



Polycystic kidney disease: Molecular understanding dictating management

Sometimes, something triggers a flashback to a patient from long ago. As I listened to Dr. William Braun's medicine grand rounds lecture on polycystic kidney disease (PKD), which is presented in this issue of the *Journal* (page 545), I remembered a time in the early 1980s when I was a resident in the University of Pennsylvania emergency room, admitting a faculty member's spouse who had fever, flank pain, hypotension, and a normal urinalysis.

Dr. Braun is an iconic figure in Cleveland Clinic medicine. He is the consummate internist, nephrologist, and transplantation physician, but he is also a critical thinker. He strives to understand (and explain) what underpins our clinical observations and therapeutic decisions. He asks the "why" questions. As he ticked through the manifestations of PKD and the diagnostic dilemmas that arise in taking care of these patients, and then transitioned into explaining the interesting though incomplete current molecular understanding of this relatively prevalent genetic disorder, I heard many of the same questions I had asked myself 30 years ago. But this time I was getting some answers.

How can one be certain a cyst is infected? How do these cysts form and expand without apparent communication with the tubular lumens? (Intracystic bleeding and infection may not be reflected in the urinalysis, although the organism isolated from infected cysts is frequently *Escherichia coli*.) If renal cysts are formed from tubular epithelial cells that are preprogrammed to self-organize into lumen-like structures, how does the same genetic defect predispose to cyst formation in organs such as the liver, or to aneurysms in blood vessels in the brain? Why does the disease take so long to express itself, and why is its expression so variable?

The patient did well during his hospital stay 30 years ago. As I recall, he had staphylococcal bacteremia with an infected cyst. We discussed the clinical scenario but had no suggestions as to how to prevent the growth of what we now know are about 60 subclinical cysts for every one that we recognize. And we certainly didn't discuss the idea that the disease process may be partially driven by dysfunctional nonmotile cilia that should respond to urine flow by appropriately directing regeneration and proliferation of renal tubular cells.

I love getting answers to questions that I didn't know enough to ask.

BRIAN F. MANDELL, MD, PhD
Editor in Chief

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