The Bench to Bedside Transition (Exceptional Cases)

Percutaneous renal sympathetic nerve ablation for loin pain haematuria syndrome

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ABSTRACT

Loin pain haematuria syndrome (LPHS) is a severe renal pain condition of uncertain origin and often resistant to treatment. Nephrectomy and renal autotransplantation have occasionally been performed in very severe cases. Its pathogenesis is controversial. A 40-year-old hypertensive lady was diagnosed with LPHS after repeated diagnostic imaging procedures had ruled out any renal, abdominal or spinal conditions to justify pain. Notwithstanding treatment with three drugs, she had frequent hypertensive crises during which the loin pain was dramatically exacerbated. Vascular causes of the pain and hypertension were investigated and excluded. Her renal function was normal. The patient was referred to a multidisciplinary pain clinic, but had no significant improvement in her pain symptoms despite the use of non-steroidal anti-inflammatory drugs, adjuvant antidepressants and opioid-like agents. The pain and the discomfort were so severe that her quality of life was very poor, and her social and professional activities were compromised. Nephrectomy and renal autotransplantation have occasionally been performed in these cases. Since visceral pain signals flow through afferent sympathetic fibres, we felt that percutaneous catheter-based radiofrequency ablation of the renal sympathetic nerve fibres (recently introduced for the treatment of drug-resistant hypertension) could be valuable for pain relief. We treated the patient with radiofrequency ablation (Medtronic Symplicity Catheter) applied only to the right renal artery. After a 6-month follow-up, the patient is pain free and normotensive with all drugs withdrawn. She has experienced no hypertensive crises in the meantime. This observation suggests that percutaneous sympathetic denervation could prove to be an effective mini-invasive strategy for the treatment of chronic renal pain, and LPHS in particular.

INTRODUCTION

Loin pain haematuria syndrome (LPHS) is a severe renal pain of uncertain origin which is often resistant to treatment. Young women are generally affected and the flank pain may be either unilateral or bilateral.

Its pathogenesis is controversial. Many hypotheses have been proposed to explain the pain and haematuria of LPHS: renal vascular disease or vasospasm, hypersensitivity and complement activation on arterioles, coagulopathy, venocalyceal fistula, abnormal ureteral peristalsis, hypercalcaemia, hyperuricosuria and intratubular deposition of calcium or uric acid microcrystals, IgA glomerulonephritis and thin membrane glomerular disease [1]. The medullary sponge kidney rarely can also manifest with LPHS [2]. However, in most cases, no precise diagnosis can be advanced and psychological factors have been suggested as having a key role in LPHS, with LPHS proposed to be a type of somatoform pain disorder [3].
The treatment of LPHS is based on an interdisciplinary approach consisting of drugs (opioids, non-opioid analgesics, anti-epileptic drugs, antidepressants, muscle relaxants etc.), and physical and behavioural medicine interventions. For cases of intractable LPHS not responding to these conservative measures, more aggressive/interventional approaches have been proposed.

While in exceptional cases, the last resort for the management of LPHS has been nephrectomy; since visceral renal denervation is a normal consequence of transplantation which leads to an insensitive kidney with no significant alteration in renal function; renal autotransplantation has also been used [4].

The perception of renal pain signals flows through afferent Aδ and C sympathetic fibres of the adventitia of the renal arteries, ascending the renal and intermesenteric plexi, the lowest splanchnic nerve and finally reaching the medial medullary reticular formation by the way of L2–T11 dorsal roots [5]. Based on this anatomical knowledge, less invasive surgical procedures for renal denervation such as laparoscopic denervation [6] and videothoracoscopic splanchnicectomy [7] have also been used, achieving at least a temporary pain relief (see also for a review [1]).

However, some of these approaches may complicate with severe orthostatic hypotension, sphincter incontinence, sexual dysfunction, paradoxical excessive sweating and renal artery stenosis [8].

The percutaneous catheter-based radiofrequency ablation of the adventitial renal sympathetic nerve fibres has been recently introduced for the treatment of drug-resistant hypertension [9, 10]. This technique uses relatively low power and precisely focused radiofrequency bursts of 8 W energy. Unlike surgical methods to renal denervation, this endovascular approach is selective, less invasive and can be carried out speedily under local anaesthesia, with a very modest peri-procedural risk.

We were following-up a patient with LPHS who was resistant to conservative measures and the condition had a severe impact on her quality of life. We thought that the percutaneous renal sympathectomy would have been effective in relieving pain in LPHS and treated the patient accordingly.

**CASE REPORT**

In 2011, a 40-year-old lady with microscopic haematuria and an intractable, severe, sometimes shooting pain against a background dullness in the right loin, which did not irradiate to the groin, came to our attention and was diagnosed with ‘LPHS’ after repeated diagnostic imaging procedures using different techniques had ruled out any renal, abdominal or spinal conditions to justify this pain. Her renal function was normal. She had passed a calcium oxalate renal stone in 2004. Two years later, she developed hypertension and chronic loin pain. Notwithstanding treatment with three drugs, she had frequent hypertensive crises during which the loin pain was dramatically exacerbated. Vascular causes of the pain and hypertension were investigated and ruled out by repeated renal angiograms. Endocrine causes of hypertension, including pheochromocytoma, were also excluded. She denied the use of oral contraceptive. None of her first-degree relatives were hypertensive. A contrast phase microscopy of the urine sediment showed isomorphic erythrocytes which, together with normal microalbuminuria (10–15 mg/24 h), was considered a sufficiently good evidence to rule out a glomerular disease. The search for a metabolic risk of renal stones was negative. In particular, the 24-h urine excretion of calcium, phosphate, oxalate, citrate and uric acid was normal as well as the pH of first morning urine. Following an episode of macroscopic haematuria and severe right loin pain, ureteroscopy of the right urinary district was performed, with negative results.

In the end, the only ‘abnormality’ identified was a slightly smaller right kidney (longitudinal diameter 9.0 cm versus 10.5), which remained stable over an observation period of 6 years with a constant separate renal function ($^{99m}$Tc-MAG3 renography, 40 versus 60%).

We suggested a formal psychiatric assessment, but the patient refused. She was referred to a multidisciplinary pain clinic, but had no significant improvement in her pain symptoms, despite the use of non-steroidal anti-inflammatory drugs, adjuvant antidepressants and opioid-like agents.

The pain and the discomfort were so severe that her quality of life was very poor, and her social and professional activities were compromised. She suggested that we subject her to nephrectomy which we denied, essentially because of the preserved renal function; however, we offered her a percutaneous renal sympathectomy. The patient signed an informed consent to undergo the procedure.

The suitability of the patient’s renal artery anatomy was checked on one previous computed tomography. The patient was treated with radiofrequency ablation (Medtronic Symplicity Catheter) applied only to the right renal artery. Percutaneous femoral access under local anaesthesia was used to introduce the catheter and selective tight renal artery catheterization was performed and the tip of the radiofrequency probe was applied to the arterial wall, in a zone close to the renal hilum, under radiographic and impedance control. Six 2 min long 8 W radiofrequency energy ablations, along the length of the right renal artery, were applied. At the end of the procedure, a global angiogram of the aorta and the renal artery was obtained, to check the integrity of the renal artery and parenchyma.

Few parietal changes of the artery at the sites of ablation were observed as usual after renal radiofrequency denervation which do not have pathological significance.

Recovery was rapid and pain vanished since the first day. Blood pressure was also normalized. After a 6-month follow-up, the patient continues to be pain free, ranking her pain ‘1’ on a scale 1 to 10. She is also normotensive with all drugs withdrawn and has experienced no hypertensive crises in the meantime. Renal function is normal, and separate renal function has not changed from values obtained before renal sympathectomy.

**DISCUSSION**

To our knowledge, this is the first case of an LPHS patient with intractable disabling chronic kidney pain in whom percutaneous, endoarterial renal sympathectomy was performed and effectively relieved pain. LPHS is a mysterious condition...
condition which unfortunately may not respond to usual conservative measures (analgesic strategies, physical medicine and behavioural medicine interventions).

Its vague pathogenesis and pathological substrate, together with non-validated diagnostic criteria and lack of optimal treatment strategies, have led to the consideration of LPHS as a type of somatoform pain disorder [3]. However, the kidney contains mechanoreceptors and chemoreceptors that evoke a number of reno-renal and cardiovascular reflexes through afferent Aδ and C sympathetic fibres of the adventitia of the renal arteries [5]. These fibres are also involved in causing the pain of renal disease [5].

Since the increased afferent activity of renal sympathetic nerves contributes to hypertension [11], in those cases in whom despite multidrug therapy blood pressure is suboptimally controlled, the interruption of the renal sympathetic fibres has been recently investigated with promising results [9, 10].

As the perception of renal pain signals flows through the same sympathetic fibres in the adventitia of the renal arteries, we applied the same technique in our patient and successfully treated her disabling pain. Although we did not investigate sympathetic activity before and after the procedure, since hypertension was also cured, we guess that the right renal afferent activity actually decreased. Most rewarding, the hypertensive crises associated with exacerbation of the flank pain completely subsided. Since it was virtually impossible to understand the timing of pain exacerbations in respect to hypertensive crisis, we cannot rule out that hypertensive crisis were a mere reaction to pain. However, we may speculate that some biological mechanisms (inflammation, ischaemia, stretch etc.) occurring only inside the right kidney was overdriving the sympathetic activity causing both pain and increased blood pressure. Although we do not have any direct proof of that, this seems to us a plausible explanation for the unexpected normalization of blood pressure too after just a single kidney sympathectomy.

Our observation lends support to the idea that the LPHS has a true biological bases and that depression, anxiety and somatoform traits are probably superimposed.

Percutaneous renal syngathectomy could also be valuable in other chronic renal pain conditions (in particular, adult polycystic kidney disease) with the advantage of a mini-invasive approach, not requiring general anesthesia at odds with other techniques of renal denervation.

The long-term pain relief from renal denervation for LPHS may not hold up over time since sympathetic reinnervation to the kidney is conceivable as has been shown in the transplanted heart. However, regrowth of sympathetic renal fibres has not been shown in patients [12], and in subjects who underwent renal sympathetic denervation, the reduction in blood pressure was still observed after a 2-year follow-up [13].

CONCLUSIONS

This case report suggests that percutaneous sympathetic denervation could prove an effective mini-invasive strategy for the treatment of chronic renal pain, and LPHS in particular. It also implies that this patient’s pain and hypertension shared some causative right renal kidney mechanism.

CONFLICT OF INTEREST STATEMENT

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REFERENCES


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