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A Case of Diffuse Endocapillary Proliferative Glomerulonephritis Associated with Polymyalgia Rheumatica

Eri Takeshima Yoshiyuki Morishita Manabu Ogura
Chiharu Ito Osamu Saito Fumi Takemoto Yasuhiro Ando
Shigeaki Muto Wako Yumura Eiji Kusano

Division of Nephrology, Department of Internal Medicine, Jichi Medical University,
Shimotsuke-shi, Japan

Key Words

Polymyalgia rheumatica · Endocapillary proliferative glomerulonephritis · Nephrotic syndrome

Abstract

A 70-year-old man complained of muscle pain in his neck, shoulders and pelvic girdle. Proteinuria and hematuria subsequently developed. Blood analysis showed increased acute phase reactants. The histology of renal biopsy showed diffuse endocapillary proliferative glomerulonephritis. There were no signs of autoimmune diseases, malignancies and bacterial or viral infections. His extrarenal symptoms and the results of blood analysis fulfilled three different criteria of polymyalgia rheumatica (PMR). Therefore, diffuse endocapillary proliferative glomerulonephritis associated with PMR was diagnosed. After low-dose prednisolone (10 mg/day) treatment, the muscle pain disappeared, acute phase reactants decreased and hematuria and proteinuria improved. The renal complication of PMR is rare but important to be considered early in the right clinical context.

Introduction

Polymyalgia rheumatica (PMR) is a clinical syndrome characterized by muscle pain and stiffness in the neck, shoulders and pelvic girdle [1]. It occurs mainly in adults over 50 years old [2]. It is often associated with giant cell arteritis (GCA), suggesting that these diseases represent different clinical manifestations of the same disease process [3]. Renal complication is extremely rare in both PMR and GCA. Only a few cases of renal AA amyloidosis have been reported as renal involvement of PMR [4, 5]. We herein

describe a case of diffuse endocapillary proliferative glomerulonephritis associated with PMR.

Case Report

A 70-year-old man complained of muscle pain and stiffness of the neck, shoulders, pelvic girdle and thighs at the end of September 2011. He also had a low-grade fever ($<38.0^{\circ}\text{C}$) with general fatigue and appetite loss. Although he took a non-steroidal anti-inflammatory drug, namely loxoprofen (180 mg/day), muscle pain and the other clinical symptoms did not improve. Seven days after taking loxoprofen, face and leg edema occurred. He suspended the use of loxoprofen and consulted a physician at a local hospital. Upon further examination at the hospital, blood analysis showed that white blood cells had mildly increased to $12,000/\mu\text{l}$, C-reactive protein (CRP) level had increased to 8.7 mg/dl, hemoglobin (Hb) level had decreased to 9.2 g/dl and creatine kinase (CK) level was in the normal range (20 mU/ml). Urinalysis showed proteinuria (2+) and hematuria (+), and urinary sediments showed red blood cells (10–15/field). Since the high fever, general fatigue, appetite loss and muscle pain continued with these blood and urinary abnormalities, the patient was admitted to the hospital. Based on the clinical course and the increase of acute phase reactants, bacterial infection was suspected as the etiology of this case at that time. Therefore, he received an antibiotic, namely meropenem (1 g/day), for 10 days; however, these symptoms as well as hematuria and proteinuria did not improve at all. Therefore, the patient was transferred to our department for diagnosis and treatment at the end of November 2011. Upon examination at admission, he had muscle pain in the neck, shoulders, pelvic girdle and thighs. He also had symptoms such as low-grade fever (37.8°C), general fatigue, appetite loss, morning stiffness in the hands and edema of the face and legs. No skin and mucosal abnormalities, arthritis, lymphadenopathy and neurological abnormalities were detected. Blood analysis showed that white blood cells mildly increased to $13,400/\mu\text{l}$, erythrocyte sedimentation rate increased to 81 mm/h, CRP level increased to 10.3 mg/dl and plasma interleukin (IL)-6 level increased to 30.5 pg/ml (normal range <4.0 pg/ml). Hb level decreased to 8.7 g/dl (mean corpuscular volume (86 fl) and mean corpuscular Hb (29.4 pg) were in the normal range), while CK level was in the normal range (23 mU/ml). Urinalysis showed proteinuria (5.2 g/day) and hematuria (3+), and urinary sediments showed red blood cells (20–30/field) with red blood cell cast (3–4/all fields) and granular cast (1–2/all fields). [Table 1](#) shows other blood analysis and urinalysis results upon admission. As shown in table 1, no autoantibody suggestive of autoimmune diseases was detected in blood analysis, and no bacterial or viral infection, including Streptococcus, Staphylococcus aureus, parvovirus B19, herpes simplex virus, cytomegalovirus and Epstein-Barr virus, was detected in sputum, blood or urinalysis specimens. The computerized tomography (CT) scan of the brain, chest and abdomen also did not show any lesions suggestive of infections or malignancies. Blood analysis showed normocytic normochromic anemia, and upper gastrointestinal endoscopy and colonoscopy did not show any lesions that caused anemia such as ulcers and malignancies. The abdominal CT scan showed that the kidneys were normal shape and not atrophied (left kidney: 10.2×5.9 cm; right kidney: 10.6×5.3 cm). The patient's extrarenal symptoms and blood analysis results led to the diagnosis of PMR because they fulfilled three different sets of diagnosis criteria for PMR [6–8]. GCA was not detected in this patient. Then, renal biopsy was performed to diagnose the patient's renal complications. The renal biopsy specimen showed glomeruli that were large and cellular, with the infiltration of polymorphonuclear leukocytes and focal and segmental increased mesangial matrix and proliferation of mesangial cells by light microscopic analysis ([fig. 1a](#)). Immunofluorescence analysis showed the deposition of IgA and C3c in the mesangial area ([fig. 1b](#)). Electron microscopy analysis showed dense deposits in the mesangial area and foot process effacement ([fig. 1c](#)). No abnormality of blood vessels suggestive of incorporation of vasculitis was observed. Taken together, these extrarenal symptoms, the results of blood and urinary analysis and the renal histological analysis led to the diagnosis of diffuse endocapillary proliferative glomerulonephritis associated with PMR. Low-dose prednisolone (PSL; 10 mg/day) was administered as treatment. Erythrocyte sedimentation rate decreased to 5 mm/h, CRP decreased to 0.55 mg/dl, body temperature was normalized, muscle pain, fatigue and appetite loss disappeared at day 4, hematuria decreased to ($<+1$) and proteinuria decreased to 0.4 g/day at 2 weeks after PSL treatment.

Discussion

We described a case of diffuse endocapillary proliferative glomerulonephritis associated with PMR. We could not detect any laboratory data suggestive of autoimmune diseases or malignancies. There were also no data suggestive of bacterial or viral infections, including streptococcal and parvovirus B19 infections, which were reported to cause endocapillary proliferative glomerulonephritis [9, 10]. The extrarenal symptoms and blood analysis results of this patient fulfilled three different sets of diagnosis criteria for PMR [6–8]. Taking these results together, we diagnosed this case as diffuse endocapillary proliferative glomerulonephritis with renal involvement of PMR. Glomerulonephritis markedly improved with low-dose PSL associated with the improvement of extrarenal symptoms and acute phase reactants of PMR.

Although the clinical course, laboratory data, and good and rapid response to low-dose PSL of this patient may support that glomerulonephritis could be a renal involvement of PMR, the possibility that acute post infectious glomerulonephritis occurred primarily and reactive arthritis was consequently developed should be considered too. The relatively low level of compliments and self-limiting clinical course may support this speculation.

Renal complication is extremely rare in PMR. Javaid et al. [4] reported a case of renal AA amyloidosis that showed nephrotic range proteinuria and rapidly deteriorating renal function within 18 months of the onset of PMR symptoms. They suggested that the patient might have had a longstanding, uncharacterized inflammatory process, and might have developed AA amyloidosis earlier on [4]. The later development of PMR may have accelerated the progression of the amyloid disease [4]. We did not detect amyloid deposition in the kidney of the patient in the present case. Although the cause of PMR remains unknown, inflammation has been considered to contribute to PMR. Mild synovitis characterized by a predominance of macrophages and CD4+ T lymphocytes has been described in specimens of shoulder synovial membranes in PMR patients [11]. Shintani et al. [12] reported that IgG, IgA and fibrinogen were deposited in the perifascicular area of the perimysium of PMR patients. In addition to these lines of evidence, the infiltration of dendritic cells and inflammatory cytokines derived from macrophages, such as IL-1 and IL-6, are detectable in histologically normal temporal arteries in PMR patients [13]. These activated immune cells may have contributed to glomerulonephritis in the present case because deposition of IgA and C3c in the mesangial area and the infiltration of polymorphonuclear leukocytes in the endocapillary space were observed. Increased plasma IL-6 level in this patient may also have contributed to glomerulonephritis because IL-6 has been reported to increase mesangial matrix and proliferation of mesangial cells [14, 15]. It was reported that PMR could be inherited in genetically susceptible individuals whose immune system can be stimulated by pathogen [16]. It has also been reported that there is an association between the genetic factors and several glomerular nephritis [17, 18]. Although we could not perform a genetic analysis in the present case, the patient's genetic factor might have contributed to the development of PMR and glomerulonephritis. Further studies will be required to investigate the mechanism and factors of glomerulonephritis associated with PMR.

The treatment of PMR mainly involves low-dose PSL. After low-dose PSL treatment, diffuse endocapillary proliferative glomerulonephritis was markedly improved in

association with the improvement of extrarenal symptoms and acute phase reactants of PMR.

In conclusion, clinical observations, laboratory data and the result of a renal biopsy specimen suggested a case of diffuse endocapillary proliferative glomerulonephritis associated with PMR, which was successfully treated by low-dose PSL. The renal complication of PMR is rare but important to be considered early in the right clinical context.

Table 1. Laboratory findings on admission

Blood analysis				Urinalysis	
WBC	13,400/ μ l	IL-2	1,430 U/ml	Volume	1,600 ml/day
RBC	2.97×10^6 / μ l	IL-6	30.5 pg/ml	Protein	5.2 g/day
Hb	8.7 g/dl	ASO	42 U/ml	Na	160 mmol/day
Ht	25.8%	ASK	$\times 160$	K	44.2 mmol/day
MCV	86 fl	AGBM	–	Cr	1.21 g/day
MCH	29.4 pg	PACA	–	RBC	20–30/field
Plt	250×10^3 / μ l	CANCA	–	WBC	3–4/field
TP	5.1 g/dl	dsDNA	–	NAG	36.8 U/l
Alb	1.9 g/dl	RNP	–	β 2 microglobulin	680 μ g/l
BUN	35 mg/dl	SM	–	Ccr	62 ml/min
Cr	0.77 mg/dl	SSA	–	Myoglobin	–
Na	140 mmol/l	SSB	–	BJP	–
K	3.7 mmol/l	SCL-70	–		
Cl	104 mmol/l	CL β 2GPI	–		
T-cho	444 mg/dl	CCP	–		
TG	162 mg/dl	Parvovirus B19 DNA	–		
AST	32 mU/ml	CMV	–		
ALT	26 mU/ml	HSV-1-IgM	–		
LDH	166 mU/ml	EBV-IgM	–		
ALP	276 mU/ml	EBNA-IgM	–		
CK	23 mU/ml	Procalcitonin	0.16 ng/ml		
γ -GTP	194 mU/ml	Endotoxin	0.8 pg/ml		
CRP	10.3 mg/dl	Beta-D-glucan	–		
IgG	1,139 mg/dl				
IgA	307 mg/dl				
IgM	88 mg/dl				
C3	84 mg/dl				
C4	15 mg/dl				
ANA	<40				

WBC = White blood cells; RBC = red blood cells; Ht = hematocrit; MCV = mean corpuscular volume; MCH = mean corpuscular hemoglobin; Plt = platelets; TP = total protein; Alb = albumin; BUN = blood urea nitrogen; Cr = creatinine; Na = sodium; K = potassium; Cl = chloride; T-cho = total cholesterol; TG = triglyceride; AST = aspartate aminotransferase; ALT = alanine aminotransferase; LDH = lactate dehydrogenase; ALP = alkaline phosphatase; CPK = creatine phosphokinase; γ -GTP = γ -glutamyl transpeptidase; ANA = anti-nuclear antibody; ASO = anti-streptolysin O antibody; ASK = anti-streptokinase antibody; AGBM = anti-glomerular basement membrane antibody; PANCA = perinuclear-anti-neutrophil cytoplasmic antibody; CANCA = cytoplasmic-anti-neutrophil cytoplasmic antibody; dsDNA = anti-double-strand deoxyribonucleic acid antibody; RNAP = anti-ribonucleoprotein antibody; SM = anti-Smith antibody; SSA = Sjögren's syndrome A antibody; SSB = Sjögren's syndrome B antibody; SCL-70 = anti-scleroderma antibody; CL β 2GPI = anti-cardiolipin antibody β 2-glycoprotein-1 complex; CMV = cytomegalovirus antigenemia; HSV-IgM = anti-herpes simplex virus type-I IgM antibody; EBV-IgM = anti-Epstein-Barr virus-IgM antibody; EBNA = anti-Epstein-Barr virus nuclear antigen antibody; NAG = N-acetyl- β -D-glucosaminidase; Ccr = creatinine clearance; BJP = Bence Jones protein.

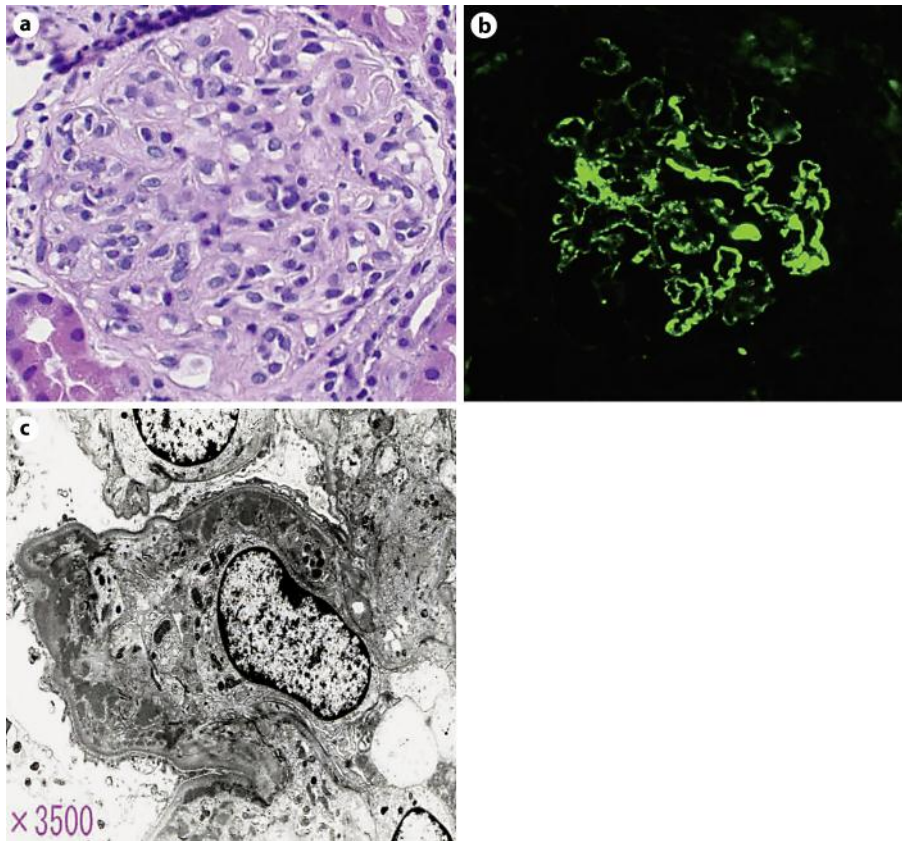


Fig. 1. Renal biopsy findings. **a** Light microscopy, HE staining. Glomeruli are diffusely large and cellular, with the infiltration of polymorphonuclear leukocytes and focal and segmental increased mesangial matrix and proliferation of mesangial cells. **b** Immunofluorescence analysis. Deposition of IgA in the mesangial area. **c** Electron microscopy. Dense deposits in the mesangial area and foot process effacement.

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