A Case of Microscopic Polyangiitis with Acute Myocardial Infarction

Daehwan Kim, M.D.,[a] Kyeong Han Yoon, M.D.,[a] Eun-So Lee, M.D.,[a] You Chan Kim, M.D.[b]

[a]*Department of Dermatology, Ajou University School of Medicine, Suwon, Korea,*[b]
Department of Dermatology, Dankook University School of Medicine, Cheonan, Korea

Microscopic polyangiitis is a systemic small-vessel vasculitis, which may involve multiple organs, but cardiac involvement is relatively rare. We report a case of microscopic polyangiitis with multiple organ involvement, in which myocardial infarction was the early manifestation of the disease. A 53-year-old man presented with sudden papulovesicular eruptions and swellings on the face, posterior neck, dorsa of both hands and fingers, and with diffuse erythematous patches on the back. He had suffered from renal dysfunction, arthralgia, and hypertension for more than 8 years. He had been admitted to the department of cardiology for acute myocardial infarction and had suffered from recurrent gastrointestinal bleeding, renal failure, acute pancreatitis and sepsis during the admission. Histopathologically, small-vessel leukocytoclastic vasculitis without granuloma was seen. Direct immunofluorescence showed no immune deposits. A high serum level of P-ANCA was detected by ELISA. (Ann Dermatol 14(3) 181~185, 2002).

Key Words : Microscopic polyangiitis; Myocardial Infarction; Gastrointestinal bleeding; ANCA

Microscopic polyangiitis (MPA) was first suggested as a microscopic form of polyarteritis nodosa (PAN) by Davson et al[1]. in 1948, which is a systemic small-vessel vasculitis primarily affecting arterioles, capillaries and venules. The disease may involve multiple organs such as kidneys, lungs, skin, joints, muscles, gastrointestinal tract, eyes, and nervous system, but cardiac involvement is relatively rare. We report a case of microscopic polyangiitis with multi-organ involvement including myocardial infarction.

CASE REPORT

A fifty three-year-old man with a 2-month history of chest pain was admitted to department of cardiology for acute substernal chest pain. He had hypertension for 8 years, and had chronic renal failure and seronegative rheumatoid arthritis for 10 years. He had no other medical history such as atopy, asthma, or allergic rhinitis. Cardiac enzymes were elevated and electrocardiography revealed acute anterior myocardial infarction. On echocardiographic examination, akinesia of anteroseptal and inferoseptal segment from mid left ventricle to apex, and hypokinesia of mid anterior, lateral apex and inferoapex were present. Left ventricular systolic function was decreased and ejection fraction was 40%. Coronary angiography showed coronary artery occlusions in 3-arteries, that is, nearly total occlusion of mid-left anterior descending artery, 67% diffuse stenosis of left circumflex artery and 78% eccentric stenosis of right coronary artery (Fig. 1. A, B). He also had anemia and hematuria of unknown origin on admission. Laboratory examination showed hemoglobin 6.2 g/dl, white cell count 11,800/μl (70.8 % neutrophils), platelet count 390,000/μl, serum blood urea nitrogen 33.9 mg/dl and serum creatinine 2.4 mg/dl. On abdominal ultrasonography, the size of both kidneys was decreased and the echo-

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Reprint request to : Kyeong Han Yoon, M.D., Department of Dermatology, Ajou University School of Medicine San 5 Wonchon-dong, Paldal-ku, Suwon, 442-721, Korea (South)
Tel. (031)219-5190, Fax. (031)219-5189
E-mail: yoon_skin@yahoo.co.kr

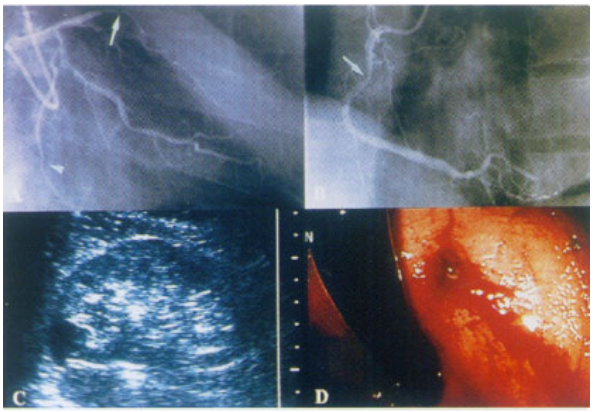
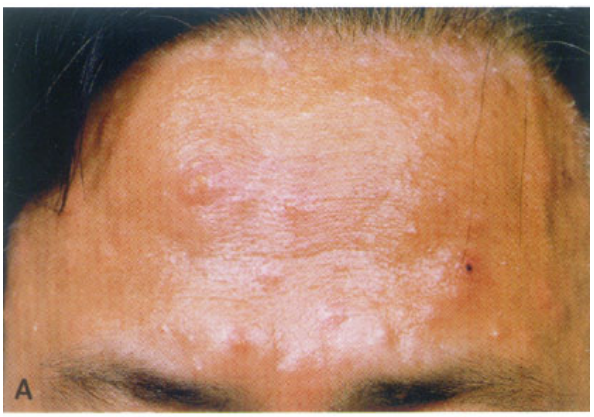
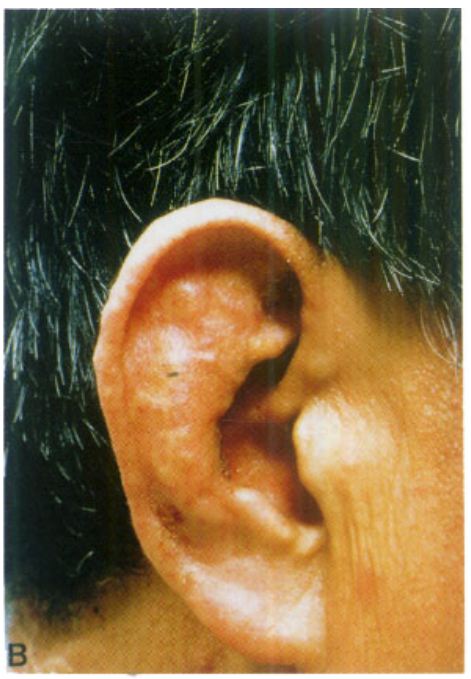
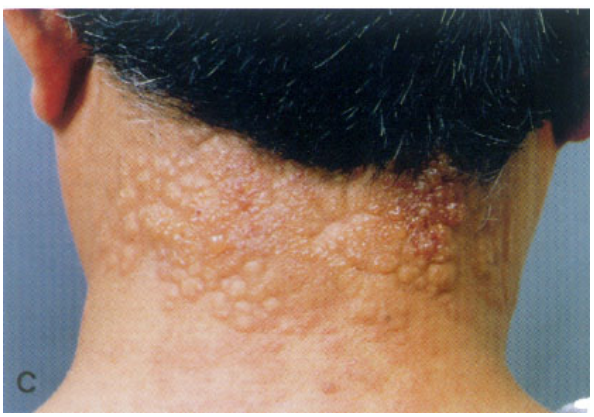


Fig. 1. A. Coronary angiogram showed nearly total occlusion of mid-left anterior descending artery (arrow) and 67% diffuse stenosis of left circumflex artery (arrow head).
B. Coronary angiogram also presented 78% eccentric stenosis of right coronary artery (arrow).
C. Abdominal ultrasonography revealed that left kidney was decreased in size and increased echogenesity of damaged cortex.
D. An exposed protruding vessel with active bleeding on lesser curvature side of upper body on stomach was observed on esophagogastroduodenoscopy.







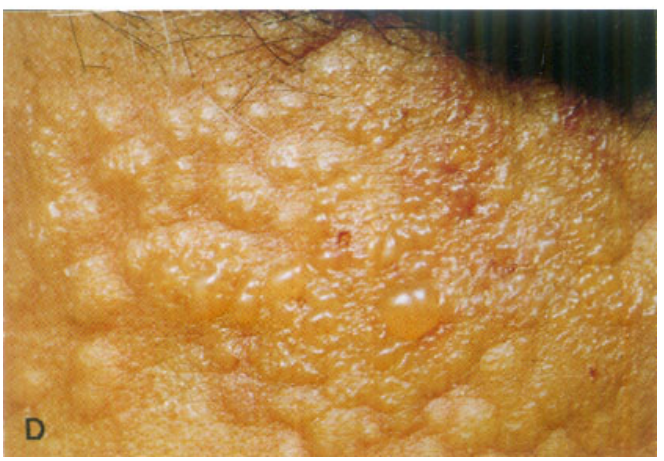
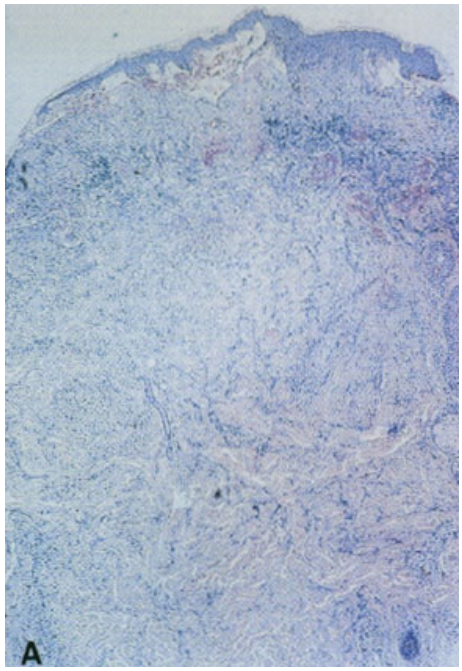


Fig. 2. A. Several erythematous papules and crusts with swelling were seen on forehead
B. Erythematous papules and vesicles were observed on external ear.
C. Multiple papulovesicular eruptions on erythematous patch were also noted on posterior neck.
D. Close-up view. Note the grouped erythematous to fleshy colored papulovesicles on erythematous or hemorrhagic base.



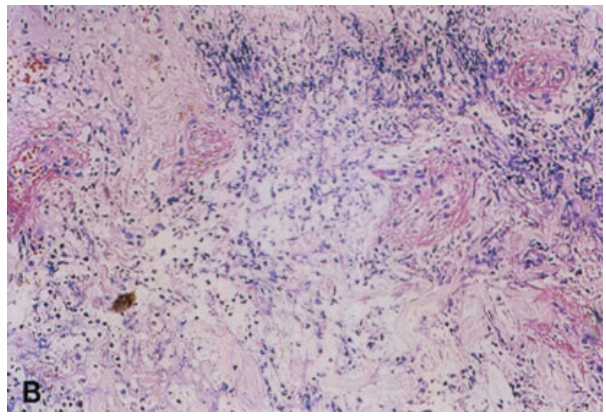


Fig. 3. A. Subepidermal vesicles and small vessel necrotizing vasculitis and cellular infiltration were found in upper dermis (H&E, × 50).
B. Multiple small-vessel leukocytoclastic vasculitis with fibrinoid necrosis and dense neutrophilic infiltration in the upper dermis (H&E, × 200).

genesity of damaged renal cortex was increased with unapparent corticomedullary differentiation (Fig 1. C). Multiple gallbladder stones were found. After anemia was recovered by transfusion, percutaneous transluminal coronary angioplasty (PTCA) with stent insertion was performed instead of operation due to co-morbid state, chronic renal failure. On the second day after PTCA with stent insertion, papulovesicular eruptions with fever developed suddenly on his face, neck, external ear and dorsa of both hands and fingers, and diffuse erythematous patches on his back (Fig. 2. A, B, C, D). These pruritic papules had been getting progressively bigger, some of which changed into hemorrhagic blisters. Investigation revealed erythrocyte sedimentation rate 104 mm/first hour, C-reactive protein 28.8 mg/dl, fibrinogen 892 mg/dl, D-dimer >1.5 μg/dl, FDP >20.0 μg/dl, hemoglobin 8.4 g/dl, white cell count 10,800/μl (80.2% neutrophils) and platelet count 386,000/μl. Renal function got worse; serum blood urea nitrogen 60.5 mg/dl, serum creatinine 5.1 mg/dl. Urinalysis still showed proteinuria and hematuria. The antibody to myeloperoxidase (Zeus Scientific, Inc. USA), a type of P-ANCA, was detected by enzyme-linked immunosorbent assay (ELISA), at a titer of 2009.0 AAU (normal, 0-150) but the antibody to proteinase 3, a type of C-ANCA, was within normal limit, 65.0 AAU (normal, 0-150). Antinuclear antibody was also detected at a titer of 1/1280, homogenous type and circulating IgG, IgM, C4 showed significant elevation. Circulating IgA, C3, anti-ds-DNA, VDRL and rheumatoid factor were within normal limit or negative. Hepatitis B surface antigen, anti-hepatitis C virus, HSV-IgM and VZV-IgM were not detected. Cultures for blood, urine and vesicles showed no significant findings. Skin biopsy specimen taken from a vesicle on posterior neck showed endothelial swelling, neutrophils infiltrate with leukocytoclasia, and fibrinoid degeneration of the vessel wall in the upper dermis (Fig. 3. A, B). Subepidermal and intraepidermal blisters were also observed. Direct immunofluorescence showed no immune deposits. General condition including renal function and skin lesions were improving with systemic antibiotics, intravenous methylprednisolone (62.5 mg/day, four consecutive days) and intravenous cyclophosphamide (750 mg/day, once) before severe anemia (hemoglobin 5.7 g/dl) with melena developed suddenly. In addition to anemia, renal function was worse again and acute pancreatitis had developed. Esophagogastroduodenoscopy revealed active bleeding in the upper body of stomach (Fig. 1D) and it was controlled by hemoclipping and transfusion. Over the subsequent 6 months, the disease has been currently well controlled with intermittent intravenous pulses of cyclophosphamide (1.25 gm, monthly). We are trying to add systemic steroid

according to the disease activity.

DISCUSSION

MPA is a systemic, non-granulomatous, small-vessel necrotizing vasculitis. Its clinical manifestations are very similar to those of PAN, but it is typically associated with focal necrotizing glomerulonephritis with crescents rather than ischemic glomerular lesions. Moreover, pulmonary involvement is usually absent in PAN. Either P-ANCA, occasionally C-ANCA, may be present in MPA, whereas both forms are less frequent in classical PAN[2]. The majority of patients with MPA are male and are over 50 years of age. Prodromal symptoms such as fever, arthralgia, myalgias are often present[3,4]. Renal dysfunction in the most cases, and occasionally pulmonary hemorrhage are associated with MPA[3,4]. Other organs such as skin, joints, muscles, gastrointestinal tract, eyes, and the nervous system may be affected, but less commonly[5-7]. Recently, a cutaneous limited variant of MPA was described[8]. Cardiac involvement is relatively rare. Sendoh et al.[7] reported a case of MPA with severe cardiac and respiratory muscle involvement. In our case, myocardial infarction with coronary artery occlusion was the early manifestation of the disease. Glomerulitis is known to be frequently associated with MPA, however, renal biopsy for confirming the disease was not done in this patient because his general condition was poor and he and his family refused it.

Cutaneous involvement is found in about 30-50% of patients and may be the primary manifestations. Palpable purpura is the most common skin manifestation, and in addition, mouth ulcers, non-specified vasculitis rashes, splinter hemorrhages and necrotizing ulceration have been described[3,5,9]. The skin findings of our patient showed a wide spectrum of clinical lesions: papules, vesicles, progressive hemorrhagic bullae and erythematous patches. Histopathologically, the absence or paucity of immunoglobulin localization in vessel walls distinguishes microscopic polyangiitis from immune complex mediated small vessel vasculitis, such as Henoch-Schonlein purpura and cryoglobulinemic vasculitis.

MPA is associated with antineutrophil cytoplasmic autoantibodies (ANCAs), in particular, antimyeloperoxidase autoantibodies[10,11]. Circulating ANCA tests are used to diagnose and monitor inflammatory activity in the primary systemic small vessel vasculitides and there are two staining patterns, cytoplasmic (C-ANCA) and perinuclear (P-ANCA) by indirect immunofluorescence of normal peripheral blood neutrophils and enzyme-linked immunosorbent assays. The majority of C-ANCAs react with proteinase 3, and most P-ANCAs are specific for myeloperoxidase. Wegener's granulomatosis is usually associated with C-ANCA and only rarely with P-ANCA, whereas MPA and Churg Strauss syndrome (CSS) are positive for P-ANCA[12-14]. MPA differs from Wegener's granulomatosis in the absence of granuloma formation and in rare involvement of upper airway. CSS is not commonly associated lesions in the upper respiratory tract, and rarely severe renal involvement, but typically accompanied by tissue and/or eosinophilia[15]. The characteristic small-vessel necrotizing vasculitis without granulomas and immune deposits on pathology, and detection of circulating P-ANCA are the key elements for the diagnosis of microscopic polyangiitis.

Although there is no good correlation between the disease activity and the titer of P-ANCA[5,16], in our patient, the titer of P-ANCA was decreased but not normalized according to the disease improvement during the course of the illness; initially 2009.0 AAU on the sixth day of admission, 1330.0 AAU on the 7th day after discharge, 1324.0 AAU and 1699.0 AAU on 2 months and 5 months after discharge. Experimental models suggest that ANCAs induce necrotizing vasculitis by activating circulating neutrophils and monocytes, which then adhere to blood vessels, degranulate, and release toxic oxygen metabolites to cause vascular injury[17]. Recently, upregulation of CD14 and CD18 on monocytes by ANCA is suggested as a pathogenetic role in systemic vasculitis[18].

In treatment of MPA, high-dose glucocorticoids remain the initial mainstay of therapy but also the combination of glucocorticoids and an immunosuppressive agent such as cyclophosphamide seems to be helpful. In a retrospective analysis of 85 patients with microscopic polyangiitis[19], the relapse rate was not significantly modified by cytoxic agents, but mortality rate was significantly lowered by them. Deaths were less frequent as many as 13 patients with steroids and immunosuppressive drugs than 15 patients with steroids alone. The 5-year survival rate was 74%. In our patient, systemic

glucocorticoid initially improved his general condition including renal function and skin lesions, but this treatment was stopped after two trials because of recurrent gastrointestinal bleeding. We are considering systemic steroid as well as intravenous pulses of cyclophosphamide (1.25 gm, monthly) because his general condition is improving.

In summary, we report a case of microscopic polyangiitis with multiple organ involvement. In addition to renal involvement, acute myocardial infarction and gastrointestinal bleeding were the major manifestations of disease in this case. This clinical report adds new information to the association between microscopic polyangiitis and acute myocardial infarction.

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