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Myeloperoxidase Anti-neutrophil Cytoplasmic Antibody Glomerulosclerosis Associated with Pulmonary Disorders

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Abstract

Seven patients presented a specific renal lesion of rapidly progressive glomerulonephritis with myeloperoxidase anti-neutrophil cytoplasmic antibody. Rapidly progressive glomerulonephritis with myeloperoxidase anti-neutrophil cytoplasmic antibody can be associated with pulmonary hemorrhage and/or pulmonary interstitial fibrosis. The patients included three men and four women with a mean age of 62.4 years. All courses of renal lesions revealed rapidly progressive glomerulonephritis and the serum creatinine levels were 7.1 ± 3.9 mg/dl and the myeloperoxidase anti-neutrophil cytoplasmic antibody was 473 ± 471 EU before treatments. Steroid therapy was administered to all patients, immunosupressive agent to four and hemodialysis in six cases. Four patients experienced a pulmonary hemorrhage and died, but all of three patients with pulmonary interstitial fibrosis survived. All of four cases died due to an infection in pulmonary hemorrhage. Although three patients with pulmonary interstitial fibrosis were survived, pulmonary hemorrhage indicated a poor prognosis. Pulmonary infection may be fetal in pulmonary hemorrhage, but pulmonary infection was a few in pulmonary interstitial fibrosis.

Keywords: Infection; Myeloperoxidase anti-neutrophil cytoplasmic antibody; Pulmonary Hemorrhage; Pulmonary interstitial fibrosis; Rapidly progressive glomerulonephritis; Steroid

Introduction

Many patients experience rapidly progressive glomerulonephritis (RPGN) with myeloperoxidase anti-neutrophil cytoplasmic antibody (MPO-ANCA) [1,2]. As RPGN with MPO-ANCA can be associated with Pulmonary Hemorrhage (PH) and/or pulmonary interstitial fibrosis (PIF), which are often fatal [3,4]. Cough, chest pain, and shortness of breath may be present and chest radiographic features consist of patchy, bilateral airspace opacities caused by alveolar hemorrhage in PIF [4]. Seven patients with renal lesions characteristic of RPGN with MPO-ANCA experienced pulmonary disorders in this study.

Cases and Methods

This study of seven patients suffering from RPGN with MPO-ANCA was performed at the Department of Internal Medicine, National Kyushu Medical Center over an approximate 5-year period. A renal biopsy was performed in 2 of 7 cases (cases 1 and 4) and case 4 was undergoing regular hemodialysis. All of the patients were suffering from RPGN and pulmonary disorders.

Table 1 show that all seven patients were diagnosed with RPGN with MPO-ANCA. The patients included three men and four women with a mean age of 62.4 years (47-72 year old). All of the renal lesions were characteristic of RPGN and the serum creatinine levels were 7.1 ± 3.9 [means ± SD] mg/dl and the MPO-ANCA was 474 ± 471 EU before treatments. Four of the patients experienced PH and died, but three patients with PIF thereafter recovered.

Case	Age/Sex (Year old)	Original Disease	Course Kidney	OB/Before Tx Cr (mg/dl)	MPO-ANCA (EU)	ABG PO_2 (mmHg)	Dx of lung
1	64 M	CrGN	RPGN	3+/4.3	22	70 (room air)	PH
2	47F	CrGN	RPGN	3+/12.8	108	88 (room air)	PH
3	72M	CrGN	RPGN	3+/4.5	924	56 (mask 10 l/min)	PH
4	57F	CrGN	RPGN, rHD	anuria/6.5	100	34 (nasal 3 l/min)	PH (4 times)
5	65F	RA, AA, MPA	CRF→MPA RPGN	3+/5.0	1000	83 (room air)	PIF
6	66F	MPA	RPGN	-/3.8	136	93 (room air)	PIF

7	66M	MPA	RPGN	±/12.6	126	102 (room air)	PIF

Table 1: Patient profiles of MPO-ANCA glomerulonephritis. Tx=treatment, ABG=arterial blood gas analysis on the admission, Dx=diagnosis,OB=urinary occult blood, Cr=creatinine, CrGN=crescent glomerulonephritis, MPA=microscopic polyangiitis, RA=rheumatic arthritis, AA=secondary amyloidosis, RPGN=rapidly progressive glomerulonephritis, rHD=regular hemodialysis, CRF=chronic renal failure, PH=pulmonary hemorrhage, and PIF=pulmonary interstitial pneumonia.

Seven patients of RPGN with MPO-ANCA and pulmonary disorders clinicopathologically examined. Table 2 shows that steroids (pulse in six cases and oral in one case) were administered to all of patients, a immunosuppressive agent (cyclophosphamide) to four patients and hemodialysis in six patients (endotoxin absorption therapy was added in case 2 and plasma exchange in case 3). Cyclophosphamide pulse and corticosteroid pulse therapy was used in case 5. Among the four patients who died from PH (all were founded by autopsy), pneumonia and disseminated intravascular coagulation were observed in case 1, fungus, cytomegalovirus infection, pneumonia, disseminate, intravascular coagulation and sepsis in cases 2 and 4 and pneumonia (haemophilus influenza) in case 3 (Title 3) . Antibiotics were used in case 1-4, but were not used in case 5-7.

Case	Steroid	Immunosupression	Hemdialysis	Other Therapy
1	pulse	-	-	-
2	pulse	+	+	endotoxin absorption
3	pulse	+	+	plasma exchange
4	pulse	+	+	-
5	pulse, oral	-	+	-
6	pulse	+	+	-
7	oral	-	+ (hemodialysis off)	-

Table 2: Treatment of MPO-ANCA glomerulosclerosis.

The serum MPO-ANCA levels remained at 48 ± 92 EU after treatments. There was no correlation between the MPO-ANCA titers and the pulmonary disorders. Although the risk of PH was high, all three patients with PIF were recovered. Pulmonary infection was a few in pulmonary interstitial fibrosis (Table 3). The autopsies of three patients revealed vasculitis in only one case. The patients were observed for a mean of 32.9 months (0-72 months). Cases 5 and 6 were undergoing maintenance hemodialysis. CRP was negative in PIF, IgG lower than 600 mg/dl in case 4, neutrophil lower than 500 /mm^3 in none, and lymphocyte lower than 500/ mm^3 in cases 2, 3, 4 and 7 (Title 3).

Case	Association	CRP (mg/dl)	WBC/N/L ($X10^2/mm^3$)	IgG (mg/dl)	Prognosis
1	pn, DIC	29.64	81/67/10	2862	died
2	fungus, CM, pn, DIC, sepsis	48.27	177/162/0.9	850	died
3	pn (hemo.inf)	27.17	204/189/4	1294	died
4	fungus, CMV, pn, DIC, sepsis	32.8	16/10/0.3	481	died
5	-	< 0.3	82/62/13	783	alive
6	-	< 0.3	70/38/9	748	alive
7	-	< 0.3	85/64/2	1975	alive

Table 3: Association and Course of MPO-ANCA glomerulosclerosis pn=pneumonia, DIC=disseminat intravascular couagulation, CMV=cytomegarovirus, hemo.inf=hemofirusu infuensa, CRP=C-reactive protein, WBC=white blood cell, N=neutrophil, and L=lymphocyte. Neutrophil and leukocyte; cases 1-4 at the time of death and cases 5-7 at the time on discharge.

Discussion

These seven patients were all thought to have a specific renal lesion known as RPGN with MPO-ANCA. As RPGN with MPO-ANCA can be associated with PH and PIF, four of the patients died from PH and clinicopathologically examined.

The acute management of systemic vasculitis may also require intensive immunosuppressive therapy [3]. However, immunosuppressive therapy can be associated with fungus, cytomegalovirus infection, pneumonia, sepsis and the patients may die due to an infection in PH.On the other hands, PIF and chronic MPO-ANCA glomerulonephritis may require the treatment of infection [5]. Especially, it is necessary that we take preventive drugs such as pentamidine, amphotericin B and itraconazole.

Three of the seven cases with cytoplasmic (C)-ANCA experienced an extensive intra-alveolar hemorrhage while four of the seven patients had perinuclear (P)-ANCA. PIF was detected in two of four cases with C-ANCA vs. three of four cases with P-ANCA. In contrast, the fatal cases include 3 of the 4 patients with C-ANCA vs. one of the five patients with P-ANCA. Therefore, P-ANCA was associated with a poor prognosis [6].

The mortally rate is higher in patients that experience a hemorrhage in Goodpasture's syndrome (56%) than those who do not (18.4%) [7]. On the other hands, five of six patients with PIF died [4]. Furthermore, three of the four patients with PIF were fatal [2]. PIF has not been commonly appreciated as an accompanying of microscopic polyangitis [8]. However, the involvement of the respiratory system is a very common and important aspect of ANCA associated systemic vasculitis [9,10]. Moreover, PIF may be an early manifestation of the disease, antedating the diagnosis of microscopic polyangititis by two or more years and is associated with a poor prognosis [4]. In the present study, all of the three patients with PIF survived.

Conclusion

RPGN with MPO-ANCA was observed in patients associated with PH and/or PIF. Steroid therapy was administered to all patients. Four of all the patients died due to the PH but those with PIF survived. Pulmonary infection was fetal in PH, but pulmonary infection was a few in PIF.

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