Temporal Arteritis Associated with Systemic Necrotizing Vasculitis

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ABSTRACT. ***Objective.*** To evaluate the clinical and laboratory characteristics of patients with systemic vasculitis associated with temporal artery involvement.

Methods. From a cohort of 120 patients fulfilling American College of Rheumatology criteria for temporal arteritis, we retrospectively identified 7 patients with systemic necrotizing vasculitis associated with histological temporal arteritis.

Results. Among the 7 patients, 2 had classic polyarteritis nodosa, one had unclassified systemic vasculitis, one had Wegener's granulomatosis (WG), and 3 had microscopic polyangiitis. The mean age of the patients was 70.2 years, and cranial symptoms revealed the disease in all but one patient. Temporal arteritis was generally associated with extracephalic manifestations suggestive of systemic vasculitis. Antineutrophilic cytoplasmic antibodies were positive in 3 of the 4 patients with small vessel vasculitis. Pathologically, the main temporal artery was involved in all but one patient, with inflammatory infiltrate of vasa vasorum and adventitia associated in 5 with small tributary involvement. Fibrinoid necrosis was rare, observed in 2 specimens; 2 patients with unclassified systemic vasculitis and WG had a classic giant cell arteritis (GCA) histologic pattern. Only one patient had exclusive involvement of small vessels, surrounding the spared main temporal artery. Muscle biopsies showed histopathological evidence of vasculitis in 2 patients, skin biopsy in one, and vein biopsy in the other.

Conclusion. Temporal artery involvement in systemic necrotizing vasculitis was generally associated with extracranial clinical features suggestive of systemic vasculitis. Temporal artery biopsy is a simple tool for diagnosis of vasculitis, but the histopathological findings do not always discriminate between necrotizing vasculitis and classic GCA. (J Rheumatol 2003;30:2165–9)

Key Indexings Terms:
TEMPORAL ARTERITIS NECROTIZING VASCULITIS MICROSCOPIC POLYANGIITIS
WEGENER'S GRANULOMATOSIS POLYARTERITIS NODOSA

Giant cell temporal arteritis (GCA) is a disease of the elderly, with predominant involvement of large vessels of terminal branches of the external carotid artery. Classical symptoms[1] are constitutional signs, headaches, jaw claudication, elevation of erythrocyte sedimentation rate, and macrophagic and lymphocytic vasculitis of the temporal artery, usually with multinucleated giant cells. Extracephalic manifestations of the disease such as aortic arch syndrome and subclavian and brachial arteritis are uncommon or atypical as respiratory, neurological, or cutaneous signs. Non-giant cell arteritis of temporal artery is quite rare and is observed in the setting of systemic necrotizing vasculitis[2-5]. We describe 7 observations of temporal artery involvement associated with systemic vasculitis.

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MATERIALS AND METHODS

Patients. From our cohort of 120 patients fulfilling the 1990 American College of Rheumatology (ACR) criteria for (giant cell) temporal arteritis[6], seen from January 1990 to December 2000, we retrospectively identified 7 patients with systemic vasculitis. Systemic necrotizing vasculitis was defined according to both ACR[7,8] and Chapel Hill criteria[9] for Wegener's granulomatosis (WG), microscopic polyangiitis (MPA), and classic polyarteritis nodosa (PAN). All patients were negative for hepatitis B and C, human immunodeficiency virus antibodies, antinuclear antibodies, and cryoglobulinemia; all were tested for antineutrophil cytoplasmic antibodies by indirect immunofluorescence. Temporal artery biopsy (TAB) was performed in all cases, and was bilateral in 5 patients. The minimum length of TAB was 20 mm, and all TAB specimens were examined by the same pathologist in a blinded manner for the definitive vasculitis diagnosis; multiple sections were cut, and a median of 92 (range 21–172) hematoxylin and eosin-stained sections per patient were reviewed. Following Esteban, *et al*[10], we focused our histopathologic study of the main temporal artery and small tributary arteries (muscular branches and arterioles) on the presence of fibrinoid necrosis, granulocytes and giant cells, involvement of vasa vasorum, and extension of the inflammatory infiltrates toward the adventitia of the temporal artery. Extra-temporal artery biopsies were muscular in 5 cases, renal in one, cutaneous in one, and venous in one. Clinical, biological, and histological findings were recorded for each patient.

RESULTS

Clinical and laboratory findings (Table 1). The patients were 4 men and 3 women with a mean age of 70.2 years

Table 1. Clinical features of the 7 patients with systemic vasculitis involving temporal artery.

Patient	Diagnosis	Age/sex	Cephalic Symptoms	Extracephalic Signs	Eosinophilia (> 1000/mm^3)	ANCA	Histology	Treatment
1	PAN	72 F	No	Fever, weight loss, mononeuritis multiplex, purpura	2220	—	TA, muscle, skin	CS, CYC
2	PAN	68 F	Headaches, jaw claudication	Fever, weight loss, PMR, hematuria (normal angiography)	No	—	TA, muscle	CS
3	SV	60 M	Headaches, jaw claudication, temporal artery nodules	Fever, weight loss, testicular pain, myalgias	No	—	TA	CS, AZA Danazol
4	WG	63 F	Jaw claudication	Fever, myalgias, arthritis, rhinitis, sinusitis, proteinuria, hematuria, digital vasculitis, nail hemorrhage, polyneuritis	No	PR3	TA	CS, CYC
5	MPA	76 M	Headaches, venous retinal occlusion	Fever, otitis, mononeuritis, proteinuria, hematuria	No	MPO	TA	CS, CYC
6	MPA	77 M	Jaw claudication	Fever, myalgias, mononeuritis multiplex	1560	MPO	TA, muscle	CS
7	MPA	76 M	Headaches, jaw claudication, diplopia	Fever, otitis, arthritis, venous angiitis, scleritis	No	—	TA, vein	CS

PAN: polyarteritis nodosa, SV: systemic vasculitis, WG: Wegener's granulomatosis, MPA: microscopic polyangiitis, PMR: polymyalgia rheumatica, TA: temporal artery, CS: corticosteroids, CYC: cyclophosphamide, AZA: azathioprine.

(range 60–77). According to the ACR and Chapel Hill criteria, 3 of them were classified as MPA, one as WG, and 2 as classic PAN. One patient had an unclassified systemic vasculitis. All patients had constitutional symptoms with fever and weight loss > 4 kg. Seven of 7 patients had signs of temporal arteritis with headaches in 5, jaw claudication in 5, and temporal nodules in one. Two patients had ophthalmologic signs, one with diplopia and scleritis, and another with venous central retinal occlusion; one patient had polymyalgia rheumatica and 3 complained of diffuse myalgias. Otitis media was observed in 2 patients with MPA. Two patients, one with WG and another MPA, had mild proteinuria and microscopic hematuria and were positive for antineutrophil cytoplasmic antibodies (ANCA) by indirect immunofluorescence — anti-PR3 antibodies and anti-myeloperoxidase antibodies, respectively, by ELISA. Four patients had peripheral nervous system involvement (one PAN, 2 MPA, one WG). The patient with an unclassified vasculitis had testicular pain and tenderness and diffuse myalgias. A PAN patient with initially isolated fever had mononeuritis multiplex and palpable purpura at the relapse. Two patients (MPA and PAN) had moderate eosinophilia (1560 and 2220/mm^3). The course of the disease was favorable in 6 out of 7 patients, with treatment by corticosteroids alone in 3 and associated with immunosuppressives in 4 patients for extracephalic manifestations of the vasculitis: cyclophosphamide as initial treatment for WG, MPA, and relapse of PAN, azathioprine for a corticosteroid dependent vasculitis.

Histological findings (Table 2). Histological analyses of TAB disclosed pathologic features in all 7 patients. All patients but one had involvement of the main temporal artery, associated in 5 with involvement of the surrounding small vessels (Figure 1). All had lymphocytic and macrophagic infiltration of media and adventitia, with giant cells in 2 and fibrinoid necrosis in one. Classic PAN involved the main temporal artery, showing mononuclear infiltration of media and adventitia, associated with vasa vasorum involvement, without fibrinoid necrosis. The TAB of the patient with WG showed a main GCA associated with small vessel involvement. Among the MPA patients, one had main temporal arteritis with mild mononeuritis and polymorphonuclear cells, vasa vasorum and adventitia infiltration, sparing the small vessels, and another had isolated necrotizing arteritis, surrounding the small vessels and sparing the main temporal artery (Figure 2). Muscle biopsy was performed in 5 patients; 2 patients with PAN and one with MPA had histologic features of non-necrotizing vasculitis. A patient with MPA had nodular superficial thrombophlebitis of the legs, and a vein biopsy disclosed angiitis; another patient with PAN had a skin biopsy showing fibrinoid necrosis and vasculitis.

DISCUSSION

The temporal artery could be involved in many diseases[3-5,11-13]. However, except for classic GCA, this finding is very rare. Our 7 patients had temporal artery involvement in the setting of systemic vasculitis. They generally fulfilled the ACR and Chapel Hill criteria for both GCA and systemic necrotizing vasculitis. Cephalic symptoms revealed the disease in all but one patient, associated with visceral manifestations, suggestive of systemic vasculitis (Table 1).

Temporal artery involvement in systemic necrotizing vasculitis has been well described by Généreau, *et al*[11] in a French multicenter cohort of 27 patients: 11 with PAN, 6 with Churg-Strauss syndrome, 3 with MPA, 3 with WG, 2

Table 2. Pathologic features of the 7 patients with systemic vasculitis involving temporal artery.

Patient	Diagnosis	Main Temporal Artery					Small Tributaries		
		Giant Cells	Mononuclear Cells/ Neutrophils	Fibrinoid Necrosis	Adventitia	Vasa Vasorum	Giant Cells	Mononuclear Cells/ Neutrophils	Fibrinoid Necrosis
1	PAN	–	++/++	–	+	+	–	+/+	–
2	PAN	–	+/–	–	+	+	–	+/–	–
3	SV	+++	++/+	–	+	+	+	+/–	–
4	WG	+	++/+	–	+	+	–	+/–	–
5	MPA	–	–	–	–	–	–	+/–	++
6	MPA	–	+/+	+	+	+	–	++/+	+
7	MPA	–	+/+	–	+	+			

– Absent; +, mild; ++, moderate; +++, severe/prominent. PAN: polyarteritis nodosa, SV: systemic vasculitis, WG: Wegener's granulomatosis, MPA: microscopic polyangiitis.

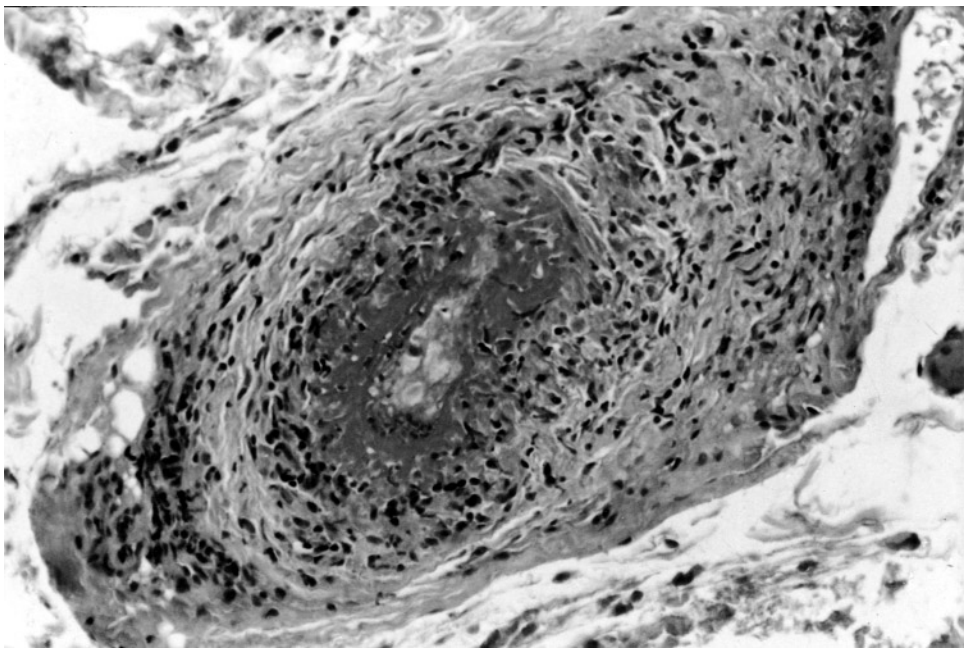

Figure 1. Isolated necrotizing vasculitis of a temporal small vessel (HPS ×200).

with hepatitis B virus-related PAN, one with hepatitis C virus-related cryoglobulinemic vasculitis, and one with rheumatoid vasculitis. In 19 of these 27 patients, fibrinoid necrosis and polymorphonuclear leukocyte infiltrates, highly suggestive of systemic necrotizing vasculitis, were present on TAB, whereas GCA was present in 5. In the TAB specimens of 13 patients, necrotizing vasculitis was seen only on a small adventitial artery. In our patients (Table 2), as in previous reports[3,10,11,14], "true necrotizing vasculitis" of the superficial temporal artery was rare[15], and the vasculitis could share the histopathological findings of classic temporal arteritis. It is interesting that large vessel vasculitis as temporal giant cell arteritis could also involve small arteries such as the tributary arteries. The significance of perivascular inflammation in the absence of arteritis in TAB has not yet been determined[16,17]. As shown by Disdier, *et al*[17], isolated vasa vasoritis is a nonspecific finding of undetermined significance, observed in necrotizing vasculitis but also in several pathologic conditions such as lymphoproliferative disorders or infectious diseases such as bacterial endocarditis. In our patients, it was generally associated with mononuclear infiltration of the main temporal artery. Esteban, *et al*[10], in a series of 28 patients with small-vessel vasculitis surrounding a spared temporal artery, found, after a complete evaluation for systemic vasculitis, that GCA was the most likely diagnosis in the majority of patients. Several histological differences between GCA and systemic necrotizing vasculitis were noted in this report. Whereas involvement of small muscle arteries and presence of granulocytes were equal in both processes, it is interesting that fibrinoid necrosis was found only in patients with systemic necrotizing vasculitis, and extension of the inflammatory infil-

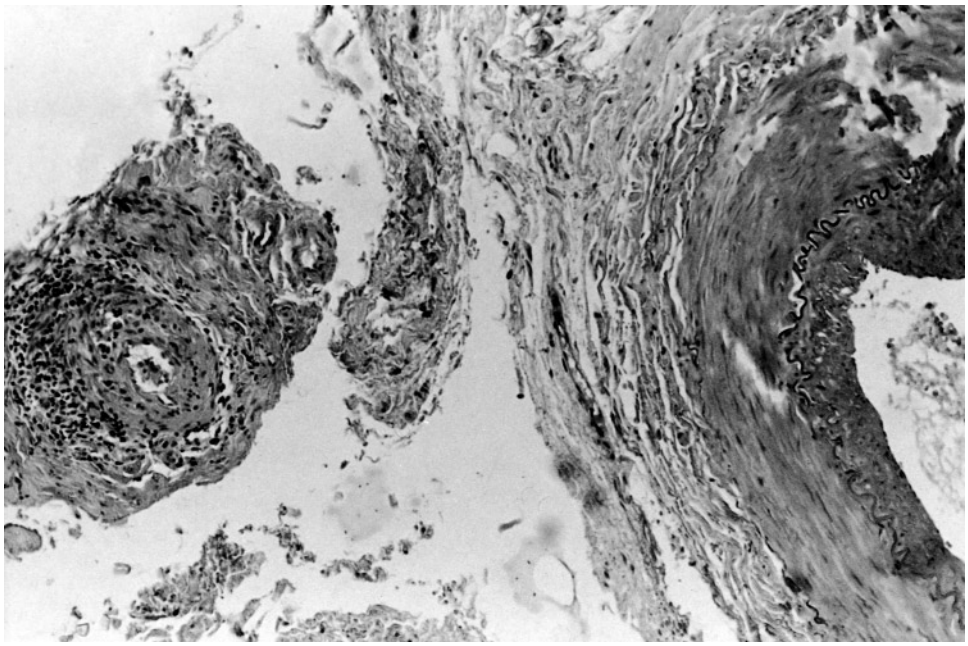

Figure 2. Small vessel vasculitis with spared main temporal artery in microscopic polyangiitis (HPS ×100).

trates toward the adventitia and inflammation of vasa vasorum were observed only in the group with GCA. According to these authors, these histologic features are essential for distinction between the 2 diseases. However, we did not find them in our 7 patients with systemic vasculitis, who all had vasa vasorum involvement. As reported[18,19], this involvement of vasa vasorum could have major significance as an early pathogenic event in GCA. ANCA and especially anti-PR3 antibodies could be useful indicators for diagnosis of systemic non-giant cell vasculitis, as they are generally absent in GCA[20]. The mean age in our group was 70.2 years, higher than usual in patients with small or medium size vessel vasculitis.

Inaugural presentation of systemic vasculitis can mimic classic GCA, and in our experience, TAB cannot discriminate histopathologically between systemic necrotizing vasculitis and GCA. Clinicians must be aware of the diagnosis of systemic necrotizing vasculitis, particularly in elderly people, and exclude it by a complete evaluation. TAB seems to be a simple and reliable tool for the diagnosis procedure of vasculitis, and prospective studies are necessary to confirm this point.

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