Polyangiitis Overlap Syndrome

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A 33-year-old man was admitted to our hospital because of intermittent claudication and finger tip ulceration with a skin rash on the upper and lower extremities. He later developed a massive melena. Angiography revealed arterial occlusion in the hand and foot, skin biopsy showed vasculitis with eosinophilic infiltration, and biopsy of the colon showed mucosal vasculitis with thrombosis. A diagnosis of polyangiitis overlap syndrome was made, and all these symptoms improved after corticosteroid therapy.
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Key words: eosinophilia, vasculitis, corticosteroid therapy

Introduction

Polyangiitis overlap syndrome proposed by Leavitt and Fauci is defined as systemic vasculitis that does not fit precisely into a single category of classical vasculitis or overlaps several of these categories (1). This new syndrome is characterized by multiple organ involvement and a good response to corticosteroids, which integrates two or more types of vasculitis previously considered to be independent and present in the same patient by chance. This is important because of differences in the prognosis, since early immunosuppressive therapy should be given in the case of polyangiitis overlap syndrome. Only a few cases of this syndrome have been reported to date (2–4). Here we present a case of polyangiitis overlap syndrome in which multiple vascular disorders were markedly improved by treatment with prednisolone.

Case Report

A 33-year-old man was admitted to our hospital in June 1995 because of an itchy rash on the lower and upper extremities, bilateral cervical lymphadenopathy, productive cough, and intermittent claudication. He also had Raynaud's phenomenon, and fingertip ulceration was found on admission. He had smoked 30 cigarettes per day for approximately 20 years, and had no previous history of allergies or bronchial asthma. The blood pressure was 110/66 mmHg in the right arm and 108/64 mmHg in the left arm, the pulse rate was 52/min and regular, and the temperature was 36.7°C. He had erythematous eruptions on the bilateral upper and lower extremities. These eruptions did

not show migration, fusion, or spontaneous remission. He complained of cold and hypesthesia of the bilateral fingers, and apical ulceration was found on the 2nd and 3rd fingers of the left hand. Laboratory data are shown in Table 1. He had leukocytosis with severe eosinophilia and an increased serum IgE level. There were no abnormalities of coagulation, biochemistry, and serology tests, except for elevation of C-reactive protein (CRP) and the erythrocyte sedimentation rate (ESR). No proteinuria or hematuria was observed. No abnormalities were observed on chest X-ray films and assessment of respiratory function, suggesting that there were no lung lesions. The biopsy specimen obtained from a cervical lymph node demonstrated lymphadenitis with severe eosinophil invasion. The punch biopsy specimen from a skin eruption on the lower extremity revealed vasculitis with severe eosinophilia, no fibrinoid necrosis, and no evidence of malignancy (Fig. 1).

Angiography revealed arterial obstruction in the upper and lower extremities (Fig. 2A). There was obstruction of the ulnar artery and radial artery at the wrist joint, and collateral circulation was inadequate, so blood flow to the 2nd finger was not visualized.

On the 53rd hospital day, he suddenly developed severe abdominal pain and melena. Colon fiberoscopy revealed hemorrhagic erosions and mucosal edema in the transverse and descending colon. Biopsy of an erosive lesion in the colon demonstrated hemorrhagic colitis with thrombotic occlusion of the mucosal vessels that suggested ischemic colitis, and no eosinophils were observed (Fig. 3). In addition, upper gastrointestinal fiberoscopy showed erosive gastritis with severe hemorrhage. These events suggested that gastrointestinal vas-

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Table 1. Laboratory Data on Admission

Hematology		Na		139 mEq/l
Red blood cell	438×10 ⁴ /μl	K		4.0 mEq/l
Hemoglobin	13.2 g/dl	Cl		99 mEq/l
Hematocrit	32.4%	C-reactive protein		0.68 mg/dl
Platelet	20.8×10 ⁴ /μl	Erythrocyte sedimentation rate		32 mm/h
White blood cell	16,800/μl	Serology		
Neutrophil	13.5%	IgG		1,601 mg/dl
Eosinophil	65%	IgA		432 mg/dl
Coagulation		IgM		384 mg/dl
Prothrombin	102%	IgE		18,100 IU/ml
Activated partial thromboplastin time	29.3 s	C3		104 mg/dl
Fibrinogen	244 mg/dl	C4		46 mg/dl
Thrombo test	148%	CH50		51.6 U
Anti thrombin III	96%	Anti-nuclear antibody		(-)
Fibrin degradation product	125 ng/ml	LE test		(-)
Lupus anticoagulant	(-)	Anti-DNA antibody		(-)
Anti cardiolipin antibody (IgG, IgM)	(-)	Immuno complex		<1.5 μg/ml
Blood chemistry		C-ANCA		<10 EU
Aspartate aminotransferase	22 U/l	P-ANCA		<10 EU
Alanine aminotransferase	32 U/l	HBs antigen		(-)
Lactate dehydrogenase	451 U/l	Urinalysis findings		
Alkaline phosphatase	358 U/l	Protein		(-)
γ-glutamyl transpeptidase	50 U/l	Sugar		(-)
Total bilirubin	0.6 mg/dl	Occult blood		(-)
Blood urea nitrogen	11 mg/dl	Ketone		(-)
Creatinine	0.6 mg/dl	Urinary sediment		np
Total protein	7.6 g/dl			
Albumin	4.3 g/dl

Figure 1. Microscopic findings of the skin rash on the lower extremity (HE stain, ×400), showing vasculitis with severe eosinophilia and no fibrinoid necrosis.

culitis formed part of an overlap syndrome of multiple vasculitis in this patient. We immediately began prednisolone therapy (60 mg/day), which improved his general condition and ab-

dominal symptoms. Gastrointestinal bleeding stopped on the 2nd day of prednisolone therapy (Fig. 4). When colonfiberscopy was repeated on the 67th hospital day, erosions and hemorrhage were no longer seen. His skin eruptions also improved and finally disappeared. The ulceration of the fingers resolved and his sensory abnormalities recovered. Thermography of the hand showed recovery of the peripheral circulation. When angiography was repeated on the 95th hospital day, recanalization of the occluded arteries was observed along with development of collateral vessels and recovery of blood flow to the 2nd finger (Fig. 2B).

Discussion

Some diseases such as Buerger's disease and Behçet's disease present an inflammatory occlusive disorder involving small and medium-sized arteries and veins in the distal upper and lower extremities. Buerger's disease often includes a triad of claudication of the affected extremity, Raynaud's phenomenon, and phlebitis migrans (5). Behçet's disease is a multisystem disorder presenting with recurrent oral and genital ulcerations as well as ocular involvement; a vascular type of Behçet's disease has also been reported (6, 7). This patient had marked

A

B

Figure 2. A) Angiography of the lower extremity before corticosteroid therapy. Arterial obstruction in the foot can be seen (arrow). B) Angiography of the lower extremity after corticosteroid therapy. Recanalization of the occluded arteries and development of collateral arteries can be seen.

Figure 3. Microscopic findings of the colon (HE stain, ×400). Hemorrhagic colitis with thrombotic occlusion of mucosal vessels is seen (arrow).

eosinophilia and elevated serum IgE, and skin biopsy showed vasculitis with eosinophilia and infiltration. Treatment with prednisolone was highly effective and reperfusion of the occluded vessels occurred. These findings differ from those of Buerger's disease and Behçet's disease. Vasculitis syndrome with eosinophilic tissue infiltration and eosinophilia are characteristic of allergic angitis and granulomatosis (Churg-Strauss syndrome) (8), and the features are occasionally observed in polyarteritis nodosa (PAN), Wegener's granulomatosis, Takayasu's disease, and the hypersensitivity group of vasculitis (9, 10). The present patient manifest clinicopathologic characteristics of vasculitis syndromes which do not fit precisely into any of these diseases, but which have overlapping features in a spectrum of systemic vasculitis-associated disease. Thus this case could be an example of a condition causing a variety of symptoms and findings, which is known as polyangiitis overlap syndrome. This syndrome was originally described by Leavitt and Fauci in 1986 (1). It is defined as a type of systemic vasculitis that does not fit precisely into a single category of classical vasculitis or overlaps several categories. The overlap syndrome occurs in a younger age group than classical vasculitis. Although various organs are involved in the overlap syndrome, cutaneous involvement is most commonly observed, and it responds promptly to corticosteroids and/or cyclophosphamide. In contrast, isolated cutaneous vasculitis frequently shows a poor response to immunosuppressive therapy. Peripheral arterial occlusion, cutaneous vasculitis with eosinophilic infiltration, and alimentary tract vasculitis affecting small mucosal vessels were observed in the present case, and all of these lesions promptly responded to corticosteroid treatment. No single classical vasculitis has all of these clinical findings (11–13), so this case satisfies the criteria for polyangiitis overlap syndrome. This syndrome is not well known to physicians, and few reports have been published previously (2, 4, 14). As far as we know, only a few cases of polyangiitis overlap syndrome have been reported in Japan, which presented features overlap-

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Figure 4. Clinical course.

ping with Wegener's granulomatosis (3, 14). This syndrome does not involve the overlap of several distinct diseases. Instead, it presents a group of symptoms from several diseases related to vasculitis. More reports on this syndrome may help to clarify the etiology of this complicated type of systemic vasculitis and lead to new treatments; it is our hope that the present report will be of some use in this respect.

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