



Cystinuria in an adult patient with polycystic kidney disease: a rare association. Case report

Cistinúria em paciente adulto com doença renal policística: uma associação rara. Relato de caso

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ABSTRACT

Cystinuria and polycystic kidney disease (PKD) are genetic disorders that affect the urinary tract and rarely reported in the same patient. Cystinuria is a metabolic disorder characterized by high urinary excretion of cystine and other amino acids accounting for 8% and 1% of kidney stones in children and adults, respectively. Patients with cystinuria present with recurrent nephrolithiasis. PKD is an inherited systemic disease characterized by the development of cysts in various organs, mainly found in the kidneys. It is a common cause of end-stage renal disease (ESRD) and nephrolithiasis. We report a 38-year old male who presented nephrolithiasis at age 26. Cystinuria was diagnosed in metabolic investigation at age 28. A computed tomography revealed PKD at age 30. On recent routine evaluation, the patient was asymptomatic and the renal function was normal. We report a rare case of cystinuria and PKD in the same patient.

Keywords: Nephrolithiasis; Polycystic kidney disease; Cystinuria; CKD; Case report.

RESUMO

Cistinúria e doença renal policística (DRP) são desordens genéticas que afetam o trato urinário e raramente foram relatadas no mesmo paciente. Cistinúria é uma desordem caracterizada por elevada excreção urinária de cistina e outros aminoácidos ocorrendo em 8% e 1% dos casos de nefrolitíase em crianças e adultos, respectivamente. Pacientes com cistinúria se apresentam com nefrolitíase recorrente. DRP é uma doença sistêmica hereditária caracterizada pelo desenvolvimento de cistos em vários órgãos, principalmente nos rins. É uma causa comum de doença renal crônica (DRC) e nefrolitíase. Relatamos o caso de um paciente masculino de 38 anos de idade que se apresentou com nefrolitíase aos 26 anos. Cistinúria foi diagnosticada em investigação metabólica realizada aos 28 anos. A tomografia computadorizada mostrou DRP aos 30 anos. Atualmente, o paciente se encontra assintomático com função renal normal. Relatamos um caso de cistinúria e DRP no mesmo paciente.

Descritores: Nefrolitíase; Doença renal policística; Cistinúria; DRC; Relato de caso.

INTRODUCTION

Cystinuria is a genetic disease that occurs due to an alteration in the intestinal and renal transport of cystine, arginine, lysine and ornithine, leading to increased urinary excretion of these amino acids and formation of calculi in the urinary tract causing symptoms such as colic, urinary tract infection and kidney failure.¹

Cystinuria is the most common cause of monogenic kidney stones and represents 1% of kidney stones in adults and 8% in children.²

Polycystic kidney disease (PKD) is the most common inherited kidney disease. It can present itself in its autosomal dominant form (ADPKD), which usually manifests in adulthood, or in its recessive form (ARPKD)

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usually begins early in childhood. However, there can be an overlap between the two forms.³ The PKD progresses with multiple liquid-filled cysts in the kidneys, but may also affect other organs and contributes to the formation of nephrolithiasis.⁴

We report a case of a patient with PKD and Cystinuria, an interesting association, only being described in three other patients in the medical literature.^{5,6}

CASE REPORT

We report a 38-year old male presented with renal colic and elimination of kidney calculi since he was 25 years old. He had no family history of renal disease, nephrolithiasis or polycystic kidney disease. At age 26, he began follow-up at the nephrolithiasis outpatient clinic, when the diagnosis of nephrolithiasis was established. Two years later, laboratorial investigation showed urine sediment with hexagonal-shaped crystals consistent with cystinuria (Figure 1) and elevated levels of urinary cystine (450mg/day; upper reference level, 30mg/day). His serum creatinine level was 0.9mg/dL (79.6 μ mol/L). When he was 30 years old, a routine computed tomography incidentally revealed multiple bilateral renal cysts (Figure 2). The patient was treated conservatively with elevated hydric ingestion, juice and fruits, restriction of protein and sodium, potassium citrate therapy (40mEq/day) and D-penicillamine (1000mg/day). Our patient still had a few colic and stone passing episodes after the beginning of the treatment of cystinuria, but without relevant clinical significance. Nowadays, with 8 years follow-up, he remains asymptomatic with no alterations in renal function.

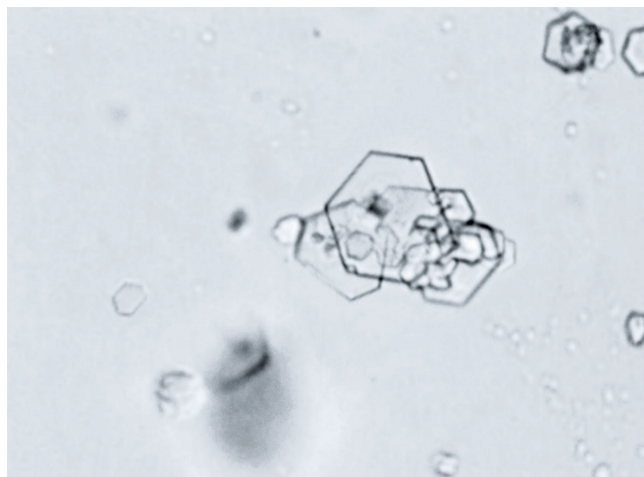


Figure 1. Hexagonal plate crystals in patient's urinary sediment.

DISCUSSION

Cystinuria is a rare genetic disorder associated with kidney stone formation. Mutations in the SLC3A1 gene on chromosome 2, the SLC7A9 gene on chromosome 19, or rarely both, have been identified as the genetic cause.⁷ Although pure cystine stones are more common among these patients, approximately 40% of stone formers may present mixed calculi.⁸ Characteristic hexagonal-shaped cystine crystals are pathognomonic and appear in 25% of cases in morning urinalysis.⁹ However, a definitive diagnosis of cystinuria requires a quantitative 24-hour urine test for cystine. Cystinuria patients generally excrete up to 100 mg/day of cystine.¹⁰

Treatment should be based on a conservative measure such as adequate diet, hydration and urinary alkalization. For refractory cases, thiol-based drug treatment may be indicated. The cystine is notoriously resistant to extracorporeal shock wave lithotripsy (ESWL).² The treatment is poorly tolerated by most patients and often ineffective requiring surgical approaches than other patients with nephrolithiasis. Chronic kidney disease and hypertension prevalence is much higher when compared to the general nephrolithiasis population.¹¹⁻¹³ For this reason, frequent clinical follow-up and cystine stones prevention are extremely important.

Polycystic kidney disease (PKD) is the most common inherited kidney disease. The main characteristic of

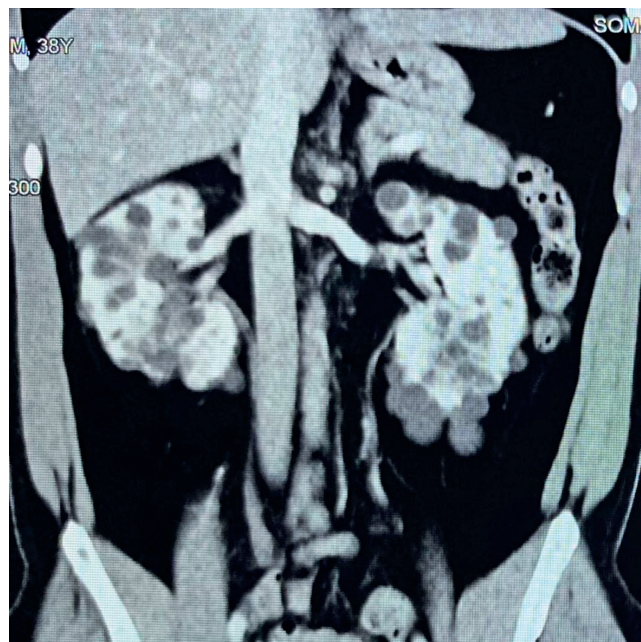


Figure 2. Computed tomography showing multiple kidney cysts bilaterally.

PKD is the presence of multiple kidney fluid-filled cysts, although other organs may also be affected. Polycystic patients are predisposed to nephrolithiasis, specially by calcium oxalate. Hepatobiliary alterations and other systemic disorders are not rare in these patients. Thus, the clinical picture of PKD can be heterogeneous, both from a genetic and phenotypic point of view. Single renal cysts are common and usually benign in adults. However, when bilateral or in children, a more advanced evaluation is required.¹⁴ Symptoms include abdominal fullness and pain, hematuria, urinary tract infections, early-onset hypertension, cerebral aneurysms and heart valve abnormalities.^{15,16}

The diagnosis is made by imaging examination, the most used method being ultrasonography, even though computed tomography can provide more data of prognostic value. This method can also be used to diagnose asymptomatic risk patients with a positive family history for PKD. Treatment includes lifestyle changes, hydration, a low-sodium and low-protein diet, and weight control. Control and treatment of hypertension and dyslipidemia may also be beneficial. Importantly, both PKD profiles (ADPKD and ARPKD) can progress to chronic kidney disease, requiring dialysis or kidney transplantation in adults and children.¹⁴

Although both diseases course with renal tubular alterations that lead to kidney stone formation, there is no genetic connection between them. Despite the high risk of nephrolithiasis in patients with PKD, these patients' stones are mostly related to hyperuricosuria and hypercalciuria, while cystine stones are uncommon.⁴

Love and Yeo (2009) reported a case of a patient with PKD who was incidentally found to have cystinuria, an interesting clinical observation not previously reported in the medical literature.⁵ In 2016, Sidhu et al. reported 2 pediatric patients diagnosed with polycystic kidney disease and cystinuria requiring surgical treatment.⁶

In conclusion, we believe that the coexistence of the two pathologies in a single patient may have occurred independently, due to its rarity. Although the association may be uncommon, patients with PKD who develop

kidney stones should undergo metabolic investigation including cystinuria. We reported a rare association of PKD and cystinuria.

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