Serum Procalcitonin Levels in Patients With Myeloperoxidase-Antineutrophil Cytoplasmic Antibodies-Associated Glomerulonephritis

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Abstract: *Introduction:* High serum procalcitonin (PCT) levels (≥0.5 ng/mL) commonly occur with systemic bacterial and fungal infections. Although several studies suggested that measuring serum PCT levels may serve as a useful marker to distinguish between active antineutrophil cytoplasmic antibodies (ANCA)-associated diseases and invasive infections, there is no information on PCT in myeloperoxidase (MPO)-ANCA-associated glomerulonephritis. *Methods:* The authors measured serum PCT concentrations before initiation of immunosuppressive therapy in 67 patients with biopsy-proven MPO-ANCA-associated glomerulonephritis. The authors compared complications and clinicopathological parameters between patients with serum PCT levels of <0.5 ng/mL (group A: 58 patients) and ≥0.5 ng/mL (group B: 9 patients). *Results:* All 58 patients in group A did not show any clinical sign of systemic infection. On the other hand, 3 of 9 patients in group B had bacterial or fungal infections of the respiratory or urinary tact. One patient had a history of chronic urinary tract infection. In the remaining 5 patients in group B, there were 3 patients with concurrent malignancies and 1 postoperative patient with malignancy. Another in group B had a long history of interstitial pneumonia of unknown origin and severe renal insufficiency. Serum levels of C-reactive protein and creatinine were significantly higher in group B than in group A. *Conclusions:* In patients with MPO-ANCA-associated glomerulonephritis, serum PCT levels of ≥0.5 ng/mL are recommended as cutoff for consideration of bacterial and fungal infections. Elevated serum PCT levels could also be observed in some patients with severe injury of the kidneys and/or lungs in the absence of infection.

Key Indexing Terms: Glomerulonephritis; Infection; Myeloperoxidase antineutrophil cytoplasmic antibodies; Procalcitonin. **[Am J Med Sci 2012;343(2):136–140.]**

Procalcitonin (PCT), a 116-amino acid prohormone of calcitonin (CT), has been proposed as a new marker that can improve recognition of patients with bacterial and fungal infections and sepsis from those with autoimmune and noninfectious inflammatory diseases.[1–3] In normal individuals, CT production results from transcription of the *CALC-I* gene, which is restricted to neuroendocrine cells, mainly C cells of the thyroid gland. In an animal model analogous to human sepsis, ubiquitous CT-messenger RNA expression in multiple tissues was observed. The signal for increased *CALC-I* gene expression is not yet known, but it is thought to be induced either directly by microbial toxins or indirectly by a humoral or cell-mediated host response.[3]

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This work was submitted by the Global COE Program from the Ministry of Education, Culture, Sports, Science, and Technology of Japan.

Submitted February 20, 2011; accepted in revised form May 13, 2011.

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Antineutrophil cytoplasmic antibodies (ANCA)-associated diseases are a spectrum of heterogeneous autoimmune diseases characterized by necrotizing small vessel vasculitis and the presence of ANCA.[4–6] ANCA have been classified mainly into cytoplasmic (C)- and perinuclear (P)-ANCA by indirect immunofluorescence microscopy using alcohol-fixed neutrophils as substrates. C-ANCA, which occur at high frequency in patients with Wegener's granulomatosis, are generally specific for proteinase 3. On the other hand, P-ANCA usually react with myeloperoxidase (MPO) and occur at high frequency in patients with microscopic polyangiitis (MPA) and kidney-limited vasculitis. Many experiments have shown the effects of ANCA in various steps of inflammatory process: neutrophils activated by binding of ANCA may release lytic enzymes and cytotoxic oxygen metabolites at the site of the vessel walls and damage vascular endothelial cells, resulting in necrotizing inflammatory injury. Patients with ANCA-associated diseases have sometimes nonspecific complaints such as fever accompanying airway disease. In addition, symptoms and signs related to involvement of the urinary tract may also be observed. These clinical manifestations may be indistinguishable from those of infections.

Most of the published observation studies on PCT in autoimmune diseases used semiquantitative assay for PCT measurement.[3] To our knowledge, there are several reports on serum PCT levels in ANCA-associated diseases including Wegener's granulomatosis and MPA.[7–11] However, there is no information on PCT in MPO-ANCA-associated glomerulonephritis. In this study, we measured serum PCT levels in 67 patients with MPO-ANCA-associated glomerulonephritis using highly sensitive immunoassay and investigated whether the serum PCT measurement may serve as a useful marker for the detection of bacterial and fungal infections. Our data suggest that a cutoff of 0.5 ng/mL can be used for this purpose, as suggested by previous studies.[1,3]

METHODS

Patients

This study was based on the renal histological records (1990–2010) of 3604 patients (excluding child patients and transplant patients) studied at Akita University Hospital and its affiliated hospitals. Renal biopsies were performed in all patients after obtaining written informed consent. We used the diagnostic criteria for MPA including MPO-ANCA-associated glomerulonephritis reported by the Research Group of Intractable Vasculitis, Ministry of Health, Labor, and Welfare of Japan.[6] There were 67 patients with MPO-ANCA-associated glomerulonephritis. These patients were evaluated in this study.

Sera were obtained from all patients at the time of renal biopsy (before initiation of immunosuppressive therapy) and

TABLE 1. Main clinicopathological characteristics of patients

Patient	Age (yr)	Gender	MPO-ANCA-associated disease	Involved organ	Serum PCT (ng/mL)	Serum CRP (mg/dL)	Serum MPO-ANCA (EU)	Serum creatinine (mg/dL)	eGFR (mL/min)	Crescent formation (%)	Complication
1	62	F	KL		0.02	3.2	464	2.5	16.1	25	
2	56	M	MPA	CNS	0.02	0.4	92	3.0	18.4	42	
3	31	M	KL		0.02	0.3	43	1.1	65.2	17	
4	36	F	MPA	S	0.02	0	85	2.1	22.8	75	Hyperthyroidism[a]
5	16	F	KL		0.02	0	446	0.6	113.1	28	
6	71	M	KL		0.02	3.4	84	1.5	36.6	20	
7	57	F	KL		0.03	0	117	1.7	25.1	43	
8	64	M	MPA	Mu	0.03	12.7	293	0.8	75.1	7	
9	53	F	KL		0.03	0	46	0.7	67.8	13	
10	43	F	KL		0.03	0.1	83	1.5	31.3	0	
11	74	F	MPA	L (IP)	0.04	7.7	92	2.8	13.5	50	
12	66	F	KL		0.04	0.3	85	1.6	25.8	68	
13	61	F	KL		0.04	0	112	1.6	26.4	40	
14	68	M	MPA	PN	0.05	5.2	384	5.2	9.5	50	
15	71	M	KL		0.05	2.4	811	1.6	34.1	52	
16	77	M	KL		0.05	0.2	150	1.9	27.6	27	
17	73	F	MPA	Mu	0.05	16.8	333	2.1	18.6	0	
18	66	F	KL		0.05	1.4	412	2.2	18.2	50	
19	53	M	KL		0.05	0.1	131	2.4	23.8	50	
20	44	M	KL		0.05	0.4	27	4.5	12.6	50	
21	57	F	CSS	L (IP), J, PN, S	0.06	1.5	148	0.5	95.9	23	
22	62	M	KL		0.06	2.1	516	1.2	48.6	33	
23	70	M	MPA	Mu	0.06	9.6	192	2.2	24.2	9	
24	77	M	MPA	L (IP)	0.06	8.4	538	1.4	38.6	10	
25	67	F	KL		0.06	1.4	1100	3.0	12.9	64	
26	79	F	KL		0.06	0.6	140	2.6	14.4	33	Large vessel vasculitis
27	69	M	KL		0.06	6.5	38	0.6	100.6	0	
28	77	F	KL		0.07	4.9	600	1.1	37.1	0	
29	69	M	MPA	J, PN	0.07	1.8	97	0.8	73.5	18	
30	68	M	MPA	L (PH)	0.08	4.5	482	1.6	34.6	7	
31	73	F	KL		0.08	0.4	138	2.8	13.6	60	[b]
32	74	F	KL		0.08	0.9	28	4.4	8.2	40	
33	66	M	KL		0.10	2.1	21	6.7	7.3	85	
34	71	M	MPA	CNS, L (IP)	0.10	12.4	513	2.1	25.4	25	
35	55	M	KL		0.13	2.5	2230	4.8	11.0	20	
36	68	F	KL		0.13	11.5	65	2.3	17.2	73	
37	71	M	KL		0.14	3.7	116	2.9	17.8	64	
38	69	F	MPA	L (IP), PN	0.14	1.0	118	2.3	17.1	63	
39	66	M	MPA	L (IP), Mu, S	0.15	8.2	28	3.0	17.5	29	
40	77	F	KL		0.15	3.1	28	1.8	21.7	30	
41	50	M	MPA	L (PL)	0.18	7.5	587	2.7	21.3	50	
42	74	F	KL		0.18	10.1	133	1.9	20.7	76	
43	72	F	MPA	Mu, PN	0.21	9.1	294	0.5	89.7	14	
44	79	M	MPA	L (IP), S	0.21	13.5	424	1.2	45.4	13	
45	66	M	KL		0.21	1.3	211	3.6	14.4	50	
46	75	F	MPA	PN	0.21	4.3	124	2.5	15.2	20	
47	62	M	KL		0.22	17.3	640	3.7	14.2	67	
48	73	F	KL		0.23	8.5	1650	3.6	10.3	40	
49	65	M	MPA	L (IP)	0.24	12.2	529	5.2	9.6	100	
50	66	F	MPA	Mu, J	0.25	0.8	360	2.2	18.2	85	Cryoglobulinemia (HCV)

(*Continued*)