Renal autotransplantation in patients with loin pain–hematuria syndrome

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Objective: To determine if renal autotransplantation is an effective treatment for the loin pain–hematuria syndrome.

Design: Retrospective chart review.

Setting: Tertiary care referral centre in Manitoba.

Patients: Four patients referred for diagnosis and management of loin pain–hematuria syndrome. Follow-up for each of the four was 2, 24, 29 and 48 months.

Intervention: Renal autotransplantation.

Main Outcome Measures: Relief of pain with preservation of renal function and blood pressure.

Results: All four patients experienced relief of the pain of loin pain–hematuria syndrome. Renal function was preserved and blood pressure maintained. Narcotic analgesia was discontinued in all cases.

Conclusion: Renal autotransplantation appears to be an effective treatment for patients with loin pain–hematuria syndrome.

Objectif : Déterminer si l'autotransplantation rénale est un traitement efficace contre le syndrome de lombalgie–hématurie.

Conception : Étude rétrospective de dossiers.

Contexte : Centre de référence de soins tertiaires au Manitoba.

Patients : Quatre patients envoyés pour se soumettre à un diagnostic et au traitement du syndrome de lombalgie–hématurie. Le suivi dans chaque cas a été de 2, 24, 29 et 48 mois.

Intervention : Autotransplantation rénale.

Principales mesures des résultats : Soulagement de la douleur et préservation de la fonction rénale et de la tension artérielle.

Résultats : Les quatres patients ont été soulagés de la douleur causée par le syndrome de lombalgie–hématurie. La fonction a été préservée et la tension artérielle, maintenue. L'analgésie narcotique a été interrompue dans tous les cas.

Conclusion : L'autotransplantation rénale semble constituer un traitement efficace pour les patients atteints du syndrome de lombalgie–hématurie.

Loin pain–hematuria syndrome (LPHS) is a chronic, painful, debilitating condition of unknown etiology. It is associated with severe, recurrent or persistent flank pain and intermittent microscopic or gross hematuria. The diagnosis is made by careful patient evaluation and thorough diagnostic testing to rule out other causes. Although LPHS is not generally regarded as a progressive disease from a standpoint of renal function, the pain often leads to narcotic dependency and serious disruption of lifestyle. Several nonsurgical options have been used to manage this condition, but results have been poor. Renal autotransplantation has shown

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promise in relieving the pain, which is thought to occur as a result of denervation of the affected kidney. The duration of pain relief is variable. We present our experience with four patients with LPHS who were treated with renal autotransplantation.

Case reports

Case 1

A 40-year-old woman presented with a 5-year history of recurrent left flank pain and intermittent microscopic hematuria. The onset of the pain coincided with the discovery of a left-sided retroperitoneal paraganglioma, for which she underwent surgical resection. Her pain returned postoperatively, and 2 years later she underwent a left percutaneous nephrolithotomy for a small (1 to 2 mm) left-sided renal calculus. In addition, she had a history of recurrent urinary tract infections, which were treated with appropriate antibiotics. Despite these treatments, her symptoms progressed to the point of constant pain, requiring acetaminophen with codeine, orally administered meperidine and morphine.

Case 2

A 36-year-old woman presented with a 9-year history of intermittent, primarily left flank pain with microscopic and occasionally gross hematuria. Her episodes of pain lasted from weeks to months at a time, eventually becoming constant. She had a history of post-streptococcal glomerulonephritis as a child. She also had a possible history of renal calculi; however, analysis of one of her stones revealed a rock fragment. She required orally administered analgesics, including acetaminophen with codeine, meperidine, oxycodone, and morphine sulfate for pain control.

Case 3

A 38-year-old woman with no history of urologic disease presented with a 10-year history of approximately 15 episodes of recurrent, severe right flank pain and gross hematuria, lasting up to 12 hours. She required orally administered acetaminophen with codeine and morphine, intravenous morphine, and epidurally administered fentanyl citrate and bupivicaine for pain relief during the attacks. She was pain-free between these episodes.

Case 4

A 44-year-old woman presented with a 10-year history of right flank pain and intermittent gross hematuria with occasional passage of clot. Three years after the onset of her pain, she underwent surgical removal of a large right renal cyst. Although this did relieve the pain for approximately 1 year, her pain returned and progressed to the point at which she had more than three episodes a week and required regular doses of meperidine orally for analgesia.

Diagnostic work-up

All patients underwent extensive investigation (Table I). Additional tests were performed on some of the patients (Table II). The diagnosis of LPHS was made after the exclusion of other causes of the symptoms.

Surgical approach

All patients underwent a standard donor nephrectomy through an ante-

Table I

Diagnostic Investigations Performed on all Patients

Investigation	Result
History and physical examination	Mild tenderness
Measurement of blood pressure	Normal
Urinalysis and urine culture	Variable red cells, sterile culture
Measurement of serum creatinine level	Normal
Intravenous pyelography	Normal
Renal ultrasonography	Normal
Computed tomography	Normal
Angiography	Normal
Cystoscopy and retrograde pyelography	Normal

Table II

Diagnostic Investigations Performed in Selected Patients

Investigation	No. of patients	Result
Urine cytologic tests	3	Normal
Renal scanning after administration of diuretic agent	2	Normal
Flexible ureteroscopy	2	Normal
Biopsy of renal tissue	1	No specific changes
Psychiatric consultation	1	No diagnosis

rior subcostal incision. All received 5000 units of heparin intravenously before clamping of the renal vessels. All harvested kidneys were perfused with Euro-Collins solution and kept cool with iced slush. The kidneys were then transplanted into the contralateral iliac fossa by way of a separate extraperitoneal incision. The renal vein was anastomosed end to side with the external iliac vein, the renal artery was anastomosed end to end with the internal iliac artery, and the ureter was anastomosed to the bladder by an extravesical approach.

Results

In all patients the postoperative course was uncomplicated. All patients had normal postoperative renal scans. At follow-up of 48, 29, 24 and over 2 months, all patients were pain-free and off analgesics. Some degree of gross or microscopic hematuria persisted in all patients. Blood pressure and serum creatinine levels were similar to preoperative values. All patients were satisfied with the results of their surgery and had resumed a normal lifestyle.

Discussion

Since its first description in 1967 by Little, Sloper and de Wardener[1] LPHS has been reported with increasing frequency, but by 1989, no more than 130 cases had been reported.[2] Early case reports described the condition only in young women; however, this condition has also been described in men.[3] Overall, more than 90% of patients with LPHS are female.[4] There is a tendency for this syndrome to become bilateral.[2,5]

The cause of the pain and hematuria is unknown. Suggestions have included estrogen-containing compounds,[5–7] abnormalities of the intrarenal vasculature,[1,8] abnormal intrarenal coagulation with focal renal ischemia,[7] renal hypersensitivity,[9] Factor XII deficiency[10] and increased intrarenal platelet activity.[6,11,12]

The diagnosis is made after extensive testing to exclude other conditions that may present with similar symptoms, such as infection, tumours or calculi. Our patients did not demonstrate any angiographic abnormalities. In several of the early descriptions of LPHS, the abnormal findings on angiography were considered crucial for the diagnosis.[1,5,7] The abnormalities noted included abnormal tortuosity, abnormal beading and wide bifurcations of the smaller intrarenal vessels.[1,5,8] Others have suggested that these same abnormalities may be the result of contrast-induced vascular spasm related to the angiography itself, possibly because the renal vessels of these patients are more prone to spasm.[13] Normal angiographic findings do not exclude LPHS.[4]

Pathological findings in LPHS are usually variable and nonspecific.[4] In one series,[14] nephrectomy specimens showed atherosclerotic-type changes in the renal vessels and areas of focal infarction. In another report,[12] 65% of patients had arteriolar or arterial hyalinosis and red blood cells in the renal tubules, without glomerular disease. Burden and associates[7] found no histologic vascular abnormalities. Several investigators[15,16] have demonstrated C_3 deposition in the basement membranes on renal biopsy specimens; however, others[2,4,7,14] have suggested that these deposits are nonspecific. Given the lack of specificity of renal biopsy for the diagnosis of LPHS, it appears to be of no value in the workup of these patients. One report[17] suggested that the biopsy itself may cause subsequent angiographic abnormalities such as arteriovenous fistulae, which may confound the diagnosis. Only one patient in our series had a renal biopsy and the findings were nonspecific. Patients who are suspected of having underlying glomerular disease may be considered for renal biopsy. However, LPHS has been reported in patients with IgA and IgM nephropathy.[18]

One patient (case 2) in our series underwent a psychiatric assessment, primarily because of her demanding personality and the clinical suspicion of underlying drug-seeking behaviour. She had also at one point apparently passed a renal calculus; however, analysis of this calculus revealed a rock fragment. It has been noted[1] that patients with LPHS may at times fabricate physical evidence to give their subjective complaints an objective correlate.[4] Her psychiatric assessment was essentially normal. Aber and Higgins[5] noted psychiatric symptoms in most of their patients with LPHS; however, subsequent evaluation showed these to be "the result of long-standing, often undiagnosed and mismanaged pain, rather than its cause." Sheil and colleagues[19] found that nine patients with LPHS had "unusual" personalities with low pain thresholds. They were all thought to have genuine organic pain. As a group these patients had psychologic characteristics that varied with the duration of their pain. Psychiatric evaluation may reveal only reactive depression.[20] Lucas, Leaker and Neild[21] found a strong history of depression, whereas Kelly[22] suggested that LPHS may represent a form of somatoform pain disorder, post-traumatic stress disorder or factitious disorder. There is a tendency for LPHS to occur more commonly in health care workers[12,22] (one of our patients was a nurse, and another was in a paramedical field). Our patients did well postoperatively and have been able to return to more or less normal lives. They were also able

to discontinue their narcotic analgesics postoperatively, a finding that has been noted by others.[2,20] Certainly, if a patient is suspected of or displays overt signs of depression, drug-seeking behaviour or personality disorder, a psychiatric assessment should be considered as part of the management plan.

Medical therapy has included the long-term use of antibiotics,[1] anticoagulants,[23] antiplatelet agents,[12] fibrinolytic agents[5] and analgesics. With the exception of analgesics, the results have been poor. Surgical therapy has focused mainly on achieving denervation of the affected kidney. The pathways mediating renal pain have been described previously.[24,25] They are primarily sympathetic pathways. Methods used to denervate the kidney have included splanchnic nerve blocks[26] and stripping of the renal pedicle.[1] These have provided temporary relief. Nephrectomy has been performed in extremely resistant cases;[14,17] however, the possibility that LPHS may become bilateral suggests that nephrectomy should be avoided.[5]

Renal autotransplantation is an attractive option, because it combines the principles of total renal denervation with nephron-sparing surgery. It was first described for the treatment of LPHS by Aber and Higgins.[5] Sheil and associates[26] described three cases; two of their patients had complete relief and one patient had near-complete relief on follow-up ranging from 10 to 13 months. These patients continued to have hematuria, which suggests that the surgery itself provided only pain relief without correcting the underlying disorder. Chin[27] described his experience with 12 autotransplants in 10 patients. Of the nine patients with a follow-up longer than 12 months (median 43 months), eight had relief of pain after renal autotransplantation. By 1993, more than 40 patients with LPHS treated by renal autotransplantation had been reported, including bilateral renal autotransplants in approximately 33%.[4] Although mostly successful (approximately 90% overall[4]), a few failures have been reported during follow-up.[20,28,29] In a recent report, Harney and associates[20] cast some doubt on the long-term efficacy of renal autotransplantation for LPHS. Although all four patients in their series were pain-free 6 months after autotransplantation, only one was pain-free at 35 months. No patient in our series experienced pain in the contralateral kidney or had a recurrence of pain over the grafted kidney.

Complete denervation of the kidney by division of the renal vascular supply and ureter is believed to be required for successful outcome and is the method used in most series.[2,26,27] Recently, however, a patient who underwent autotransplantation for severe loin pain (without hematuria) was followed up for 21 years with no recurrence of pain.[25] In this case the ureter was left in situ and not divided. Although the concept of performing a less extensive operation by avoiding a separate procedure on the ureter is appealing, it is too early to recommend this technique until more is known about the specific pain mechanisms involved in this syndrome. It is likely that the return of the pain is secondary to reinnervation of the transplanted kidney.[30]

Although the long-term sequelae of LPHS are not known, long-term follow-up of such patients suggests that the condition does not lead to progressive renal impairment.[1,2,5,12,23] Aber and Higgins[5] described the natural history of 51 patients with LPHS. They showed that approximately 30% of these patients underwent spontaneous resolution of their symptoms over a mean period of 3.5 years. Therefore, a patient who presents with suspected LPHS should be managed with analgesics for 3 to 4 years before surgical intervention is considered. For the remaining patients, however, the pain experienced is severe and often leads to narcotic analgesic dependency,[2] poor social adjustment and extreme frustration on the part of both the patient and the health care provider.

In our experience renal autotransplantation for LPHS has been a safe treatment for these patients, allowing them to end their narcotic dependency and resume a normal life.

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