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Unveiling Adult Polycystic Kidney Disease: Historical Perspectives and Evidence-Based Management Approaches

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Abstract

Background: Adult polycystic kidney disease is an important contributor to chronic renal failure, marked by a highly variable clinical trajectory and progression to chronic renal failure. Diagnosis typically relies on ultrasound imaging, with genetic testing being less commonly necessary. Management strategies aim to delay the onset of chronic renal failure or slow its progression, involving interventions such as antihypertensive medications, dietary protein restriction, and prompt treatment of urinary tract infections.

This paper aims to present the case of an Iraqi patient diagnosed early, prior to the onset of renal failure, and to outline evidence-based treatment options.

Patients and methods: A thirty-year-old female with recurrent urinary tract infections sought evaluation following her uncle's recent diagnosis of chronic renal failure due to adult polycystic kidney disease. Her uncle had developed progressive symptomatic uremia at age 52, accompanied by gradual hearing loss, a rare association with this condition. Her aunt had succumbed to chronic renal failure.

Results: The patient exhibited normotension and renal function tests revealed normal values. A renal ultrasound depicted normal-sized kidneys with multiple cysts observed bilaterally, with the largest measuring 3 centimeters, confirming the diagnosis of adult polycystic kidney disease.

Conclusion and expert opinion: This article delves into the realm of adult polycystic kidney disease, offering insights into its historical context, diagnostic methods, and evidence-based management strategies. Beginning with the earliest recorded case in history, the narrative progresses through key milestones in understanding the disease, emphasizing diagnostic techniques such as ultrasound imaging. The current evidence-based expert opinion suggests that the long-term use simvastatin plus octreotide-long-acting release monthly injection in patients with adult polycystic kidney disease to slow the growth of cysts and the deterioration in renal function. The use of tolvaptan can also be considered, but it is associated increased adverse effects such as thirst, polyuria, and hepatic injury.

Keywords: Adult polycystic kidney disease, early diagnosis, evidence-based therapies, expert opinion.

Introduction

Adult polycystic kidney disease is an important contributor to chronic renal failure, marked by a highly variable clinical trajectory and progression to chronic renal failure. Diagnosis typically relies on ultrasound imaging, with genetic testing being less commonly necessary. Management strategies aim to delay the onset of chronic renal failure or slow its progression, involving interventions such as antihypertensive medications, dietary protein restriction, and prompt treatment of urinary tract infections [1, 2, 3, 4].Stephen Báthory (Figure-1A), a Polish king, is the earliest recorded individual with adult polycystic kidney disease. After dying at about the age of 53 years, and during post-mortem procedures aimed at preserving his body as a mummy, his surgeon, Jan Zigulitz, assisted by Dr. Buccella, noted the enlarged, irregularly surfaced kidneys resembling those of a bull.

Figure-1A: Stephen Báthory (September 27, 1533-12 December 12, 1586), King of Poland and Grand Duke of Lithuania (1576-1586)

However, at that time, the king's death was not attributed to renal disease. In 1933, Franciszek Walter (Figure 1B), a professor from Krakow Medical School, convened a meeting of physicians and historians to analyze the abnormalities observed during the king's autopsy. It was concluded that the king succumbed to uremia resulting from polycystic kidney disease.

In 1793, Matthew Baillie (Figure 1C) distinguished the vesicular cysts characteristic of this disorder from hydatid cysts, coining the term "False hydatids of the kidney."

Figure-1B: Professor Franciszek Ksawery Walter (1885-1950)

Figure-1C: Matthew Baillie (October 27, 1761-September 23, 1823), a British physician and pathologist

In 1888, Félix Lejars (Figure-1D) from Paris emphasized that the cysts in this condition were present on both sides and named the condition “Polycystic kidney”.

Figure-1D: Félix Lejars from Paris

In 1983, Szabó and colleagues highlighted the utility of diagnostic ultrasound for early detection of polycystic kidney disease, a practice increasingly recognized as reliable [2].

This paper aims to present the case of an Iraqi patient diagnosed early, prior to the onset of renal failure, and to outline evidence-based treatment options.

Patients and methods

A thirty-year-old female with recurrent urinary tract infections sought evaluation following her uncle's recent diagnosis of chronic renal failure due to adult polycystic kidney disease. Her uncle had developed progressive symptomatic uremia at age 52, accompanied by gradual hearing loss, a rare association with this condition. Her aunt had succumbed to chronic renal failure.

Results

The patient exhibited normotension and normal echocardiographic findings. Renal function tests revealed normal values (serum creatinine: 0.6 mg/dL, blood urea: 19 mg/dL). A renal ultrasound (Figure-2) performed on January 6, 2024, depicted normal-sized kidneys with typical texture and cortical thickness. Multiple cysts were observed bilaterally, with the largest measuring 3 centimeters, confirming the diagnosis of adult polycystic kidney disease.

Discussion

Management strategies for adult polycystic kidney disease focus on delaying the onset or slowing the progression of chronic renal failure through interventions such as antihypertensive therapy, dietary modifications, and prompt treatment of urinary tract infections.

In 1996, Maschio et al. reported a three-year placebo-controlled study which included 583 patients with renal insufficiency resulting from a variety of diseases, and included 64 patients with adult polycystic kidney disease. Three hundred patients were treated with an angiotensin-converting-enzyme inhibitor, benazepril, while 283 patients were treated with placebo.

After three years, thirty-one patients who received benazepril experienced doubling of the base-line serum creatine level or required for dialysis, while fifty-seven patients who received placebo experienced doubling of the base-line serum creatine level or required for dialysis (P<0.001). However, the study found that although benazepril had a protective effect against the progression of renal insufficiency in several kidney diseases, it was not effective in polycystic kidney disease [5].

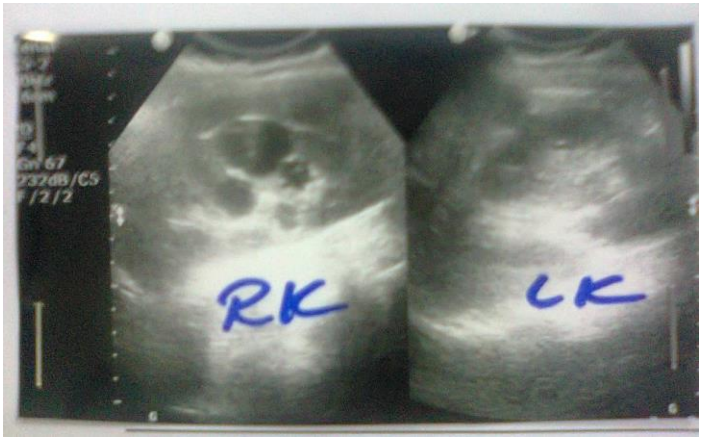

Figure-2: Renal ultrasound confirming the diagnosis of adult polycystic kidney disease

In 2001, van Dijk et al. from the Netherland emphasized that experimental animal studies showed that Hydroxymethylglutaryl-CoA (HMG-CoA) reductase inhibitors, the statins can retard the progression of chronic renal insufficiency. They reported a clinical study which included ten patients adult polycystic kidney disease who had normal cholesterol level whom were treated in random order for one month with simvastatin 40 mg a day or placebo.

Simvastatin treatment was associated with marked increase in glomerular filtration rate and, effective renal plasma flow (P<0.05). Treatment was also associated with a marked decrease in cholesterol level (P<0.001). van Dijk et al suggested that simvastatin treatment can improve renal function in patients with adult polycystic kidney disease by improving renal plasma flow, possibly through improving endothelial function [6].

In 2005, Piero Ruggenenti from Italy and his research group proposed somatostatin as a therapeutic avenue, theorizing its inhibitory effect on fluid secretion within renal cysts, thereby impeding cyst expansion. The renal cysts in adult polycystic kidney disease are filled with fluid secreted mostly by the tubular epithelium lining the cysts through secondary chloride transport.

They thought that the fluid filling can possibly be inhibited by somatostatin resulting in shrinkage of the cysts. They reported a six-month cross-over, placebo-controlled study which included patients with mild-to-moderate renal insufficiency caused by autosomal-dominant adult polycystic kidney disease. Twelve patients were treated with octreotide-long-acting release (A long-acting somatostatin) 40 mg intramuscularly four weekly.

The increase in renal volume was markedly lower in patients treated with somatostatin than in patients who received placebo. Ruggenenti and his research group reported that the use of somatostatin for six months was well tolerated and safe, and can slow the expansion of renal volume in adult polycystic kidney disease. Therefore, somatostatin treatment can inhibit growth of smallest cysts.

Their study demonstrated reduced renal volume expansion in patients with adult polycystic kidney disease treated with octreotide-long-acting release [7].

In 2010, Anna Caroli from Italy and her research group reported a post hoc analysis of the study of Piero Ruggenenti from Italy and her research group reported that octreotide treatment also reduced liver volumes in the patients with adult polycystic kidney disease [8].

Also in 2010, Marie C Hogan from the United States and her research group reported favorable outcomes with octreotide treatment in patients with autosomal dominant

polycystic kidney and liver disease, with reductions in liver and kidney volumes.

They reported a one-year placebo-controlled study which included 42 patients with autosomal dominant polycystic kidney and liver disease (34 patients had polycystic kidneys and 8 had polycystic liver disease). Twenty-eight patients were treated with octreotide-long-acting release depot (A long-acting somatostatin analogue) up to 40 mg every four weeks (+/-5 days), and fourteen patients received placebo.

Octreotide treatment was associated with reduction in liver volume, while liver volume almost remained unchanged in the patients who received placebo (P=0.048). Octreotide treatment prevented the increase kidney volume, while the patients who received placebo experienced an increase in kidney volume (P=0.045). Changes in GFR were similar in both groups. Octreotide was found to be well-tolerated and was considered to have acceptable side effects.

In 2011, Maria V Irazabal from the United States and her research group emphasized the preliminary evidence from experimental studies suggesting that tolvaptan (Specific vasopressin receptor antagonists) can retard disease progression in polycystic kidneys animal models.

They reported a study which included twenty patients with adult polycystic kidney disease which showed that tolvaptan treatment can markedly decrease total kidney volume and renal cyst volume especially of larger cysts when the renal function is maintained. The effect of tolvaptan was attributed to inhibition of V (2)-driven adenosine cyclic 3, 5-monophosphate generation and to the aquaretic effect (Promotion of the excretion of water without electrolytes) [10].

Also in 2011, Higashihara et al. from Japan showed highlighted tolvaptan's efficacy in cyst growth retardation in adult polycystic kidney disease in 2011, despite concerns regarding its long-term safety [11].

In 2012, Torres et al from the United States and their collaborators reported a placebo-controlled study which included 1445 patients adult polycystic kidney disease, and showed that a three-year tolvaptan treatment retarded the increase in total renal volume and slowed the loss of renal function, but tolvaptan was associated with a higher discontinuation rate than placebo because of the occurrence of adverse side effects [12].

In 2013, Caroli et al. from Italy and their collaborators reported a three-year placebo-controlled study which included 75 patients with adult polycystic kidney disease. 38 were treated with two 20 mg intramuscular injections of octreotide-long-acting release, and 37 patients received placebo.

At one year, MRI studies showed that octreotide-long-acting release treatment was associated with much less increase in total kidney volume. It was possible to study thirty-five patients treated with octreotide-long-acting release, and thirty-five patients who received placebo with MRI at three years. Octreotide-long-acting release treatment was again associated with less increase in total kidney volume

Thirty-seven patients treated with octreotide-long-acting release, and thirty-two patients received placebo experienced at least one adverse effect (p=0·16). Patients with serious adverse effects were similarly distributed in the treated patients and in the patients received placebo. Nevertheless, four patients treated with octreotide-long-acting release experienced acute cholecystitis or cholelithiasis [13].

In 2019, Norberto Perico from Italy and his research group reported octreotide's efficacy in slowing cyst and kidney growth and delaying progression to end-stage renal disease, with fewer serious infections compared to placebo. They reported a study which included 100 patients adult polycystic kidney disease who had glomerular filtration rate between 15 to 40 ml/min/1.73 square meters.

Fifty-one patients were treated with two intramuscular injections of 20 mg octreotide-long-acting release every four weeks for 3 years, forty-nine patients received placebo.

The study showed that octreotide-long-acting release treatment can slow growth of cysts and kidneys and slow the progression to end-stage renal disease. Of 63 patients with chronic kidney disease stage 4, three of the patients treated with octreotide-long-acting release, and eight of the patients received placebo developed end-stage renal disease (P = 0.036). Three of the patients who received placebo experienced a serious renal cyst rupture/infection and one patient developed a serious urinary tract infection/obstruction. However, only one patient of the patients treated with octreotide-long-acting release experienced a serious infection of renal cyst [14].

In 2023, Lu et al. from China conducted a meta-analysis affirming tolvaptan's efficacy in preserving renal function and reducing complications in adult polycystic kidney disease, notwithstanding increased adverse effects. Their meta-analytic study included 13 placebo-controlled studies which included 3575 patients with adult polycystic kidney disease. The study showed that tolvaptan treatment was associated with slowing of the deterioration in renal function, slowing the increase in total kidney volume, and reduction of complications including renal pain, urinary tract infections, hematuria, and hypertension.

However, tolvaptan increased adverse effects such as thirst, polyuria, and hepatic injury [15].

Conclusion and expert opinion

This article delves into the realm of adult polycystic kidney disease, offering insights into its historical context, diagnostic methods, and evidence-based management strategies. Beginning with the earliest recorded case in history, the narrative progresses through key milestones in understanding the disease, emphasizing diagnostic techniques such as ultrasound imaging.

The current evidence-based expert opinion suggests that the long-term use simvastatin plus octreotide-long-acting release monthly injection in patients with adult polycystic kidney disease to slow the growth of cysts and the deterioration in renal function. The use of tolvaptan can also be considered, but it is associated increased adverse effects such as thirst, polyuria, and hepatic injury.

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