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INTERNAL MEDICINE

Reprinted from Internal Medicine
Vol. 50, Pages 2899-2904
December 2011

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□ CASE REPORT □

Percutaneous Renal Artery Embolization in a Patient with Severe Nephrotic Syndrome which Continued after the Introduction of Hemodialysis

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Abstract

We treated a woman with membranous nephropathy in whom serious nephrotic syndrome (NS) continued even after the introduction of hemodialysis (HD). No response was seen with conservative treatment, including administration of steroids and albumin transfusion and body fluid management with HD. Hypoalbuminemia continued, and management of her general condition was problematic because of the hypotension, edema, pleural and peritoneal effusions. We performed percutaneous renal artery embolization (RAE), voluntary urine output disappeared for a short time, and good clinical course was subsequently seen with sustainable serum albumin levels of around 3 g/dL.

Key words: percutaneous renal artery embolization, nephrotic syndrome, hemodialysis, medical nephrectomy, membranous nephropathy

(Intern Med 50: 2899-2904, 2011)
(DOI: 10.2169/internalmedicine.50.5880)

Introduction

Even with the introduction of HD, severe NS has been reported to persist during the time that remaining renal function was seen, and various complications have been described, including malnutrition from hypoproteinemia, edema, increased susceptibility to infection, delayed wound healing, hypotension, hypercoagulation, thrombosis, and vascular access occlusion. These problems include the adverse effects of steroids or immunosuppressants and economic and social problems resulting from the use of large volumes of albumin transfusion. We performed medical nephrectomy for the present case using non-steroidal anti-inflammatory drugs (NSAIDs), but this proved ineffective. Following RAE, voluntary urine output disappeared, and good clinical course was subsequently seen. This case is reported together with a brief discussion of the literature.

Case Report

A 60-year-old woman present with the chief complaints of edema of the entire body. Her family and medical history were unremarkable. The patient was diagnosed with hypertension by a local doctor in 2004, but no abnormal urinary finding or renal failure was evident. In September 2007, edema of both legs appeared and the patient was examined in our department for increased body weight (+10 kg) in late November 2007. Renal failure and NS were diagnosed based on the following findings: serum creatinine (S-Cr), 5.6 mg/dL; urinary protein (UP), 4+; UP-to-creatinine ratio (UP/UCr), 40.4; and serum albumin (S-Alb), 1.3 mg/dL. The patient was hospitalized the same day. Examination on admission showed the following: height, 144.0 cm; body weight, 83.0 kg; body mass index, 40.0; blood pressure (BP), 130/74 mmHg; heart rate, 70 beats/min and regular; and body

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Received for publication May 23, 2011; Accepted for publication August 23, 2011
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Table 1. Laboratory Data on Admission

<Urinalysis>		<Blood cell count>		<Serological study>	
pH	6.5	WBC	7800/μL	HBs Ag	(-)
Protein	(3+)	Ht	40.6%	HCV Ab	(-)
Glucose	(2+)	Hb	12.9 g/dL	RPR	(-)
Occult blood	(+)	RBC	420 ×10⁴/μL	TPHA	(-)
Ketones	(-)	PLT	33.1 ×10⁴/μL	IgG	419 mg/dL
Bilirubin	(-)			IgA	253.6 mg/dL
		<Blood chemistry>		IgM	107.8 mg/dL
<Sediment>		TP	4.8 g/dL	CH50	59.6 U/mL
WBC	0-1/HPF	Alb	1.3 g/dL	C3	142.3 mg/dL
RBC	0-1/HPF	GOT	16 U/L	C4	46.1 mg/dL
Granulated cast	0-1/HPF	GPT	13 U/L	ANA	<40
		LDH	274 U/L	ASO	8 U/mL
<24-h urine>		ALP	249 U/L	RA test	23 U/mL
Protein	31.3 g	γGTP	6 U/L	PR3-ANCA	<10 EU
		chE	129 U/L	MPO-ANCA	<10 EU
		CPK	222 U/L		
<Urine chemistry>		T-Bil	0.3 mg/dL	<Coagulation test>	
Na	44.0 mEq/L	BUN	58 mg/dL	PT-INR	0.94
K	24.9 mEq/L	Cr	5.6 mg/dL	APTT	32.8 s
		UA	6.8 mg/dL		
<Others>		Na	139 mEq/L	<Others>	
Selectivity index	0.28	K	3.6 mEq/L	TSH	2.86 μIU/mL
UP/UCr	40.4	Cl	115 mEq/L	FT4	0.76 ng/dL
		Ca	7.7 mg/dL	I-PTH	283.0 pg/mL
		P	7.3 mg/dL		
		TCHO	581 mg/dL		
		LDL-C	382 mg/dL		
		TG	408 mg/dL		
		CRP	0.07 mg/dL		
		HbA1c	5.2%		

temperature, 36.0℃. No anemia was evident in the palpebral conjunctivae, and no jaundice was seen from the bulbar conjunctivae. The jugular veins showed no distension or collapse. Respiratory and cardiac sounds were normal and no cardiac murmurs were audible. Her abdomen was flat and soft without tenderness, and no vascular murmurs were identified. Distinct edema was apparent in her legs. Neurological examination showed no abnormalities.

The test findings on admission are shown in Table 1. In urine tests, daily urinary protein volume was 31.3 g/day, and selectivity index was also poor, at 0.28. Blood biochemistry tests showed a total serum protein level of 4.8 g/dL, S-Alb of 1.3 g/dL, and total serum cholesterol of 581 mg/dL. Based on these findings, NS was diagnosed. In addition, renal failure was identified based on a blood urea nitrogen (BUN) level of 58 mg/dL and S-Cr of 5.6 mg/dL.

The course after admission is shown in Fig. 1-5. Atrophy of the kidneys was seen on both ultrasonography (US) (Fig. 2) and computed tomography (CT) (Fig. 3), and chronic renal failure was diagnosed.

Treatment was started with anticoagulant therapy using warfarin and diet therapy using salt restriction. Diuretics were then administered (furosemide, 160 mg; thiazide, 4 mg; spironolactone, 100 mg) with the combined use of an albumin transfusion (25% albumin, 100 mL), achieving a daily urine volume of around 2,000 mL and a decrease in body weight from 83 kg to 73 kg.

In early December 2007, BUN rose to 84 mg/dL and S-Cr to 8.3 mg/dL. Nausea, loss of appetite and other uremic symptoms also appeared. As a result, HD was started. Body fluids were then removed as BP allowed. When body weight had reached 68.0 kg, daily urine volume decreased to around 700 mL, but daily urinary protein continued at about 10 g and S-Alb also remained around 1.5 g/dL. Control of hypotension, pleural and peritoneal effusions, and edema of the limbs was poor, and frequent transfusions of albumin were necessary.

The underlying etiology was unclear, but prednisolone was started at 40 mg/day in mid-January 2008, giving priority to decreasing the urinary protein level. However, no improvement was seen. To identify the underlying etiology and determine a suitable treatment plan, open renal biopsy was performed in mid-February (Fig. 4). Membranous nephropathy (Stage II) was diagnosed based on the findings. Extensive interstitial damage and many glomeruli with global sclerosis were seen, renal failure was thus considered irreversible and the renal prognosis was poor.

Abolition of renal function from body fluid removal by HD or extracorporeal ultrafiltration method (ECUM) was performed, but high urinary protein ($\geq$10 g/day) and hypoalbuminemia ($\leq$2 g/dL) continued, and management of her general condition was problematic because of the hypotension, edema, pleural and peritoneal effusions. For the purpose of medical nephrectomy to decrease urinary protein, administration of 600 mg of indomethacin farnesil (standard dose, $\leq$200 mg) was initiated in early March. However, urine volume did not decrease. The dose was increased to 1,000 mg, but no effect was seen. After we explained the

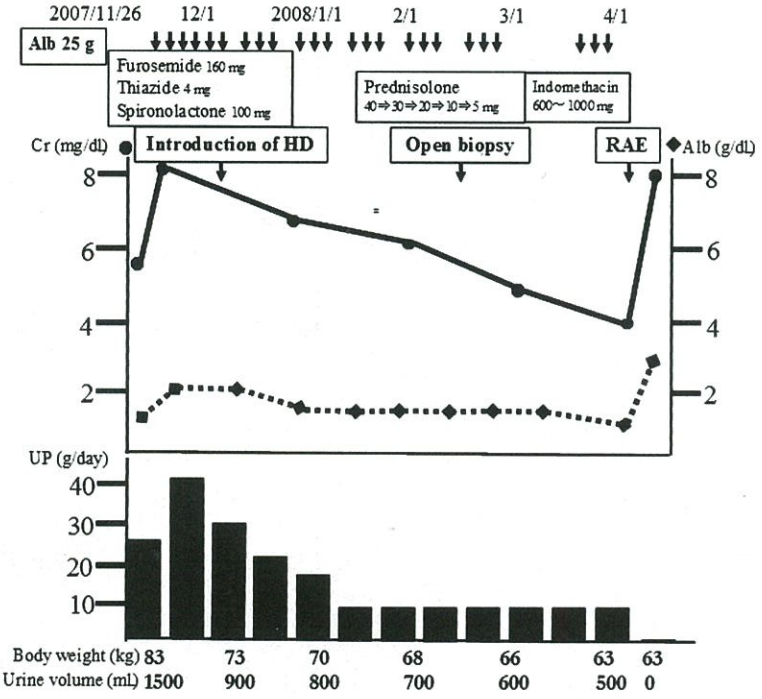

Figure 1. **Clinical course.**

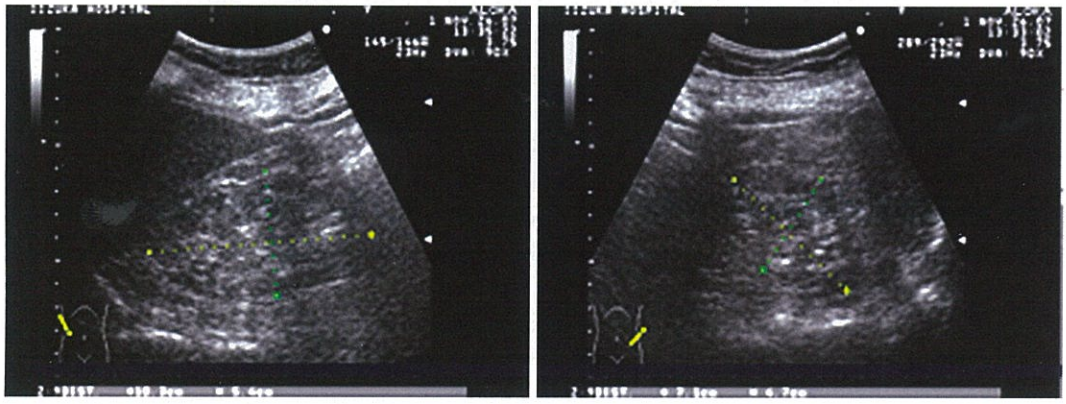

Figure 2. **US of kidneys. Both atrophic kidneys are shown.**

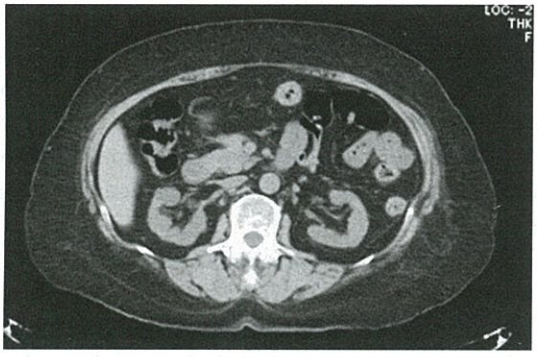

Figure 3. **Abdomin al CT findings. Both atrophic kidneys and a large amount of subcutaneous fat are shown.**

risk of hypoalbuminemia, poor prognosis of renal failure, and the risk of RAE (anuria, fever, back pain, nausea, hypertension, anemia, hypocalcemia, vitamin D deficiency), the patient consented to operation.

RAE was performed with absolute ethanol in the first part of April (Fig. 5). A balloon was dilated peripherally to the inferior suprarenal artery bifurcation to block blood flow, and after confirming with contrast medium that there was no leakage or reflux (Fig. 5A), 5 mL of absolute ethanol was injected. After 10 min, blood flow block was released. This was performed on each kidney, and the procedure was completed after confirming with contrast medium that no blood flow was present in the kidney (Fig. 5B). After RAE, the patient had a slight fever, and LDH rose to 486 U/L, WBC rose to 21,000/μL, and CRP rose to 24.8 mg/dL, but it recovered for several days. Postoperatively, the patient was anuric and S-Alb, BP, edema, pleural and peritoneal effusions improved. The patient was discharged from hospital in mid-May 2008.

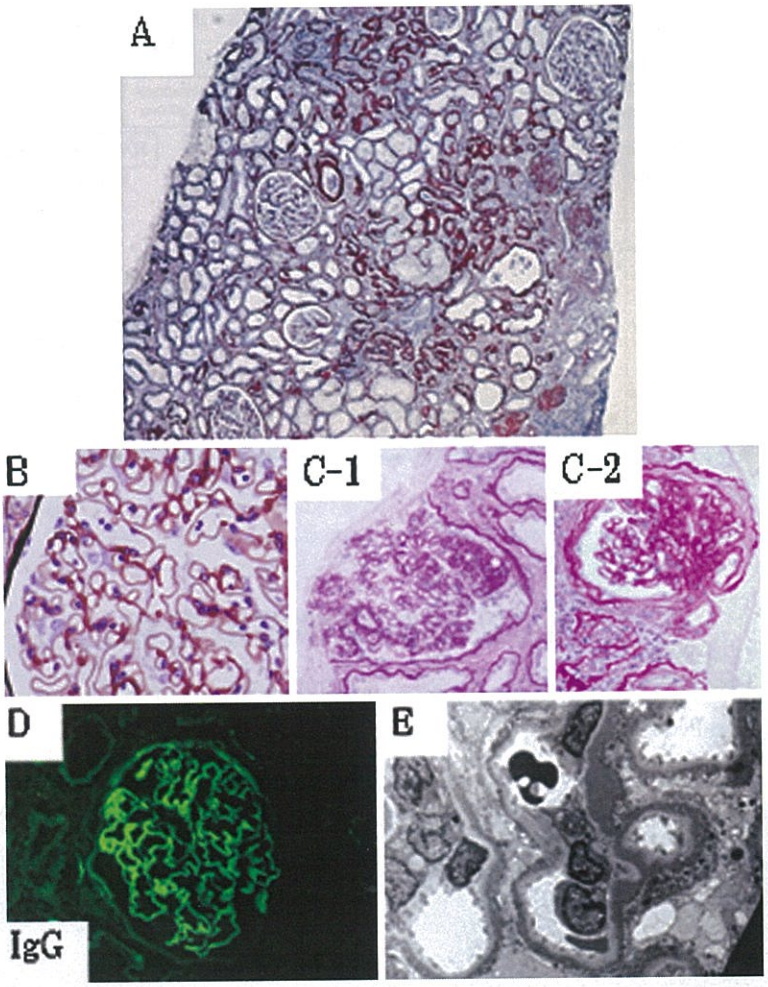

Figure 4. **Renal biopsy findings. A) Severe interstitial inflammatory infiltrate, tubular atrophy, and global sclerosis. B) No thickening of glomerular capillary walls, no spike and no mesangial proliferation. C) Glomeruli with segmental sclerosis. D) Granular deposition of lgG along the capillary walls. E) Dense deposits in the subepithelial space area and spike.**
A, B: Periodic acid silver methenamine (PAM) stain. C: Periodic acid-Schiff (PAS) stain. D: Immunofluorescence statning. E: Electron microscopy.

Discussion

Ehrenreich and Churg classified membranous nephropathy into Stages I-IV based on electron microscopy findings (1). The present patient was thought to be in a relatively early stage, Stage II. However, many reports have found that these disease classifications do not correlate with renal prognosis (2), and the present patient showed a poor prognosis despite the early stage.

In multivariate analyses of the risk factors for renal failure following membranous nephropathy in Japan, sex (male), advanced age (≥60 years), BUN ≥20 mg/dL, Cr ≥1.5 mg/dL on initial examination, segmental sclerosis ≥20% of glomeruli seen in renal biopsy, and interstitial lesions in more than ≥20% of glomeruli have been reported as significant (3), similar to reports in Western countries (2). The present patient met these conditions other than male sex, and based on the 45 glomeruli showing global sclerosis (75% of observed glomeruli), renal failure was already complete and recovery with steroids or immunosuppressants was considered unlikely. In addition, the patient also had steroid diabetes, leg phlegmon, a high level of obesity, and hypogammaglobulinemia (IgG <500 mg/dL), considering the risk of side effects, continued administration of steroids or the start of immunosuppressants was judged to be inappropriate.

It takes several months for abolition of renal function from body fluid removal in HD or ECUM, and serious complications such as shock or thrombosis are considered possible (4-9), we performed medical nephrectomy using NSAIDs, but no effect was seen. We found reports of 5 cases in which medical nephrectomy using NSAIDs was attempted in patients with severe NS that continued after the introduction of HD (4-6, 10, 11). This approach was successful in 3 cases, while 2 cases showed no decrease in urine volume and required RAE (Table 2). Even in the 3 successful cases, several weeks to several months were nec-

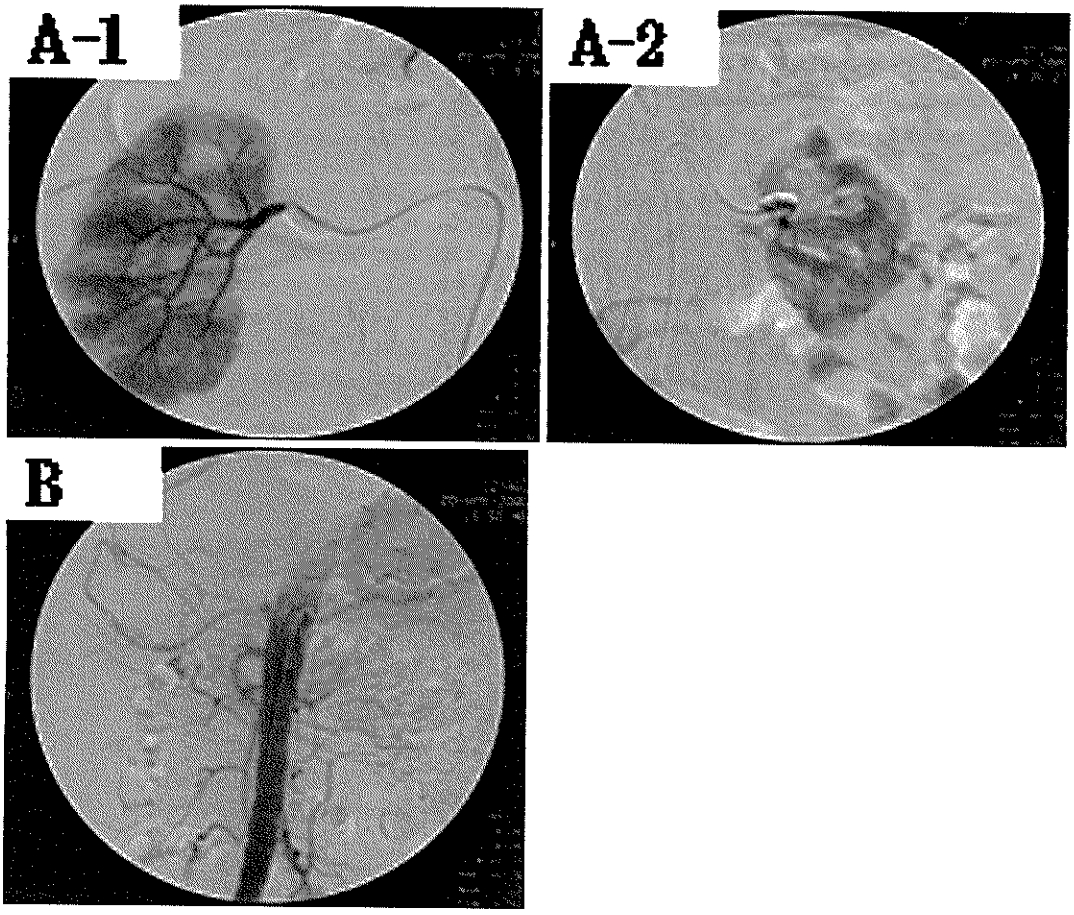

Figure 5. Angiography of renal arteries. A-1: Right renal artery wedged by 8-mm balloon. A-2: Left renal artery wedged by 8-mm balloon. B: After embolization.

Table 2. Medical Nephrectomy with Non-steroidal Anti-inflammatory Drugs

Study	Primary renal lesions	Drug and doses	Anuria
Kamijyou (4)	Diabetic nephropathy	Indomethacin 150 mg/day	Yes
Hagerty (5)	Membranoproliferative glomerulonephritis	Naproxen 500 mg/day	Yes
Duda (6)	Amyloidosis	Indomethacin 200 mg/day	No
Baumelou (10)	Membranous nephropathy	Indomethacin 150 mg/day	Yes
Miyauchi (11)	Focal glomerular sclerosis	Indomethacin 150 mg/day	No
Present report	Membranous nephropathy	Indomethacin farnesil 1000 mg/day	No

essary before the urine volume decreased, and thus we performed RAE.

RAE was first reported for kidney cancer by Lang in 1970 (12), and was first reported for persistent NS by Heinrich et al in 1976 (7). Many reports of RAE have described the disappearance of urinary output within several days after surgery and no serious side effects.

Embolic agents include gelfoam, metal coils, and absolute ethanol. With gelfoam and metal coils, the procedure must be repeated several times because reopening tends to occur with gelfoam and collateral circulation tends to develop with metal coils. With absolute ethanol, on the other hand, the embolic effect is strong because the blockage extends to the glomeruli and tissue necrosis of the entire kidney tends to occur, so this approach is often successful on the first try (13, 14). Absolute ethanol was selected in the present patient to obtain a reliable effect. Sóme reports have described a burning sensation or back pain following RAE (13, 14), but pain management in the present patient was good with preoperative epidural anesthesia and use until postoperative day 2.

The possibility of anemia from erythropoietin production

deficiency, hypocalcemia from active vitamin D deficiency, and hypotension from renin production deficiency have been indicated as potential long-term complications following RAE (8, 9). With the current erythropoietin and active vitamin D formulations, however, supplementation is possible and no particular problems have been encountered. Hb in the present patient continued at around 11 g/dL, corrected calcium level was maintained at around 9.5 mg/dL, BP was maintained at around 120/70 mmHg, daily urinary volume was 0 mL and S-Alb was >3.0 g/dL in May 2011. The present case indicates that good results can be obtained with the selection of RAE for patients with severe NS that continues after the introduction of HD.

The authors state that they have no Conflict of Interest (COI).

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