vital signs showed elevated blood pressure; above the 97th percentile for age. Abdominal examination revealed hepatosplenomegaly and fullness in the renal angles. Bedside echocardiography showed septal hypertrophy. Abdominal ultrasound showed enlarged both kidneys with loss of corticomedullary differentiation and picture consistent with polycystic kidney disease. Computed tomography of the urinary tract (CTUT) was done and showed enlarged, attenuated kidneys with lobulated outline and very faint medullary calcifications as well as enlarged liver with mild diffuse dilatation of the intrahepatic biliary radicals (Figure 1). Magnetic Resonance Imaging (MRI) showed enlargement of both kidneys with loss of corticomedullary differentiation and hyperintense renal parenchyma (Figure 2). He was started on antibiotics for urinary tract infection. Upper endoscopy performed as work up for anemia showed distal esophagitis. The child received methylprednisolone 30mg/kg/day for 5 days then was shifted to prednisone 2mg/kg/day for 4 weeks and gradually tapered over a period of 2 months. He improved markedly and achieved a stable hemoglobin level around 10gm %. He also received erythropoietin for 3 months. Kidney functions returned to normal following
the treatment of urinary tract infection. Blood pressure was maintained by a calcium channel blocker.

![Image](image-url)

**Figure 2.** Axial & coronal T2WIs showing enlargement of both kidneys with loss of corticomedullary differentiation & hyperintense renal parenchyma.

**Discussion**

Anemia is a common complication of CKD. It impairs physical activity, reduces energy level, neurocognitive functions and quality of life. Causes of anemia are multifactorial. Progressive reduction in erythropoietin levels is one of the most important causes of anemia with CKD. Other factors that contribute to anemia in patients with CKD include iron deficiency due to loss of blood or impaired absorption of iron, ineffective use of iron stores due to high hepcidin levels, systemic inflammation, reduced bone marrow response to uremic toxins, reduced red blood cell life span, vitamin B12 or folic acid deficiencies (10). Anemia associated with ARPKD may result from the aforementioned factors or may result from other causes such as bleeding varices due to portal hypertension. We report autoimmune hemolytic anemia as an atypical and rare cause of anemia associated with ARPKD.

Autoimmune hemolytic anemia was previously reported in an adult female patient with ADPKD but, to our knowledge, was never reported in patients with ARPKD nor in the pediatric age group. We are the first to report this rare association (8). Corticosteroid therapy is usually the first line of therapy of autoimmune hemolytic anemia. Corticosteroid therapy is widely used in the treatment of patients with different kidney diseases. However, there are several adverse effects of corticosteroids on the cardiovascular system, glucose and lipid metabolism, immune system, and central nervous system that are well described in literature (11). Our patient received corticosteroids and his vital signs showed high blood pressure. It is unclear whether it was steroids-induced or a consequence of the underlying kidney disease. Benefits of corticosteroid therapy outweigh the risks in this patient as it was life-saving since the patient presented with life-threatening anemia and there was great difficulty to secure blood for blood transfusion. Several medications were used to control the high blood pressure and following corticosteroid withdrawal, it is now maintained on calcium channel blocker only. The patient received erythropoietin for a presumed diagnosis of erythropoietin deficiency since it is one of the commonest causes of anemia associated with CKD. Evaluation of iron stores and erythropoietin levels could not be done at first presentation and before receiving blood transfusion as the patient’s condition was unstable. After diagnosing autoimmune hemolytic anemia and initiation of corticosteroid therapy, erythropoietin was discontinued and the patient hemoglobin level was stable and maintained at 10 gm/dL making erythropoietin deficiency as a cause for anemia less likely.

Drug induced hemolytic anemia is a rare cause of anemia that is difficult to diagnose. Antibiotics including penicillin and cephalosporins are the drugs most often implicated in the development of AIHA (12). Autoimmune hemolytic anemia associated with other classes of antibiotics such as trimethoprim sulfamethoxazole has also been reported in few cases in literature (13, 14). Our patient received trimethoprim-sulfamethoxazole in the past for
recurrent attacks of urinary tract infection. However, given the remote history of antibiotics use, drug-induced hemolytic anemia was considered a remote yet, a possible etiology. Some antihypertensive medications have also been reported to cause autoimmune hemolytic anemia such as hydralazine and alpha methyldopa (15); however, our patient was not on any antihypertensive medications prior to presentation.

Conclusion

ARPKD remains a rare and severe condition with high morbidity and mortality rates. Complications should be monitored properly and treated to improve the patients’ quality of life and delay the progression to end stage renal disease. Anemia is a common complication that should be monitored and treated properly. Herein we describe, to our knowledge, the first case of autoimmune hemolytic anemia associated with ARPKD.

Author Contributions: All authors searched medical literature, databases, conceptualized, conducted the case review and reviewed the final manuscript. All authors have read and agreed to the published version of the manuscript.

FUNDING

Authors declare there was no extramural funding provided for this study.

CONFLICT OF INTEREST

The authors declare no conflict of interest in connection with the reported study. Authors declare veracity of information.

References
