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Polyangiitis Overlap Syndrome : Cutaneous Leukocytoclastic Vasculitis associated with Polyarteritis Nodosa

Chan-Kum Park, M.D., Young-Hae Ko, M.D., Moon-Hyang Park, M.D.,
Jung-Dal Lee, M.D., Chang-Woo Lee, M.D.*

Departments of Pathology and Dermatology, College of Medicine,
Han Yang University, Seoul, Korea*

A rare case of polyangiitis overlap syndrome is described. The patient was a 25-year-old man who had palpable purpura on his legs which showed leukocytoclastic vasculitis, and polyarteritis nodosa. Superior mesenteric arteriography showed microaneurysms in jejunal branches with focal segmental necrotizing arteritis of small and medium sized muscular arteries in the jejunum. Deposits of IgA and C3 in the superficial blood vessels of the lesional skin were consistent with the features of Henoch-Schönlein purpura. The patient died about two months after initial admission in spite of cytotoxic agent and steroid administration.

Key Words : *Polyangiitis overlap syndrome, Leukocytoclastic vasculitis, Polyarteritis nodosa.*

INTRODUCTION

Certain vasculitic disorders can be clearly recognized as distinct entities, with clinical, pathologic, and immunologic criteria, whereas in others there is clinical and pathologic overlap among these disorders(DeShazo et al., 1977; Fauci et al., 1978; Pischel and Zvaifler, 1984 ; Leavitt and Fauci, 1986 ; Pons et al., 1987). The polyangiitis overlap syndrome proposed by Fauci represents a heterogeneous group of disease entities that do not fit precisely into any single category but exhibit characteristic features of several distinct vasculitic diseases(Fauci et al., 1978 ; Leavitt and Fauci, 1986).

Hypersensitivity angiitis usually affects blood vessels that are seldom involved in classic polyarteritis, such as the small arteries and veins as well as the arterioles and venules (Lie, 1987). Henoch-Schönlein purpura belongs to subgroups of hypersensitivity vasculitis and characteristically show deposition of IgA in blood vessels(Fauci et al., 1978 ; Heng, 1985 ; Van Hale et al., 1986 ; Piette and Stone, 1989). The disease usually runs a self-limited course and does not require intense immunosuppressive treatment(Fauci et al., 1978 ; Leavitt and Fauci, 1986).

Classic systemic polyarteritis nodosa is a disease of small or medium-sized muscular arteries, and is not associated with the characteristic dermal lesions of small vessel vasculitis(Arkin, 1930). It is a chronic systemic disease characterized by exacerbations and remissions and, if untreated, is associated with a high mortality rate(Fronert and Sheps, 1967 ; Sack et al., 1975 ; Fauci et al., 1979). Recent reports have suggested that favorable clinical responses occur in patients with systemic necrotizing vasculitis when cytotoxic agents are used(Melam and Patterson, 1971 ; Glanz et al., 1976 ; Reimold et al., 1976 ; Tuma et al., 1976 ; Fauci et al., 1979). Recognition of polyangiitis overlap syndrome is important, because early diagnosis may lead to successful treatment with cyclophosphamide(Leavitt and Fauci,

Address for correspondent : *Chan-Kum Park, M.D., Department of Pathology, College of Medicine, Han Yang University, 17. Haengdang-dong, Sungdong-gu, Seoul, 133-791, Korea. Tel : 293-2111, 3111(Ext : 2640, 2646, 3666).*

1986).

We report a patient presenting with palpable purpuric skin rashes showing the histologic features of leukocytoclastic vasculitis with IgA deposits. He had concurrent classic systemic polyarteritis nodosa characterized by microaneurysms in the jejunal branches of the superior mesenteric arteries and segmental necrotizing vasculitis of the small and medium sized muscular arteries in the jejunum.

CASE REPORT

A 25-year-old man was admitted to our hospital because of palpable purpuric skin rashes and acute renal failure. He had been in good health until six weeks before admission, when he had noticed chills and febrile sensations, rhinorrhea, nasal stuffness, and headache.

Abdominal pain occurred four weeks before admission and was followed by palpable purpuric skin rashes, hematochezia, hematuria, blood tinged sputum, and nasal bleeding. Purpuric red spots on both upper and lower extremities became more numerous and spread to abdomen. Under the impression of Henoch-Schönlein purpura, he was given prednisone 40 to 60mg per day which did not relieve symptoms. Clinical symptoms and signs progressed rapidly. And then abdominal distention developed with anuria.

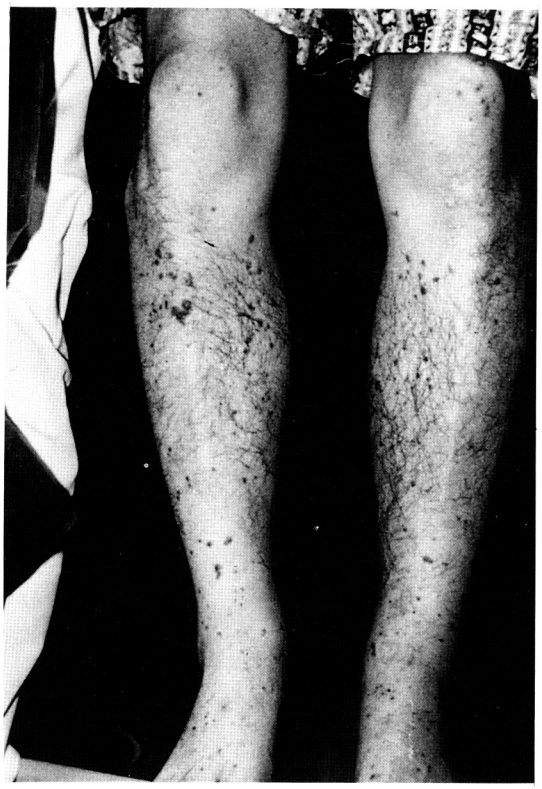

Fig. 1. Discrete palpable purpura on the lower extremities.

Physical examination on admission showed that the patient appeared acutely ill. Purpuric spots and palpable petechiae intermingled with vesicles and bullae covered both upper and lower extremities(Fig. 1), and the abdomen. Pretibial edema was noted. The lungs showed decreased breathing sound in both lower lung fields. The heart was normal. Abdominal tenderness was noted. Temperature was 36.7℃ pulse 96, and respirations 22 per minute. Blood pressure was 170/110mmHg.

The admission laboratory data were as follows. Urine gave a ++++ test for protein ; sediment contained 5-10 white blood cells and innumerable red blood cells per high-power field. White-cell count was 45,600/cu mm, with 88 percent neutrophils, 2 percent band forms, 6 percent lymphocytes, 2 percent monocytes and 2 percent eosinophils. Platelet count was 312,000/cu mm; prothrombin time was 83.3 percent(12.8 seconds). Partial thromboplastin time was 31 seconds. Urea nitrogen was 177mg per 100ml, creatinine 10.6mg per 100ml. Sodium was 125 mEq, potassium 6.4 mEq, chloride 8.1 mEq, and carbon dioxide content 25.9 mEq per liter. Fibrinogen was 215mg/dl, FDP 10ug/ml, and paracoagulation test was negative. Tests for antinuclear antibody and for cryoglobulins were negative. The fourth component of complement(C'4) was 36 mg(normal, 20 to 50mg). Radial immunodiffusion disclosed IgG 332mg/dl, IgA 393mg/dl, IgM 771mg/dl. ; agarose gel electrophoresis gave a normal pattern with a moderate increase in the gamma globulin and alpha 2 globulin fractions. A hepatitis panel was negative. In a 24-hour specimen of urine the creatinine was 800mg, and the protein 12gm. X-ray films of the chest showed pneumonic infiltration in both lung fields and pulmonary edema.

Superior mesenteric arteriography showed microaneurysms in the jejunal branches(Fig. 2). On the sixth hospital day symptoms and signs of panperitonitis developed, and laparotomy confirmed jejunal perforation.

Gross examination of the segmentally resected

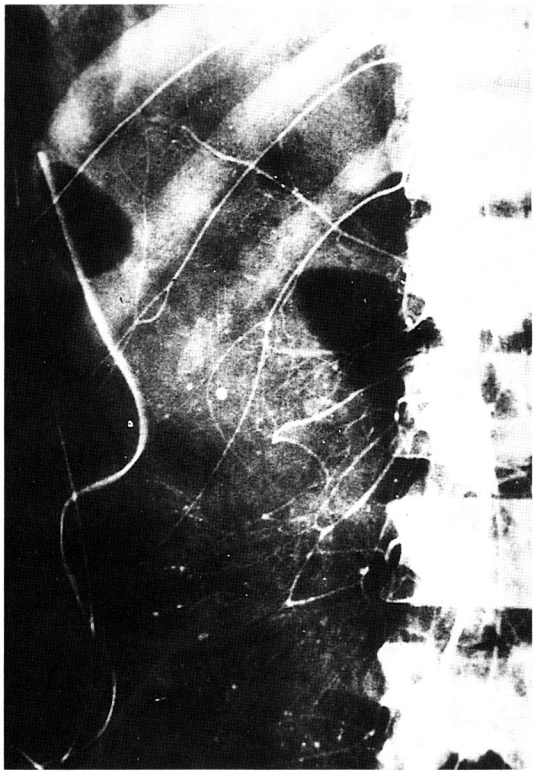

Fig. 2. Superior mesenteric arteriogram showing microaneurysms in the jejunal branches.

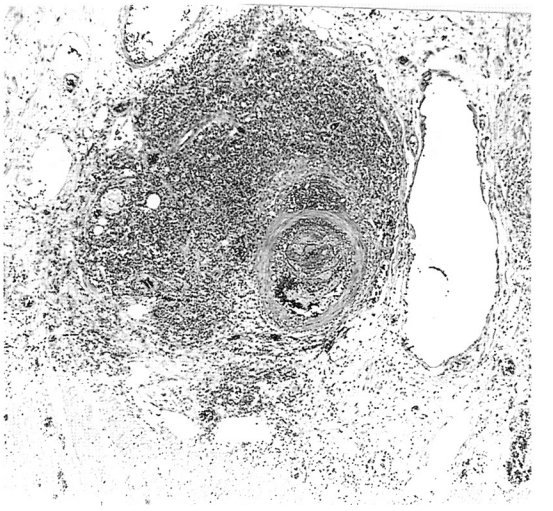

Fig. 3. Polyarteritis nodosa involving the jejunum. There is segmental fibrinoid necrosis in the wall of a medium sized muscular artery with periarterial inflammation in the submucosa.(Hematoxylin-eosin stain.×40).

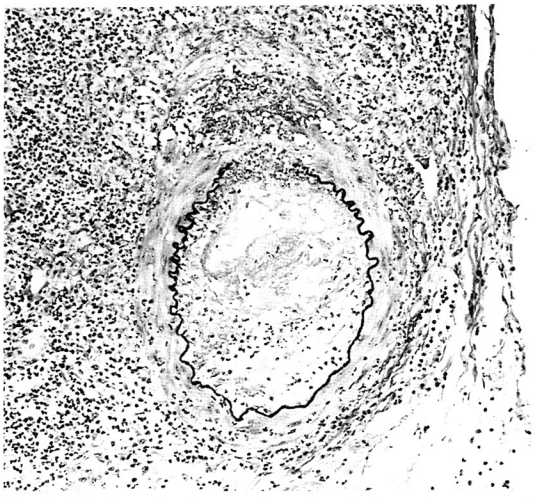

Fig. 4. Medium sized muscular artery in the submucosa of the jejunum showing necrotizing arteritis with destroyed internal elastic lamina, intravascular thrombus, and fibrinoid necrosis.(Elastic tissue stain.×100).

jejunum showed multiple patchy ulcerations in the mucosal surface. Microscopically, there was focal segmental necrotizing arteritis involving small and medium sized muscular arteries in the jejunum and mesentery (Fig. 3). The vascular lumina showed fibrinous or organizing thrombi. In more acute lesions we observed extensive fibrinoid necrosis of the walls of small arteries, arterioles, venules and capillaries, and an infiltrate composed of lymphocytes and neutrophils.

In most of the affected arteries there was marked destruction of the elastic lamina, associated with aneurysm formation(Fig. 4). The jejunum had been ulcerated due to underlying vasculitis with perforation leading to peritonitis. A diagnosis of polyarteritis nodosa was made.

Findings of a skin biopsy specimen from a purpuric skin lesion on his left upper arm on the eighth hospital day showed leukocytoclastic vasculitis. There was perivascular infiltration of polymorphonuclear leukocytes, lymphocytes and some eosinophils involving venules in the papillary and upper reticular dermis. Fibrinoid necrosis of vessel walls, nuclear dusts and extravasation of red cells around the affected venules were conspicuous(Fig. 5).

Two weeks after the skin biopsy a second skin biopsy of a purpuric lesion was performed. Im-

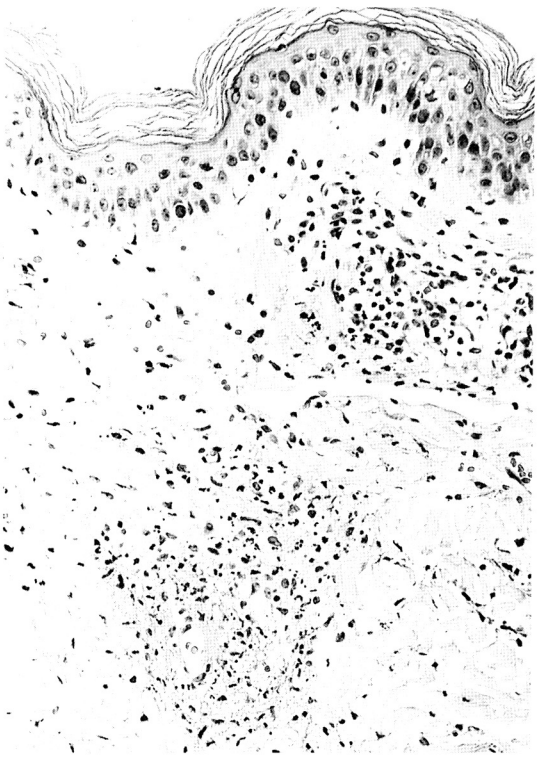

Fig. 5. Leukocytoclastic vasculitis involving venules in the reticular dermis. There is RBC extravasation, fibrinoid necrosis of the vessel wall, and infiltration of polymorphonuclear leukocytes with leukocytoclasis.(Hematoxylin-eosin stain. X200).

munofluorescence study revealed weak IgA deposits in the walls of small vessels in the upper dermis as well as C3, and fibrin or fibrinogen. No deposits of IgG and IgM were noted. The findings of leukocytoclastic vasculitis, with weak positive IgA and C3 staining were consistent with Henoch-Schönlein purpura. The patient was on a downhill clinical course despite cytoxan and steroid pulse therapy. On the 50th hospital day the patient died due to cerebral infarction and hemopneumothorax.

DISCUSSION

In conjunction with the findings of skin biopsies, angiographically documented microaneurysms in the superior mesenteric arteries and segmental necrotizing arteritis of the small and medium sized arteries in the jejunum, we think that this patient had Henoch-Schönlein purpura associated with classic systemic polyarteritis nodosa, and that this case can be included in the category of polyangiitis overlap syndrome.

A strict distinction of medium-sized vessel polyarteritis-type vasculitis from small-vessel hypersensitivity angiitis-type vasculitis cannot always be made in some cases(DeShazo et al., 1977 ; Pischel and Zvaifler, 1984). These vasculitic syndromes with overlapping clinical and pathologic features remain constant sources of nosologic confusion(Leavitt and Fauci, 1986). However, early and correct diagnosis of vasculitis becomes vital not only for prompt and aggressive immunosuppressive treatment of certain 'malignant' forms of vasculitis but also for withholding cytotoxic agents in situations where their use is unwarranted and may cause serious side effects and complications(Lie, 1987).

Of the 10 patients Leavitt and Fauci(1986) studied, three had overlap of classic polyarteritis nodosa and allergic angiitis and granulomatosis, two had overlap of giant cell arteritis and polyarteritis nodosa, one had overlap of cutaneous vasculitis and polyarteritis nodosa, one had overlap of Henoch-Schönlein purpura and polyarteritis nodosa, and three had overlapping syndromes that could not be clearly classified under any well-defined clinical syndrome. Our case illustrates the importance of the recognition of the polyangiitis overlap syndrome as a distinct clinical entity.

As Cupps and Fauci(1983) have previously reported, isolated cutaneous vasculitis is frequently not responsive to a combination of corticosteroids and cyclophosphamide. However, when it is associated with an underlying systemic vasculitis, cutaneous vasculitis of any type usually responds promptly to immunosuppressive therapy (Fauci et al., 1978 ; Cupps and Fauci, 1983 ; Fauci, 1983).

There are several striking differences between patients with the polyangiitis overlap syndrome and those with the classic systemic necrotizing vasculitic syndromes (Fauci et al., 1979 ; Leavitt and Fauci, 1986). The overlap syndrome is seen in a younger group of patients than classic systemic necrotizing vasculitis (mean age of onset 25 years versus 41 years)(Leavitt and Fauci, 1986). In addition, as in our case none of the patients with polyangiitis overlap syndrome had hepatitis B antigenemia, whereas six of the 17 previously described patients in the systemic necrotizing vasculitis group did have hepatitis B antigenemia(Fauci et al., 1979 ; Leavitt and Fauci, 1986). The clinical course in patients

with the polyangiitis overlap syndrome is similar to that in patients with systemic necrotizing vasculitis-(Fauci et al., 1979). All of the patients had aggressive diseases that ultimately required therapy with both corticosteroids and cyclophosphamide in nine cases out of 10 (Fauci, 1983).

Most vasculitic syndromes are caused by deposition of immune complex in the vessel wall (Fauci et al., 1978). The factors which influence the sites of inflammation in polyarteritis nodosa and leukocytoclastic vasculitis are not known but probably include : the charge of the immune complex, the size, chronicity, amount, and uniformity of the complexes, and immunoglobulin properties such as class and affinity (Pischel and Zvaifler, 1984). A single antigen can cause more than one vasculitic syndrome. In hepatitis B infection, the same immune complexes may be deposited in muscular arteries, producing polyarteritis nodosa, and in venules, producing hypersensitivity angiitis, and elicit the production of anti-immunoglobulin antibodies directed against the Fc portion of HBs Ab, leading to the development of cryoglobulinemia (Sergent et al., 1976 ; Sergent, 1980). Therefore, it can be expected that a single antigen will trigger different pathologic responses in different patients as well as elicit varied pathologic responses in an individual patient.

Alternatively, the overlap case may result from a mixture of immune complex, each with its own pattern of distribution (Pischel and Zvaifler, 1984).

In conclusion, since cutaneous vasculitis is a common feature of the syndrome, clinicians should be aware of the existence of the polyangiitis overlap syndrome. This is a systemic vasculitic syndrome with real potential for irreversible organ damage if not treated promptly and adequately.

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