Chapter 5

Chronic kidney pain in ADPKD, a case report of successful treatment by catheter-based renal denervation

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Abstract

Chronic pain is a common concern in patients with autosomal dominant polycystic kidney disease (ADPKD). We report what to our knowledge is the first catheter-based renal denervation procedure in a patient with ADPKD resulting in successful management of chronic pain. The patient was a 43-year-old woman whose chronic pain could not be controlled by pain medication or splanchnic nerve blockade. Transluminal radiofrequency renal denervation was performed as an experimental therapeutic option with an excellent result, indicating that this procedure should be considered for chronic pain management in ADPKD.
Introduction

Up to 60% of all patients with autosomal dominant polycystic kidney disease (ADPKD) experience some pain, which in some individuals can be debilitating enough to lead to decreased psychosocial functioning and limitation in daily activities (1). Chronic pain in ADPKD may be multifactorial, and can be caused by cystic enlargement of the kidneys resulting in distension of the renal capsule; by pressure on adjacent tissues; or may be unrelated to ADPKD. Bajwa et al. introduced a stepwise approach for effective pain management in ADPKD, beginning with non-pharmacological therapies, such as ice pads and psychological behavioral modification, stepping up to non-opioid analgesics, opioids, transcutaneous electrical nerve stimulation, and finally surgical procedures (2). Several surgical procedures, such as cyst aspiration and cyst fenestration, have been tried with success to relieve ADPKD-related pain. However, pain relief is often only temporary, and aspiration and fenestration are associated with a high risk for infection (2). Renal denervation also has been proposed for patients with intractable ADPKD-related pain and was performed by laparoscopic and thoracoscopic procedures with satisfactory results (3, 4). Recently a catheter-based percutaneous transluminal method has been introduced to ablate efferent and afferent renal sympathetic nerve fibres. This procedure now is applied mainly in patients with therapy-resistant hypertension.

We report a case of a patient with ADPKD and chronic pain who underwent catheter-based renal denervation for pain treatment, with an excellent result.

Case report

A 43-year-old woman with ADPKD was referred to our tertiary-care hospital with a history of pain that was difficult to treat since 2008. The diagnosis of APDKD was made based upon the revised Ravine criteria (5).

At presentation in May 2013, the patient reported progressive abdominal pain, in particular on the left side in the epigastric region with a visual analogue scale score ranking 6-8 of 10. The pain was constant and described as stabbing and nagging, with radiation toward the left upper abdomen. On the right side, she also experienced pain, but this was less intense. Because of the pain, she could not sleep on her left side and woke up at least 5 times every night, leading to progressive fatigue. Inspiration increased her pain sensation, suggesting a visceral origin. Defecation and micturition did not influence pain, whereas exercise worsened it. Her symptoms were debilitating, influencing her social life and leading to an inability to work full-time. For blood pressure control, the patient used losartan, 100 mg, once daily; amlodipine, 10 mg,
once daily; and hydrochlorothiazide, 25 mg, once daily, on which her mean daytime blood pressure was 139/95 mm Hg during a 24-hour ambulatory blood pressure measurement.

Previous attempts at pain control using non-pharmacologic therapies or acetaminophen had not been effective. Buprenorphine patches (regulated dose release, 10 µg/h) were tried, but the pain remained and the patient experienced side effects of drowsiness and progressing fatigue that precluded dose increases. Two years earlier, a successful temporary blockade of the left splanchnic nerve had been performed for pain control. Therefore a long-term neurolytic nerve block with phenol was given on both sides with some success. Unfortunately, after 2 months the pain returned with the same intensity as before. A second long-term neurolytic nerve block was attempted with only temporary limited pain relief. In the patient’s eyes, the best option was now to remove her left kidney, although this procedure might shorten her time to end-stage renal disease.

Spiral computed tomography was performed and showed the presence of multiple bilateral renal and hepatic cysts, leading to enlargement of kidneys and liver (Figure 1). The patient’s right kidney volume was 1142 mL; left kidney volume, 1472 mL; and liver volume, 2004 mL. These images did not show cyst bleeding, cyst infections, kidney stones or extra-renal abnormalities that might cause pain. This scan also showed no signs that her kidneys compressed adjacent tissue, indicating that this theoretical
cause of intractable pain also was less likely. Given her serious situation, we decided to try catheter-based renal denervation of the afferent sensory nerves using the Simplicity Catheter System, a 6F-compatible single-use radio frequency (RF) probe. Before introducing the RF probe, a renal angiogram was performed and showed no contra-indications for the procedure. Subsequently, the system was introduced into the renal artery and the catheter electrode was positioned in contact with the vessel wall at the most distal location possible. The catheter was connected to an automated RF generator, and 5 applications of RF energy in a spiral pattern along the renal artery from distal to proximal and with 5-mm interspaces were performed (Figure 2).

Figure 2. Angiography of the renal denervation procedure. The solid line represents the Simplicity Catheter System (a 6F-compatible, single-use radio frequency probe) that was introduced into the renal artery. The catheter electrode is positioned at the most distal location possible in the renal artery.

Immediately after the procedure, the pain was different and more intense, which was thought to be the result of using too low a dose of fentanyl during the procedure. The patient was discharged without complications on the day after the procedure. In the following days, her pain completely disappeared on the left side and she needed
only half the dosages of her pain medication. Because of this satisfactory result, the patient requested to denervate the right kidney as well. Four months later, a rightsided renal denervation was performed. The procedure was uncomplicated and she was pain free immediately. Moreover, her blood pressure had decreased to 117/79 mm Hg. Therefore, we reduced her antihypertensive medication before discharge the next day.

Four months later, the patient was still pain free, reported a visual analogue scale score of 0 of 10, did not use pain relief medication and had resumed her normal working and social life. Office blood pressure had decreased from a pre-intervention level of 145/96 mm Hg to 120/75 mm Hg, even though her antihypertensive medication had been reduced from 3 to 2 agents. Her eGFR had not changed (76 mL/min/1.73m² pre-intervention vs. 78 mL/min/1.73m² post-intervention).

Discussion

Chronic abdominal pain in ADPKD can be directly or indirectly related to the cystic enlarged kidneys (2). The renal nerves, which carry both sympathetic efferent and sensory afferent nerve fibers, are distributed circumferentially in the adventitia around the renal artery. Two previous case reports have described the possibility of renal denervation for direct ADPKD-related pain by thoracoscopic or laparoscopic procedures (3, 4). However, these invasive techniques are difficult to perform and require surgical experience, which is difficult to gain because there is only a limited number of patients with intractable ADPKD-related pain. We performed transluminal RF renal denervation as an alternative procedure to surgery with an excellent result.

Recent studies demonstrated the beneficial effect of renal denervation for treating resistant hypertension, heart failure and insulin resistance (6). Catheter-based renal ablation may be effective for pain-related syndromes as well. This procedure has been shown to be successful in a single patient with the loin pain haematuria syndrome (7). One case report suggested that catheter-based renal denervation also might have a beneficial effect on pain in cystic disease (8). However, in this case, the procedure was performed for therapy-resistant hypertension and the patient only had several one-sided renal cysts, rather than ADPKD (8).

The present evidence suggests that this procedure is safe up to 3 years after intervention (9). Another reason aside from pain management to apply renal denervation in patients with ADPKD is to treat hypertension. Hypertension in patients with ADPKD is associated with higher sympathetic activity (10-12). This indicates that
patients with ADPKD could benefit from renal denervation for hypertension treatment. Our patient’s blood pressure control improved after the procedure. Contra-indications for this procedure are a history of renal artery stenting, renal artery stenosis > 50%, the presence of multiple arteries, or the renal artery having an average diameter ≤ 4 mm or being < 20 mm long. Because contrast is used during the procedure, local prevailing guidelines to prevent contrast nephropathy should be followed.

In conclusion, this case report suggests that percutaneous catheter-based renal denervation may be a simple and effective procedure for pain relief in selected patients with ADPKD in whom chronic pain is likely to be related directly to the increase in size of the kidneys and for whom oral analgesics did not result in effective pain treatment. Further research will have to be performed to indicate the place that renal denervation could have in the stepwise approach for effective pain management in ADPKD.

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Conflicts of interest
The authors declare that they have no relevant financial interests.
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References

Renal denervation in ADPKD