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Case Report Open Access

Lipid-rich Glomerular Capillary Thrombi, of a Patient with Waldenstrom's Macroglobulinemia

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Abstract

A 77-year-old woman was diagnosed nephrotic syndrome with Waldenström's macroglobulinemia (WM). Renal biopsy revealed MPGN-like lesions with extensive glomerular capillary thrombi which were positive for anti-IgM and anti-lambda-light chain immunofluorescence. The electron microscopy showed characteristic thrombi intra glomerular capillary walls which were occupied with a lot of vacuoles. These structures were similar with them of lipoprotein glomerulopathy. The patient was started to treat with R-CHOP, and then nephrotic syndrome and her renal insufficiency were completely recovered. There were no previous reports of nephrotic syndrome and acute renal failure caused by oil-rich intracapillary thrombi in WM in the literature.

Keywords Glomerular capillary thrombi; Waldenstrom's macroglobulinemia; Acute renal failure; Rituximab

Case Report

A 77-year-old woman was admitted our nephrology unit because of systemic edema and hypertension. She showed proteinuria and microhematuria. Additionally, she had hematological abnormalities, such as positive M-peak for IgM lambda-light chain in electrophoresis (but sIgM 192 mg/dl was normal-range), and a monoclonality of IgM positive plasma cells in bone marrow and lymph node (Table 1).

Laboratory Data			
			Normal range
Hematology	White blood cells	4300/μl	4300-8400
	neutrophils	75.1%	43.0-75.0
	lymphoid cells	13.1%	21.0-53.0
	monocytes	6.6%	2.8-9.0
	eosinophils	4.8%	0-10.0
	basophils	0.4%	0-3.0
	Red blood cells	315 × 10^4/μl	427-555 × 10^4/μl
	Hemoglobin	9.7 g/dl	12.5-16.7
	Hematocrit	29.3%	38.4-49.5
	Platelets	11.2 × 10^4/μl	140-322 × 10^4/μl
Blood chemistry			
	Total protein	5.5 g/dl	6.5-8.2
	Serum albumin	3.5 g/dl	3.8-5.3

	Blood urea nitrogen	25.6 mg/dl	8.0-20.0
	Creatinine (Cre)	0.85 mg/dl	0.4-1.1
	Uric acid	8.9 mg/dl	2.0-7.6
	Sodium	138.3 mEq/L	134-147
	Potassium	4.3 mEq/L	3.5-5.0
	Chloride	107.5 mEq/L	98-108
	Calcium	8.4 mg/dl	8.4-10.8
	Phosphate	4.4 mEq/L	2.7-4.5
	Aspartate aminotransferase	25 IU/L	8-40
	Alanine aminotransferase	23 IU/L	4-44
	Lactate dehydrogenase	176 IU/L	119-229
	Alkali phosphatase	210 IU/L	104-338
	Total bilirubin	0.54 mg/dl	0.20-1.00
	Creatine kinase	28 IU/L	28-180
	Blood glucose	117 mg/dl	70-110
	Total cholesterol	141 mg/dl	130-220
Lipid subfraction			
	HDL cholesrerol	30%	23-48
	LDL cholesterol	63%	47-69
	VLDL cholesterol	7%	2.0-15
	Apo-E	4.4 mg/dl	2.8-4.6
Coagulation			
	%Prothrombin time	106%	80%
	Active partial thromboplasmin time	25.7 sec	33 ± 3
	Fibrinogen	417 mg/dl	250 ± 50
Urinalysis			
	Specific gravity	1.014	1.005 -1.035
	pH	5.5	5.0-7.5
	Protein	(3+)	(-)
		0.8 g/day	
	Creatinine clearance rate (Ccr)	58.4 ml/min	
	Suger	(-)	(-)
	Occult blood	(3+)	(-)
	Urine sediment		
	Erythrocytes 20-29 per high-power field		
	Leukocytes, 1-4 per high-power field		

	Granular casts (+) per high-power field.		
	Fatty cast (+) per high-power field.		
	β_2-microglobulin (U-β-2MG)	562 μg/L	<230
	N-acetyl-β-D-glucosaminidase	14.7 U/L	<7.0
Serology			
	C-reactive protein (CRP)	0.4 mg/dl	<0.3
	IgG	512 mg/dl	870-1740
	IgA	109 mg/dl	110-410
	IgM	192 mg/dl	46-260
	IgE	<5.0 IU/ml	<173
	C_3	62 mg/dl	79-140
	C_4	1 mg/dl	13-35
	CH_{50}	<12.0/ml	25.0 – 48.0
	IgG-rheumatoid factor	negative	negative
	Antinuclear antibody	negative	negative
	PR3-ANCA	<10 EU	<10
	MPO-ANCA	<10 EU	<20
	Antistreptolysin-O	<50 U/ml	<156
	Ferritin	209.0 ng/ml	12-119
	Direct Coombs test	negative	negative
	Indirect Coombs test	negative	negative
	Haptoglobin	69 mg/dl	25-176
	Rapid plasma regain	(-)	(-)
	Hepatitis B surface antigen	(-)	(-)
	Anti-hepatitis C virus antibody	(-)	(-)
	Cryoglobulin	(±)	(-)
	Serum immunoelectrophoresis	Positive M-peak for IgM lambda-light chain	
	Urine immunoelectrophoresis	Nonspecific pattern	
	Bone marrow and Lymph node biopsy	CD20 positive/lambda positive cells infiltration	
		compatible for Waldenstrom's macroglobulinemia	

Table 1: Monoclonality of IgM positive plasma cells in bone marrow and lymph node Laboratory test.

Also, she was diagnosed nephrotic syndrome and acute renal failure with Waldenstrom's macroglobulinemia. To confirm her renal involvement, a renal biopsy was examined.

Renal biopsy revealed membrane proliferative glomerulonephritis (MPGN)-like lesions with extensive glomerular capillary thrombi which were positive for anti-IgM and anti-lambda-light chain immunofluorescence.

The electron microscopy showed characteristic thrombi intra glomerular capillary walls which were occupied with a lot of vacuoles.

These structures were similar with them of lipoprotein glomerulopathy. We therefore confirmed that the glomerular thrombi included with rich lipids including apoE by lipid-staining (oil-red and anti-apoE) (Figures 1 and 2).

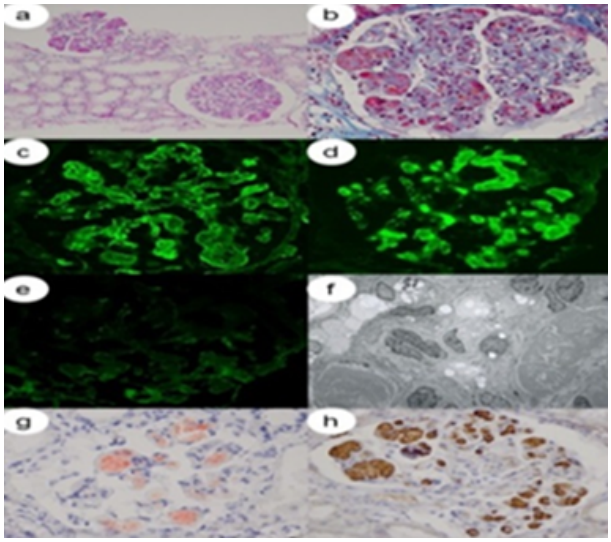

Figure 1: (a): Periodic acid-Schiff (PAS) stain, b: Masson's Trichrome (MT) Stain, c: IgM stain, d: Lambda stain, e: Kappa stain, f: Electron Microscope (X1000), g: oil-red stain, h: anti-apoE stain; Light microscopy: Two cortical tissues were submitted. Twenty-six glomeruli including 3 globally sclerosed ones were observed. Most glomerli showed MPGN-like features with focal or global thrombi. Tubulo-interstitial damage was 10% of tissue. Moderate lympho-plasmocytic infiltration was focally seen (a, b). Immunofluorescence: IgM periphery and mesangium positive, other immunoglobulins and complements negative. Thrombi: IgM weak positive (c), lambda light chain positive (d), kappa negative (e). Electron microscopy: Electron dense deposit was unremarkable in glomerulus. Thrombi were filled with abundant lipid particles, which were similar with lipoprotein glomerulopathy (f). Special stain of thrombi: Oil-red stain positive (g); Anti-apoE stain positive (h) DNA sequence of apoE gene showed no mutation. The patient was started to treat with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone), we could see of the therapy effectively at first, but recurred. After that, we try to treat with R-CHOP (including rituximab), and then nephrotic syndrome and renal failure were completely recovered (Figure 2).

Discussion

Renal complications occur rather infrequency in WM, compared to multiple myeloma, and about 15% of WM patients are reported to show mild to moderate impaired renal function [1]. Although kidney involvement in WM is well documented, only approximately 80 biopsy-confirmed cases of have been published. AL amyloidosis is commonly considered as the main cause of nephrotic syndrome [2]. One report from single academic institution performed a retrospective 44 cases study of WM-related nephropathy [3]. The report showed the most common histiologic findings were AL amyloidosis (n=11, 25%), and there were no histiologic findings included intracapillary thrombi. Another previous 32 cases report of WM with histologically proven renal involvement report showed that most common histiologic findings were intracapillary thrombi (n=5, 16%) and membrane proliferative glomerulonephritis (n=5, 16%) and cryoglobulinemic glomerulonephritis (n=5, 16%) followed by AL amyloidosis (n=4, 14%), and cast nephropathy (n=4, 14%) [4].

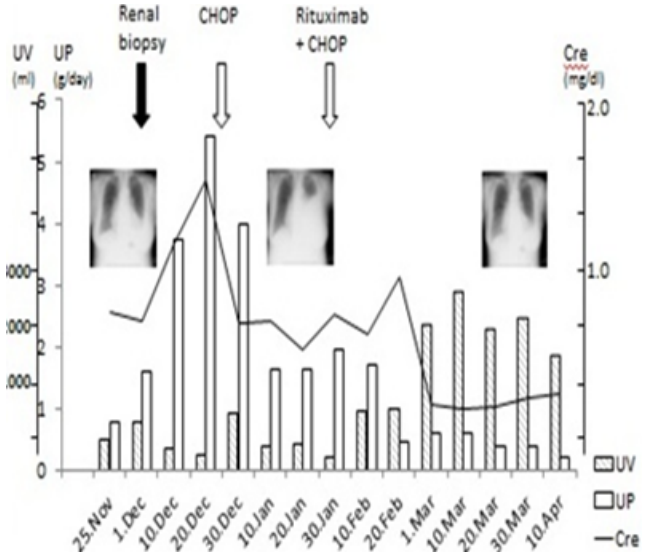

Figure 2: Clinical course after hospitalization, the patient showed nephrotic syndrome and acute renal failure. Treatment with R-CHOP was started, and then nephrotic syndrome and her renal insufficiency were completely recovered.

The intracapillary thrombi which caused nephrotic syndrome and acute renal failure were constructed mainly from protein of IgM paraprotein [5]. But, to our knowledge, there were no previous reports of nephrotic syndrome and acute renal failure caused by oil-rich intracapillary thrombi in WM in the literature. Therapy of WM is indicated in patients with clinically relevant symptoms. Therapeutic plasmapheresis should be performed in cases with hyperviscosity [5]. Rituximab, a monoclonal antibody against CD20, is being widely used for WM. In the prospective, randomized trial involving 64 WM patients, a significantly higher response rate (91 vs. 60%) was obtained among patients receiving R-CHOP (rituximab, cyclophosphamide, vincristine, and prednisone) vs. CHOP [6]. We used CHOP therapy, at first, because we were not able to have a diagnosis of the WM at that point. After diagnosis and recurrence, we used R-CHOP therapy. In our case, R-CHOP therapy was effective, but the efficacy of rituximab-based therapy on WM-related nephropathy is not well known [7].

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