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Case Report

Laparoscopic Bilateral Nephrectomy Followed by Live-Related Kidney Transplant for the Treatment of Persistent Severe Nephrotic Syndrome and Advanced Chronic Renal Failure: A Case Report and Review of the Literature

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Abstract

Hypoalbuminemia, secondary to urinary protein wasting, is central to much of the metabolic and clinical complications of the nephrotic syndrome. The management of patients with persistent significant proteinuria despite the progression to end-stage renal failure, is a challenge. These patients may become massively edematous, malnourished, and susceptible to infections, thromboembolism, and atherosclerotic complications. At times, resolution of proteinuria can be achieved by early initiation of maintenance hemodialysis, with the goal of accelerating the onset of oliguria/anuria. Alternatively, different thromboembolic agents have been used to occlude the renal arteries, and induce anuria. However, such measures may have undesirable side effects such as allergic and systemic toxic effects, as well as infections, which may be particularly hazardous in patients in whom a live donor is available, and renal transplant is considered. Under such circumstances, bilateral laparoscopic nephrectomy may represent a reasonable alternative for the induction of anuria, and the elimination of massive urinary protein losses.

We present a case of persistent heavy proteinuria due to idiopathic membranous nephropathy complicated by acute tubular necrosis and irreversible renal failure, bilateral renal veins thrombosis and progression over short period of time to end-stage renal failure. The patient was successfully treated with laparoscopic bilateral nephrectomy followed by live-related kidney transplant with the resolution of all manifestations of the nephrotic syndrome.

Keywords: Acute Renal Failure; Chronic Renal Failure; Laparoscopic Nephrectomy; Membranous Nephropathy; Nephrotic Syndrome; Proteinuria; Renal Transplantation

Introduction

Urinary protein wasting is the hallmark of a variety of glomerular disorders. Heavy proteinuria, irrespective of its cause, is associated with a spectrum of clinically important systemic complications that are usually responsible for much of the morbidity and/or mortality seen with the nephrotic syndrome [1,2]. Sodium retention leads to edema, which may become generalized and massive (anasarca). Other common, but probably less well appreciated, manifestations of the nephrotic syndrome include protein malnutrition, intravascular hypovolemia, which at times may lead to acute renal failure, hyperlipidemia [3] and the potential for accelerated atherosclerosis [4], hypercoagulability [5] with a tendency to venous thrombosis [6], increased susceptibility to infection [7]. In addition, urinary losses of binding proteins lead to several abnormalities in the endocrine system and in trace metals. Finally, heavy proteinuria is a predictor of rapid progression of renal failure, and this relation is probably causal. Progressive renal failure occurs in 20-25% of patients with idiopathic membranous

glomerulonephritis [8-13].

Interventions aiming at lowering urinary protein excretion in patients with the nephrotic syndrome have therefore emerged as a major therapeutic goal. Specific immunologic interventions are available for only a few causes of the nephrotic syndrome [14,15]. In all other cases, nonspecific immune intervention may be attempted [16-22]. However, the response rate is quite variable, and proteinuria, and its complications may persist in a substantial number of patients. Other interventions that are directed at reducing proteinuria in the nephrotic syndrome, include the use of ACE inhibitors [23-26], and NSAIDs [27]. Although NSAIDs may reduce proteinuria [28] more than can be explained by the reduction in the glomerular filtration rate [29], their use has been limited because of their potentially serious side effects, particularly acute renal failure, gastrointestinal bleeding, and hyperkalemia. Patients with the nephrotic syndrome, in whom severe proteinuria persists, despite the progression to advanced chronic renal failure, present a therapeutic challenge. In these patients, renal ablation by medical nephrectomy through embolization of the renal arteries, followed by the initiation of chronic hemodialysis, may be indicated to avoid the serious risks of severe hypoproteinemia [30].

We present a case of persistent severe proteinuria (21.5 gm/day) due to idiopathic membranous nephropathy complicated by acute irreversible renal failure due to Acute Tubular Necrosis (ATN), bilateral renal veins thrombosis and rapid progression to end-stage renal failure. The patient was successfully treated with laparoscopic bilateral nephrectomy followed by live-related kidney transplant with the resolution of all manifestations of the nephrotic syndrome.

Case Report

A 34-year-old Hispanic male from El Salvador with unremarkable past medical history was admitted to Los Angeles County-University of Southern California Medical Center with chief complains of progressive bilateral leg swelling and 15 lbs weight gain. Initial physical examination was significant for blood pressure of 122/80 mmHg and severe bilateral pitting edema of the lower extremities up to the knees. Urinalysis showed specific gravity of 1.026, pH 5.0, proteins >300, and large blood. Microscopic examination of urinary sediment showed 5-10 RBCs, 0-1 WBCs, and no urinary casts. Urine culture was negative. 24-hour urine collection showed 11 gm of protein, and creatinine clearance was 148 ml/min. other significant laboratory results showed serum albumin 0.9 g/dl, hemoglobin of 14.2 g/dl, and platelets 239,000. Serum cholesterol was 510 mg/dL, and triglycerides 454 mg/dL. The patient had normal transaminases, C3, C4 and negative serology for HIV, HCV, HbsAg, ANA and syphilis. Renal ultrasound showed right kidney 11.6 cm, left kidney 12.5 cm, both with increased echogenicity and patent bilateral renal veins by Doppler study. A percutaneuos renal biopsy was performed. Light microscopy showed mild focal and segmental mesangial hypercellularity, without crescents or sclerosis. There was minimal segmental basement membrane thickening. The tubules contained protein reabsorption droplets and small amounts of lipid droplets in a focal distribution. The interstitium was unremarkable. Electron microscopy (Figure 1).

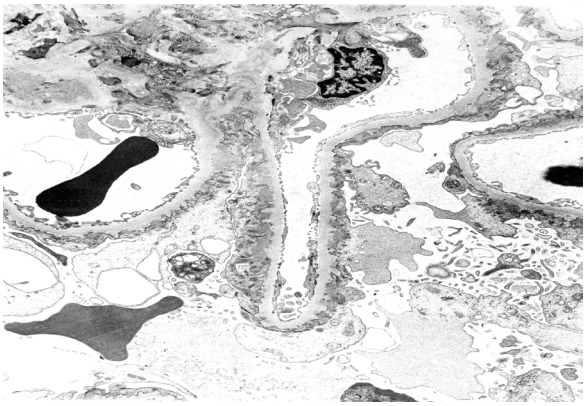

Figure 1: Electron Microscopy picture showing thickened glomerular basement membrane and numerous small sub-epithelial electron-dense deposits.

Demonstrated a normal configuration to the capillary loops with numerous small sub-epithelial electron-dense deposits reported along the glomerular basement membranes. The glomerular basement membranes were mildly thickened segmentally with small segmental spikes of basement membrane. The mesangium showed paramesangial electron-dense deposits. Extensive obliteration of visceral epithelial cell foot processes was present. Immunofluorescence microscopy showed diffuse staining for IgG (2+), C3 (1+), and trace IgA. These findings were consistent with the diagnosis of idiopathic membranous glomerulonephritis stage 2 of Churg.

(Figure 1) The Patient refused immunosuppressive therapy with either chlorambucil or cytoxan but agreed to a trial of prednisone 120 mg orally every other day for two months followed by a tapering-off over 2-3 months. The patient's symptoms were treated with furosemide 40 mg plus amiloride 5 mg BID for his significant edema, atorvastatin 80 mg/d for his severe hypercholesterolemia, and benazapril 10 mg BID, which later increased to a maximum of 40 mg BID to control his urinary protein excretion. INH 300 mg/d plus vitamin B_6 50 mg/d were also started for positive PPD skin test and negative chest x-ray.

Patient's 24-hour urinary protein excretion progressively increased from 11 gm/day at presentation to 15 gm/day over four-month with serum albumin remained low at 0.9 g/dl and serum creatinine remained stable between 0.8 to 1.2 mg/dL. Six months after the initial presentation, the patient was readmitted with

worsening bilateral leg swelling and acute deterioration of his renal function, serum creatinine of 3.7 mg/dL. ACE inhibitor and diuretics were held, and repeat kidney ultrasound was unchanged, urinalysis showed 3+ protein, 5-10 RBC/hpf, 1+ glucose and few epithelial cells but no casts seen. A repeat kidney biopsy showed acute tubular necrosis in addition to his base line membranous nephropathy. Few weeks later the patient was re-admitted with bilateral flank pain and increasing leg and scrotal edema. A Doppler renal ultrasound showed right renal vein thrombosis that warranted chronic anticoagulation with cumadin. Over the course of the subsequent year, renal function did not recover and continued to deteriorate, reaching a creatinine clearance level of 13 ml/min. Despite advanced renal failure, severe nephrotic syndrome persisted, with proteinuria reaching 21.5 gm/day. Renal replacement therapy was offered to the patient, who refused initiation of hemodialysis and elected to have a preemptive renal transplant from his sister. The patient was admitted to USC University Hospital and underwent laparoscopic bilateral nephrectomy, followed by one-haplotype-matched kidney transplant from his sister with complete and prompt resolution of the nephrotic syndrome (Table 1). Below summarizes pre-and post-nephrectomy and live-related kidney transplant laboratory results in a chronological order. Pathology of both removed kidneys showed advanced membranous nephropathy, chronic tubulointerstitial fibrosis and arteriosclerosis.

DATE	**10/12/1998**	**4/22/1999**	**5/14/1999**	**4/27/2000**	**5/8/2000**	**8/22/2000**
CHRONOLOGY OF EVENTS	Initial diagnosis N.S.* (**MGN**)	ARF (**ATN**)*	RVT*	Before Nephrectomy (Advanced CRF*)	1 week post Nephrectomy & Kidney Transplant	Post Transplant F/U
BUN (mg/dL)	18	34	23	33	23	31
Serum Creatinine (mg/dL)	0.7	3.7	3.1	5.8	3.1	1.1
Serum Albumin (g/dL)	0.9	1.2	1.8	1.9	3.6	4.3
24-hour Urine Protein (gm/day)	11	14.8		21.5		0.035
24-hour Urine Creatinine (mg/day)	1480	1300		1134		1680
Creatinine Clearance (ml/min)	148	24		13		107
Hematocrit (%)	42.1	22.3		29.6		42
Cholesterol (mg/dL)	510	428		326	132	135
Triglyceride (mg/dL)	454	622		359	186	104
HDL (mg/dL)		43		34	23	41
LDL (mg/dL)				220	72	

*N.S.: nephrotic syndrome; MGM: membranous glomerulonephritis; ATN: acute tubular necrosis; RVT: renal vein thrombosis; CRF: chronic renal failure.

Table 1: Pertinent Laboratory Results of Pre-and Post-Nephrectomy and Live-Related Kidney Transplant.

Discussion

The appropriate treatment for idiopathic membranous glomerulonephritis, the most common cause of nephrotic syndrome in adults, is controversial [16,17]. This disease places many patients at risk for end-stage renal failure, and the complication of hyperlipidemia and hypercoagulable states. Progressive renal failure occurs in 20-25% of patients with idiopathic membranous glomerulonephritis [8-13]. Risk factors for an unfavorable course can often be identified at the discovery of the disease. These risk factors include older age at onset, male sex, heavy proteinuria (>10 gm/d), impaired renal function, sustained hypertension and significant chronic tubulointerstitial lesions in the initial renal biopsy. Hypoalbuminemia, secondary to urinary protein wasting, is central to much of the metabolic and clinical complications of the nephrotic syndrome. The management of patients in whom significant proteinuria persists despite the progression to end-stage renal failure, is a challenge. Albumin replacement therapy is costly and of limited efficacy because of its rapid loss in the urine. These patients may, therefore, become massively edematous, malnourished, and susceptible to infections, thromboembolism, and atherosclerotic complications.

Interventions aimed at reducing these massive losses of proteins in the urine become an important goal of therapy. One strategy is to start maintenance hemodialysis earlier with the goal of accelerating the onset of oliguria. If the initiation of dialysis fails to significantly correct the urinary protein wasting, "medical nephrectomy" has been used [31]. Different thromboembolic agents such as autologous blood clots [31,32], wool coils [33], absolute ethanol [34], gelatin sponges, isobutyl-2-cyanoacrylate, and mercury [35], have been used to occlude the renal arteries. However, such measures for the induction of "medical" nephrectomy may have undesirable side effects such as infections, allergic and systemic toxic effects. Such complications may be particularly hazardous in patients in whom a living donor is available, and a renal transplant is contemplated. Under such circumstances, bilateral surgical nephrectomy may represent a preferable alternative for the induction of anuria, and the elimination of massive proteinuria. Traditional "Open" surgical nephrectomy can be associated with significant morbidity, particularly in such debilitated patients. Currently, when bilateral surgical nephrectomy is considered, the less invasive laparoscopic procedure is preferred. Indeed, since its introduction in 1990, laparoscopic nephrectomy has been shown to be associated with decreased morbidity, much shorter recovery time, and probably cost-saving [36-38]. Furthermore, Glassman's, et al. [39] recommended that, in patients with autosomal dominant polycystic kidney disease, if bilateral nephrectomy is to be performed as an adjunct to transplantation, it should be done at the time of renal grafting, in view of the superior outcome of concomitant bilateral nephrectomy and renal transplantation compared to those who did not undergo concomitant procedures. Bilateral laparoscopic nephrectomy of the native kidneys has also been performed for the treatment of severe hypertension after renal transplantation [40].

Finally, some as a measure to reduce the likelihood of recurrence of glomerular disease after renal transplantation have advocated bilateral pre-transplant native nephrectomy [41]. However, Odorico, et al. [42] compared the rates of recurrence and graft loss between patients treated with bilateral native nephrectomy (n = 61) and those who were not (n = 303), and reported that pretransplant bilateral nephrectomy did not prevent or delay the onset of recurrent glomerulonephritis after renal transplantation. In conclusion, we suggest that bilateral laparoscopic nephrectomy should be considered as a therapeutic option for the treatment of persistent sever nephrotic syndrome associated with advanced chronic renal failure, particularly when a living donor is available, and renal transplant is elected for renal replacement therapy.

References

1. Harris RC and Ismail N (1994) Extrarenal complications of the nephrotic syndrome. Am J Kidney Dis 23: 477-497.
2. Cameron JS (1987) The nephrotic syndrome and its complications. Am J Kidney Dis 10: 157-171.
3. Joven J, Villabona C, Vilella E, Masana L, Alberti R, et al. (1990) Abnormalities of lipoprotein metabolism in patients with the nephrotic syndrome. N Engl J Med 323: 579-584.
4. Ordonez JD, Hiatt RA, Killebrew EJ, Fireman BH (1993) The increased risk of coronary heart disease associated with nephrotic syndrome. Kidney Int 44: 638-642.
5. Llach F, Papper S, Massry SG (1980) The clinical spectrum of renal vein thrombosis: acute and chronic. Am J Med 69: 819-827.
6. Trew PA, Biava CG, Jacobs RP, Hopper J Jr. (1978) Renal vein thrombosis in membranous glomerulonephropathy: incidence and association. Medicine (Baltimore) 57: 69-82.
7. Ogi M, Yokoyama H, Tomosugi N, Hisada Y, Ohta S, et al. (1994) Risk factors for infection and immunoglobulin replacement therapy in adult nephrotic syndrome. Am J Kidney Dis 24: 427-436.
8. Remuzzi G, Ruggenenti P, Benigni A (1997) Understanding the nature of renal disease progression. Kidney Int 51: 2-15.
9. Glassock RJ, Adler S, Ward H, et al. (1990) Primary Glomerular Diseases in the Kidney, in Brenner B, Rector F (editors). The Kidney. Philadelphia, PA, Saunders 1990: 1238-1244.
10. Donadio JV, Torres VE, Velosa J, Wagoner RD, Holley KE, et al. (1988) Idiopathic Membranous Nephropathy: The Natural History of Untreated Patients. Kidney Int 33: 708-715.
11. Ponticelli C and Passeririni P (1990) The Natural History and Therapy of Idiopathic Membranous Nephropathy. Nephrol Dial Transplant 5: 37-41.
12. Wehrmann M, Bohle A, Bogenschutz O, Eissele R, Freislederer A, et al. (1989) Long-Term Prognosis of Chronic Idiopathic Membranous Glomerulonephritis. Clin Nephrol 31: 67-76.

13. Murphy BF, Fairley KF, Kincaid-Smith PS (1988) Idiopathic Membranous Glomerulonephritis: Long-Term Follow-Up in 139 cases. Clin Nephrol 30: 175-181.

14. Lin C-Y (1995) Treatment of hepatitis B virus-associated membranous nephropathy with recombinant alpha-interferon. Kidney Int 47: 225-230.

15. Dimitrov Y, Heibel F, Marcellin L, Chantrel F, Moulin B, et al. (1997) Acute renal failure and nephrotic syndrome with alpha interferon therapy. Nephrol Dial Transplant 12: 200-203.

16. Cameron JS (1992) Membranous nephropathy: Still a Treatment Dilemma. N Engl J Med 327: 638-639.

17. Wasserstein AG (1995) Membranous Glomerulonephritis, in The Principles and Practice of Nephrology (2nd ed), edited by Jacobson HR, Striker GE, Klahr S, St. Louis, Mosby-Year Book Inc 1995: 149-154.

18. Black DAK, Rose G, Brewer DB (1970) Controlled trial of prednisone in adult patients with the nephrotic syndrome. BMJ 3: 421-426.

19. Meyrier A, Noel L-H, Auriche P, Callard P, Collaborative Group of the Societe de Nephrologie (1994) Long-term renal tolerance of cyclosporin A treatment in adult idiopathic nephrotic syndrome. Kidney Int 45: 1446-1456.

20. Tune BM and Mendoza SA (1997) Treatment of the idiopathic nephrotic syndrome: regimens and outcomes in children and adults. J Am Soc Nephrol 8: 824-832.

21. Ponticelli C, Zucchelli P, Passerini P, Cesana B, Locatelli F, et al. (1995) A 10-year follow-up of a randomized study with methylprednisolone and chlorambucil in membranous nephropathy. Kidney Int 48: 1600-1604.

22. Ambalavanan S, Fauvel J-P, Sibley RK, Myers BD (1996) Mechanism of the antiproteinuric effect of cyclosporine in membranous nephropathy. J Am Soc Nephrol 7: 290-298.

23. Nosrati S, Khawaja S, El-Shahawy MA, Massry SG (1997) Effects of Angiotensin Converting Enzyme inhibition by perindopril on proteinuria of primary renal diseases. Am J Nephrol 17: 511-517.

24. Gansevoort RT, Sluiter WJ, Hemmelder MH, de Zeeuw D, de Jong PE (1995) Antiproteinuric effect of blood-pressure-lowering agents: a meta-analysis of comparative trials. Nephrol Dial Transplant 10: 1963-1974.

25. Hemmelder MH, de Zeeuw D, Gansevoort RT, de Jong PE (1996) Blood pressure reduction initiates the antiproteinuric effect of ACE inhibition. Kidney Int 49: 174-180.

26. Gansevoort RT, de Zeeuw D, de Jong PE (1994) Is the antiproteinuric effect of ACE inhibition mediated by interference in the renin-angiotensin system? Kidney Int 45: 861-867.

27. Arisz L, Donker AJM, Brentjens JRH, van der Hem GK (1976) The effect of indomethacin on proteinuria and kidney function in the nephrotic syndrome. Acta Med Scand 199: 121-125.

28. Donker AJM, Brentjens JRH, van der Hem GK, Arisz L (1978) Treatment of the nephrotic syndrome with indomethacin. Nephron 22: 374-381.

29. Golbetz H, Black V, Shemesh O, Myers BD (1989) Mechanism of the antiproteinuric effect of indomethacin in nephrotic humans. Am J Physiol 256: F44-F51.

30. Henrich WL, Goldman M, Dotter CT, Rosch J, Bennet WM (1975) Therapeutic renal artery occlusion for elimination of proteinuria. Arch Intern Med 136: 840-842.

31. Olivero JJ, Frommer JP, Gonzalez JM (1993) Medical nephrectomy: the last resort for intractable complications of the nephrotic syndrome. Am J Kidney Dis 21: 260-263.

32. Rosen RJ, Feldman L, Wilson AR (1978) Embolization for postbiopsy renal arteriovenous fistula: Effective occlusion using homologous clot. Am J Roetgenol 131: 1072-1073.

33. Wu JM, Moorthy AV, Beirne GJ, Crummy AB (1980) Renal infarction with Gianturco wool coils: Use in the management of massive proteinuria. JAMA 243: 2425-2426.

34. Nadalini VF, Zambelli S, Bruttini GP, Pacella M, Giglio C (1984) L'embolisation liquide de l'artere renale avec l'ethanol absolu. J Radiol 65: 301-305.

35. Avram MM, Lipner HI, Gan AC (1976) Medical nephrectomy: The use of metallic salt for the control of massive proteinuria in the nephrotic syndrome. Trans Am Soc Artif Intern Organs 22: 431-438.

36. Clayman RV, Kavoussi LR, Soper NJ, Dierks SM, Meretyk S, et al. (1991) Laparoscopic nephrectomy. N Engl J Med 324: 1370-1372.

37. Eraky I, El-Kappany H, Shamaa MA, Ghoneim MA (1994) Laparoscopic nephrectomy: an established routine procedure. J Endourology 8: 275-279.

38. Ono Y, Katoh N, Kinukawa T, Matsuura O, Ohshima S (1997) Laparoscopic radical nephrectomy: The Nagoya experience. J Urol 158: 719-724.

39. Glassman DT, Nipkow L, Bartlett ST, Jacobs SC (2000) Bilateral nephrectomy with concomitant renal graft transplantation for autosomal dominant polycystic kidney disease. J Urol 164: 661-664.

40. Fornara P, Doehn C, Fricke L, Durek C, Thyssen G, et al. (1997) Laparoscopic bilateral nephrectomy: results in 11 renal transplant patients. J Urol 157: 445-449.

41. Cochat P, Schell M, Ranchin B, Boueva A, Said MH (1996) Management of recurrent nephrotic syndrome after kidney transplantation in children. Clinical Nephrology 46: 17-20.

42. Odorico JS, Knechtle SJ, Rayhill SC, Pirsch JD, D'Alessandro AM, et al. (1996) The influence of native nephrectomy on the incidence of recurrent disease following renal transplantation for primary glomerulonephritis. Transplantation 61: 228-234.