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Managing Cyst Infections in ADPKD: An Old Problem Looking for New Answers

Ahsan Alam, and Ronald D. Perrone

[+] Author Affiliations

Correspondence:
Ronald D. Perrone, MD, Division of Nephrology, Tufts Medical Center, 800 Washington Street, Hospital Box 391, Boston, MA 02111. Phone: (617) 636-2372; Fax: (617) 636-8329; E-mail: rperrone@tuftsmedicalcenter.org

Kidney and liver cyst complications are frequent in patients with autosomal dominant polycystic kidney disease (ADPKD). It has been estimated that 30 to 50% of patients with ADPKD experience some form of kidney infection during their lifetime (1,2). Patients may experience symptoms from cyst infections, cyst hemorrhage, or pain from ruptured or expanding cysts.

The clinical determination of an infected kidney cyst may be difficult in a patient with ADPKD. The typical presentation of fever and abdominal pain carries a broad differential that includes pyelonephritis, infected kidney stones, perinephric or perihepatic abscess, cyst hemorrhage, or even intra-abdominal pathology unrelated to ADPKD. Conventional imaging with ultrasound, computed tomography, or magnetic resonance imaging scan may not be definitive in isolating the location of infection or even in differentiating cyst infection from cyst hemorrhage or pyelonephritis (3). A urine culture is often negative because kidney cysts become separated from their parent nephron, and one must rely more on blood cultures or cyst fluid aspiration when they can be obtained.

The accurate diagnosis of cyst infection is of great importance, because it can influence the prompt initiation of antibiotics (particularly one that is widely known to penetrate cyst membranes), it can determine the need for extending the duration of antibiotic therapy, or it can guide toward percutaneous or surgical drainage when empiric therapy has been ineffective. An additional concern is the delivery of antibiotics to an infected cyst, because drug delivery becomes independent of glomerular filtration when cysts are detached from the renal tubules.

For decades, reports have documented various challenges in the successful diagnosis and treatment of infected cysts in ADPKD. Unfortunately, our scientific understanding has not extended very far beyond the level of case series and expert opinion. There has been a paucity of clinical studies and a void of randomized clinical trials in the published literature. Implementing an evidence-based strategy becomes a thorny issue, and additional data are a valuable asset to the field.

In this issue of *CJASN*, Sallée *et al.* (4) take on the study of this important and relatively common complication of cyst infection in ADPKD. The authors retrospectively reviewed 389 hospital admissions during a 10-yr period at their hospital. They were able to assemble a cohort of 31 patients with 41 episodes of cyst infection, suggesting that cyst infection accounts for 11% of all hospital admissions of patients with ADPKD. They highlight the complexity of diagnosing and managing renal and hepatic cyst infections. They found that microbiologic diagnosis from urine or even blood is far from universal, particularly in cases of renal cyst infections. The authors also present their criteria for a "likely" diagnosis of cyst infection. This operational definition uses the clinical features of abdominal pain, fever >38°C, and a C-reactive protein level >50 mg/L. They report that these factors are in keeping with criteria commonly used in clinical practice, and it certainly deserves consideration after further validation. Whether this definition performs as well for patients who have ADPKD and are on hemodialysis, in which C-reactive protein may be elevated for other reasons, remains to be tested. Overall, the findings in their study reinforce previous

experiences that show fluoroquinolones, either alone or in combination with another antibiotic, provide the most favorable treatment response (5,6). They also note that larger hepatic cysts often required d ıge in addition to antibiotics (7), and positron emission tomography (PET) scans may provide valuable diagnostic information in the patient whose ailment is difficult to diagnose (8,9).

There are certainly limitations with this study. The design is limited to a retrospective examination of patients who were hospitalized at a single institution. Whether their observations generalize to other cohorts with ADPKD or even ambulatory patients with less severe or more occult presentations remains to be addressed. In this study design, we cannot evaluate the performance of a diagnostic test without considering which factors led the physician to order that test. Clinical judgment may not always follow a systematic diagnostic algorithm. The authors suggest in their discussion that a PET scan may be the optimal first-line tool in detecting cyst infections in ADPKD. As sensible as this may sound, it demands further and more rigorous scientific testing. Conventional diagnostic test performance characteristics, such as sensitivity, specificity, and likelihood ratios, need to be understood, and only then can we appropriately integrate this procedure into routine clinical practice. Other modalities such as tagged white blood cell scans have also been used, and it is not clear how this would perform in comparison (10).

The article by Sallée *et al.* (4), nevertheless, plays an important role in adding to the existing literature and attempts to address the basic questions that still exist. Have the risk factors for cyst infection changed over time, and are they modifiable? With ultrasound, computed tomography, magnetic resonance imaging, tagged white blood cell, and PET scans at the clinician's disposal, which test is most appropriate for diagnosis, and in which settings does one outperform another? Upon diagnosis, which antibiotic should be chosen as empiric therapy? Studies have shown that lipid-soluble antibiotics penetrate into cysts better as compared with lipid-insoluble ones. How well (or poorly) do newer classes of antibiotics penetrate kidney and liver cysts, and how should they fit into our existing armamentarium? What is the impact of recently emerging highly antibiotic-resistant bacterial strains? When should interventional approaches be implemented? How does management affect longer term outcomes? These and many other questions still have to be addressed and reflect the challenges in studying this field.

Recent clinical research surrounding ADPKD has been centered on novel and promising therapeutics aimed at slowing cyst initiation or expansion or biomarkers of ADPKD disease progression, such as volumetric measures of kidney size or genetic factors. These have been exciting areas of scientific advancement and perhaps focus attention away from “old” problems that seem to be resolved. Nevertheless, cyst complications are arguably as consequential to patients as any other. We have much to learn about the treatment of patients with ADPKD and cyst infections. The challenge is up for the taking.

Disclosures

None.

Footnotes

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See related article, “Cyst Infections in Patients with Autosomal Dominant Polycystic Kidney Disease,” on pages 1183–1189.

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