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Clinical Report

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Renal ablation using bilateral ureteral ligation for nephrotic syndrome due to renal amyloidosis

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Abstract
Nephrotic syndrome is common in immunoglobulin light chain amyloidosis (AL). In patients who do not achieve renal recovery, renal ablation has been reported for intractable proteinuria. We describe a patient with renal-limited AL who failed therapy and developed disabling proteinuria. He underwent laparoscopic ligation of the native ureters. Post-operatively, blood pressure improved. Hemodialysis was initiated. We conclude that bilateral ureteral ligation is a novel and minimally invasive method of renal ablation and may be considered for patients with refractory nephrotic syndrome.

Keywords: amyloidosis; nephrotic; ureteral ligation

Background

Immunoglobulin light chain amyloidosis (AL) presents with renal involvement in up to half of all patients at the time of diagnosis. Renal manifestations of AL vary depending on the site of amyloid deposits. Glomerular deposits are most commonly associated with proteinuria. Nephrotic range proteinuria (>3.5 g/24 h) is present in 86% of patients with biopsy-proven renal AL [1]. The chances of renal recovery and improvement in proteinuria depend on the degree of proteinuria and hypoalbuminemia at the time of presentation and whether a hematological response was achieved with chemotherapy [2]. Approximately 42% of patients will progress to end-stage renal disease and require renal replacement therapy [1]. For patients not yet on dialysis, management of nephrotic syndrome is challenging. The use of standard therapy such as angiotensin-converting enzyme inhibition and diuretics is often limited by hypotension and hypoalbuminemia.

Medical and/or surgical ablation of filtration has been utilized to achieve remission from massive proteinuria associated with the nephrotic syndrome [3, 4]. The role of bilateral ureteral ligation for renal ablation for this purpose has not been previously described. We report a case of renal-limited AL with severe nephrotic syndrome associated with orthostatic hypotension and anasarca in a patient who failed conventional chemotherapy. The patient underwent laparoscopic hand-assisted bilateral ureteral ligation with successful ablation of renal function and improvement in edema and postural hypotension. He was subsequently treated with long-term intermittent hemodialysis.

Case report

A 59-year-old Caucasian male developed 3 weeks of progressive lower extremity edema and was found to have proteinuria on urinalysis. Twenty-four-hour urine protein was 16 g and serum protein electrophoresis showed a monoclonal immunoglobulin G lambda type. A renal biopsy established the diagnosis of lambda light chain amyloidosis. Evaluation for other organ involvement including serum troponin, echocardiogram, esophagogastroduodenoscopy and colonoscopy with random biopsies was negative for amyloid involvement. Treatment included melphalan- and dexamethasone-based chemotherapy followed by autologous stem cell transplantation. Despite therapy, total serum-free light chain levels and massive nephrotic syndrome persisted. Three months after his stem cell transplant, he received an additional 5-month course of bortezomib therapy with no hematological response. The following 9-month period was marked by increasing proteinuria (15.8–24.4 g/24 h) and autonomic dysfunction with disabling orthostatic hypotension with postural syncope such that he became wheelchair dependent. Renal function worsened with 24-h creatinine clearance of 15 m/min and 24.4 g of urinary protein excretion in 24 h. Serum albumin fell to 1.2 g/dL. He was treated with alternate day albumin infusion with temporary symptomatic improvement. Due to poor functional status thought to be related to ongoing proteinuria, the decision was made to pursue therapeutic renal ablation to decrease daily urinary protein loss and restore plasma oncotic pressure. A trial of naproxen therapy did not improve his proteinuria. He was referred for consideration of surgical nephrectomy. As an alternative approach, with the aim of minimizing hypotension related to nephrectomy, the patient underwent hand-assisted laparoscopic ligation of both native ureters. Urine output and protein losses ceased immediately. Post-operative renal ultrasound confirmed mild hydronephrosis. Recovery was uneventful and the patient did not complain of pain associated with the procedure. Blood pressure, serum albumin and postural symptoms gradually improved (Table 1). During 12-day hospitalization, nutritional and functional status improved and he was dismissed home on long-term hemodialysis requiring minimal assistance for ambulation.

Table 1. Summary of patient's vitals and labs before and after renal ablation[a]

Pertinent vitals and labs	Before renal ablation	After renal ablation (2 weeks later)
Weight (kg)	90.5	65.5
Blood pressure (mmHg)	114/62	156/80
Albumin (g/dL)	1.9 (nadir 1.2)	3.4
Creatinine (mg/dL)	2.4	6.7 (dialysis)
Creatinine (μmol/L)	212.16	592.28
eGFR (mL/min)	28	9 (dialysis)
Urine protein (g/24 h)	16 (peak 24.4)	N/A

[a]N/A, Not applicable.

Discussion

Despite advances in medical therapy for specific causes of nephrotic proteinuria, some patients remain disabled from ongoing massive protein losses. Such patients are often considered for therapeutic renal ablation as in the case described here. Medical renal ablation with the goal of cessation of proteinuria has been attempted using a variety of medical treatments including mercury salt (sodium mercaptomerin) [5], angiotensin II and cyclosporine [6] and inhibitors of prostaglandin synthesis [7]. Bilateral renal infarction has been carried out by percutaneous renal artery embolization using ethanol and irritant coils as a successful substitute to nephrectomy in patients with chronic kidney disease and massive proteinuria [8]. These maneuvers are sometimes complicated by flank pain and incomplete ablation of renal function. Moreover, a constellation of signs and symptoms (fever, nausea, vomiting, leukocytosis and flank pain) referred to as 'post-infarction syndrome' has been connected with renal artery embolization [8].

Surgical removal of the kidney offers complete relief from urinary protein losses but carries the hazards of an open operation in severely debilitated patients. Laparoscopic nephrectomy may offer a less invasive procedure, although this procedure has been applied infrequently for this purpose. Any renal operation poses a particular challenge for patients suffering from nephrotic syndrome due to complications of hypoalbuminemia with hypotension, increased bleeding tendency and impaired renal function. We chose laparoscopic ligation of the ureters adjacent to their entry into the native bladder as a potentially minimally invasive procedure that would accomplish the same objective.

Bilateral ureteral ligation for cessation of nephrotic proteinuria associated with renal amyloidosis is a novel low-risk method of renal ablation. Ligation of the ureters has been previously performed in patients who required reconstruction of the urinary system at the time of renal transplantation. It has been shown to be associated with minimal complications except for the need for nephrectomy later on primarily in patients with polycystic kidney disease as the underlying cause of renal dysfunction [9]. A retrospective study of 17 patients who underwent bilateral ureteral ablation did not show any evidence of post-operative pain or infection and was suggestive of short-term safety of the procedure [10]. Eighty-eight percent of the patients had underlying focal segmental glomerulosclerosis and 65% were not yet on dialysis.

To our knowledge, this is a unique case of the impact of renal nephrectomy by bilateral ureteral ligation on the quality of life of a patient with renal amyloidosis not yet on dialysis. Renal ablation therapy in this case led to a major improvement in hemodynamic stability allowing function in the upright position for a patient with nephrotic syndrome secondary to treatment refractory AL amyloid. Laparoscopic ligation of both ureters is a novel and safe surgical approach to renal ablation and may be considered for patients with disabling refractory complications of proteinuria.

Conflict of interest statement. None delcared.

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