Case Series

Lower Limb Giant Cell Arteritis and Temporal Arteritis: Followup of 8 Cases

CLAIRE Le HELLO, HERVÉ LÉVESQUE, MARTINE JEANTON, NICOLE CAILLEUX, FRANÇOISE GALATEAU, CHRISTOPHE PEILLON, PIERRE VEYSSIER, JACQUES WATELET, PHILIPPE LETELLIER, HUBERT COURTOIS, and DOMINIQUE MAÏZA

ABSTRACT. Among 8 patients with giant cell arteritis (GCA) (6 women, 2 men) whose clinical presentations were compatible with temporal arteritis (TA), 6 were followed for 37–105 (mean 74.9) months, one died shortly after treatment onset, and the last was asymptomatic (10 mg steroids/day) when lost to followup at 29 months. All 8 patients had bilateral leg claudication of recent onset; for 6 patients, this was the first symptom. All leg angiograms showed multiple, bilateral, long and smooth stenoses, thromboses, or both. Biopsies of diseased leg arteries from 4 patients provided histological proof of GCA; another case was histologically proven post mortem. Among the 5 patients who met at least 3 American College of Rheumatology criteria of GCA or TA, 3 without histologically documented leg GCA also had biopsy proven temporal GCA (n = 1), or headaches and claudication and angiographic inflammatory arteritis of the arms (n = 2). All patients received steroids; 3 had bypasses, one with endarterectomy. Five are asymptomatic after 24–100 months of steroids (mean 50.6). Revascularization was not successful; one amputation was necessary. Large artery involvement in GCA can affect the legs. Bilateral and rapidly progressive intermittent claudication of recent onset is the most common symptom, even in the absence of headaches or the presence of a silent inflammatory syndrome. Early diagnosis allows rapid initiation of steroid therapy, which is usually able to generate a sufficiently good response to avoid vascular surgery. (J Rheumatol 2001;28:1407–12)

Key Indexing Terms:
GIANT CELL ARTERITIS LEGS INFLAMMATORY ARTERITIS TEMPORAL ARTERITIS

Horton, *et al*[1] published the first histological description of giant cell arteritis (GCA) of the temporal vessels in 1932. Thereafter, the disease was termed temporal arteritis (TA) or GCA because the authors thought it was a localized affliction of the cranial arteries in elderly patients. Jennings and Camb[2] and others[3,4] subsequently drew attention to the possible extracranial large vessel involvement of GCA especially because of bruits over upper or lower limb arteries. Among the 52 patients studied by Hamrin *et al*, 58% had at least a bruit, compared to only 12% of the 52 controls[3]. GCA has since been recognized as a systemic vascular disease. The first documented proof of lower limb involvement was based on autopsies and suggested that occult localizations of GCA occur more commonly than is clinically recognized[5-7]. A larger necropsy study revealed the disseminated nature of this pathology, especially aorta and lower limb involvement[8]. In the largest clinical study (248 patients with TA), 34 had evidence that the disease affected the aorta or its major branches[9]. The frequencies of GCA involvement of extracranial large vessels range widely because different diagnostic criteria are used. Except for autopsy findings, leg artery involvement seems rare, because only 18 well documented cases with histological proof of lower limb GCA have been published in the English and French literature[10-27]. However, it is essential to identify this entity at an early stage because in the absence of appropriate treatment, rapid progression to critical ischemia and gangrene is possible. Clinical and biological signs of TA may be absent and may result in a potentially dangerous delay in obtaining the diagnosis and initiating the corticosteroids (CS). GCA should therefore be included in the differential diagnosis of any unexplained peripheral vascular disease occurring in middle aged or elderly patients. We describe 8 patients with lower limb GCA compatible with TA first seen

From the Departments of Thoracic and Cardiovascular Surgery, Pathology and Internal Medicine, Centre Hospitalier Universitaire de Caen, Caen; the Departments of Internal Medicine and Vascular Surgery, Centre Hospitalier Universitaire de Rouen, Rouen; and the Department of Internal Medicine, Centre Hospitalier Général de Compiègne, Compiègne, France.

C. Le Hello, Staff Physician; D. Maïza, Head, Department of Thoracic and Cardiovascular Surgery; F. Galateau, Staff Physician, Department of Pathology; P. Letellier, Head, Department of Internal Medicine, Centre Hospitalier, Universitaire de Caen; M. Jeanton, Staff Physician; N. Cailleux, Staff Physician; H. Lévesque, Head; H. Courtois, Head, Department of Internal Medicine; C. Peillon, Staff Physician; J. Watelet, Head, Department of Vascular Surgery, Centre Hospitalier Universitaire de Rouen; P. Veyssier, Head, Department of Internal Medicine, Centre Hospitalier Général de Compiègne.

Address reprint requests to Dr. C. Le Hello, Department of Thoracic and Cardiovascular Surgery, Centre Hospitalier Universitaire de Caen, avenue de la Côte de Nacre, 14000 Caen Cedex, France.

Submitted July 10, 2000 revision accepted September 22, 2000.

in 3 university hospital centers in northern France between 1982 and 1997.

CASE REPORTS

The mean age of the 8 Caucasian patients (6 women, 2 men) was 56.3 years (Table 1). Patient 7 has been reported[28]. Five patients had at least 3 of the 5 American College of Rheumatology (ACR) criteria for the diagnosis of GCA[29]. For Patients 3, 4, and 8, who had less than 3 ACR criteria, the latter 2 were over 50 years old and histological examination of their leg artery biopsies provided proof for definitive diagnosis of GCA; Patient 3, despite her young age and only one ACR criterion, suffered from shoulder pains, but Takayasu's arteritis was excluded[30] and she was diagnosed based on angiograms and superficial femoral artery biopsy. All patients presented with poor general status. Common symptoms of GCA were not present in all patients: only 4 had headaches, one had indurated temporal arteries, 2 had hip and shoulder girdle pains, and 2 had jaw claudication. The mean erythrocyte sedimentation rate (ESR) was 89.6 (range 24–140) mm/h. A unilateral temporal artery biopsy was performed in 7 patients and revealed GCA in only 3 cases.

Cardiovascular risk factors. Some patients had cardiovascular risk factors (Table 2). No patient had history of symptomatic coronary atherosclerosis (no angina, no electrocardiographic manifestations, no chronic ischemic heart disease) or cerebrovascular disease (e.g., cerebral embolism, lacunae, or intracranial hemorrhage). There was no clinical or biological argument for diabetes mellitus, elastic tissue disease, connective tissue disease, or Buerger's disease. Patient 2 had a protein S deficiency.

Vascular manifestations. All patients had bilateral leg claudication of recent onset that occurred with exercise, and progressed rapidly; it was the initial symptom for 6 patients. This claudication was severe enough to lead to necrosis in 2 of them. Claudication appeared one year after TA diagnosis for Patient 2 when daily prednisone had been tapered to 10 mg/day; for Patient 8 claudication appeared 8 months after untreated jaw claudication. Examination of all patients revealed symmetrical, total or near total abolition of pulses distal to the popliteal arteries (posterior tibial, dorsal foot). Femoral bruits were noted in 2 of them. Upper limb pulse abolition and/or bruit were present only for Patients 5 and 7: angiograms showed bilateral subclavian and/or axillary stenoses or thromboses.

Angiograms. Each patient underwent lower limb arteriography. Multiple, long segments of smooth arterial stenoses or smooth tapered occlusions of affected large arteries alternating with areas of normal caliber were present in all patients (Figures 1 and 2, Patient 3). Involvement was bilateral in all cases and symmetrical in 7 cases. The most commonly affected were superficial femoral arteries (15/16), deep femoral arteries (9/16), and anterior tibial arteries (5/16) (Table 2). Typical localizations of atheroma were absent for all but Patient 5, and irregular plaques, ulcerations, and calcifications of atherosclerosis were not seen.

Histological examinations. Biopsies of a lower limb artery were taken from 4 patients, twice for diagnosis (superficial femoral artery, posterior tibial artery) and twice during revascularization. Another patient died of a stroke and proof of lower limb involvement was obtained during autopsy. No biopsy was taken for Patients 5–7, who had at least 3 ACR criteria and lower limb angiograms consistent with inflammatory arteritis. Two of them also had angiographically detected bilateral subclavian stenoses or thromboses as described in GCA[31]. The third had biopsy proven temporal GCA. Histological examination of Patient 3's superficial femoral artery found a narrow lumen, thickened intima and media, and disruption of internal elastic lamina with giant cells and granulomas (Figure 3, Patient 3) (Table 1).

Treatment and followup. CS were prescribed to all patients, with one or more

Table 1. Principal characteristics of patients and lower limb histology.

Patient	Age/Sex	Headache	TAA	ESR	Abnormal TAB	ACR Criteria, n	Leg Histology	Other Signs
1	58 M	+	–	45	+	3	GCA (autopsy)	
2	44 M	+	–	120	+	3	GCA (bypass)	
3	42 F	–	–	70	–	1	GCA (biopsy)	
4	60 F	–	–	24	ND	1	GCA (bypass)	
5	57 F	+/–	+	88	–	4	ND	Arm claudication
6	67 F	–	–	120	+	3	ND	
7	60 F	+	–	140	–	3	ND	Arm claudication
8	63 F	–	–	110	–	2	GCA (biopsy)	

TAA: temporal artery abnormality, TAB: temporal artery biopsy, ND: not done, GCA: giant cell arteritis.

Table 2. Cardiovascular risk factors and arteries involved on angiograms.

Patient	Tobacco Use	Hyperlipidemia	HTA	A+I	CF	DF	SF	POP	TPT	AT	PT
1	+	–	–			2	1	1			
2	+	–	–			2	2			2	
3	–	–	–			1	2		1	1	1
4	–	–	+			2	2				
5	–	–	+	2	2		2				
6	–	–	+				2			2	
7	–	–	+				2				
8	+	+	+			2	2	2			1

HTA: hypertension, A + I: aorta + iliac arteries, CF: common femoral artery, DF: deep femoral artery, SF: superficial femoral artery, POP: popliteal artery, TPT: tibioperoneal trunk, AT: anterior tibial artery, PT: posterior tibial artery.

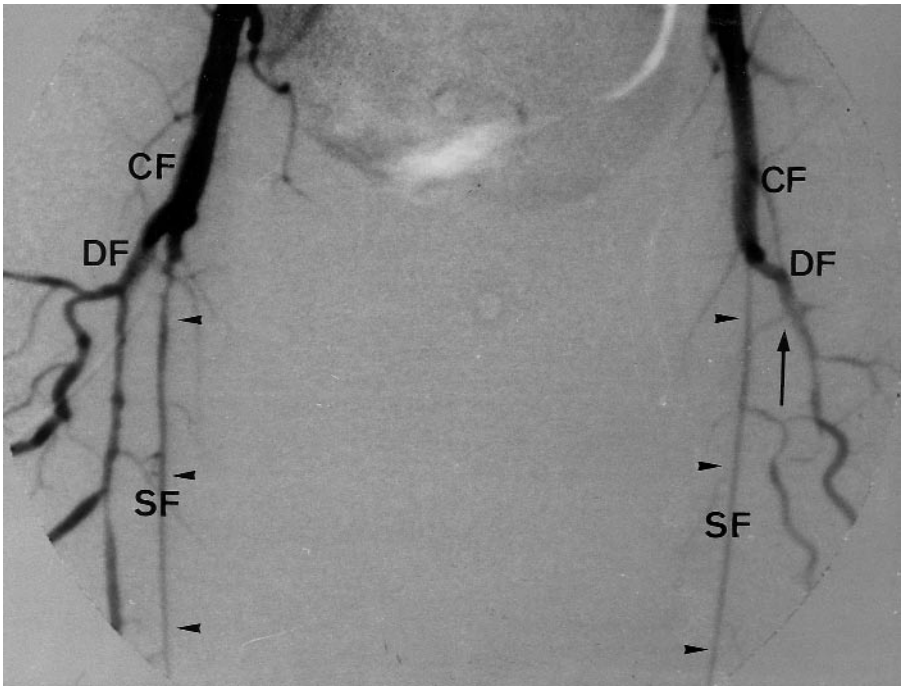

Figure 1. Patient 3. Angiogram: long segments of smooth stenoses of both superficial femoral arteries (arrowheads) and thrombosis of the left distal deep femoral artery (perforating artery) (arrow). CF: common femoral artery, DF: deep femoral artery, SF: superficial femoral artery.

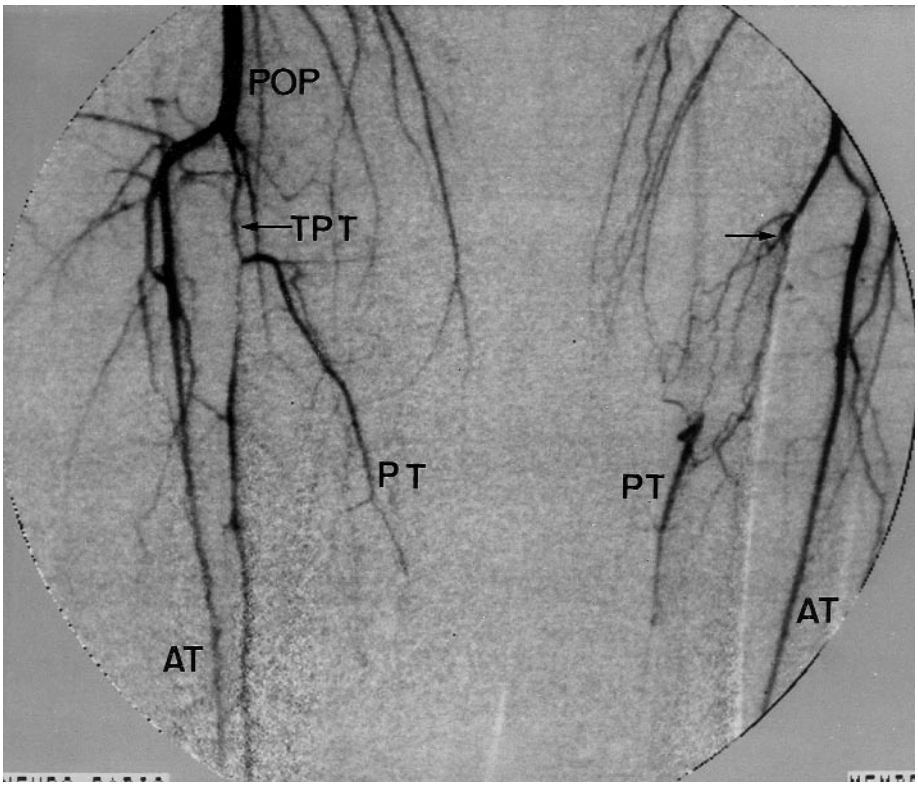

Figure 2. Patient 3. Angiogram: smooth stenoses of the right tibioperoneal trunk and the left anterior tibial artery, occlusion of the left posterior tibial artery. POP: popliteal artery, TPT: tibioperoneal trunk, PT: posterior tibial artery, AT: anterior tibial artery.

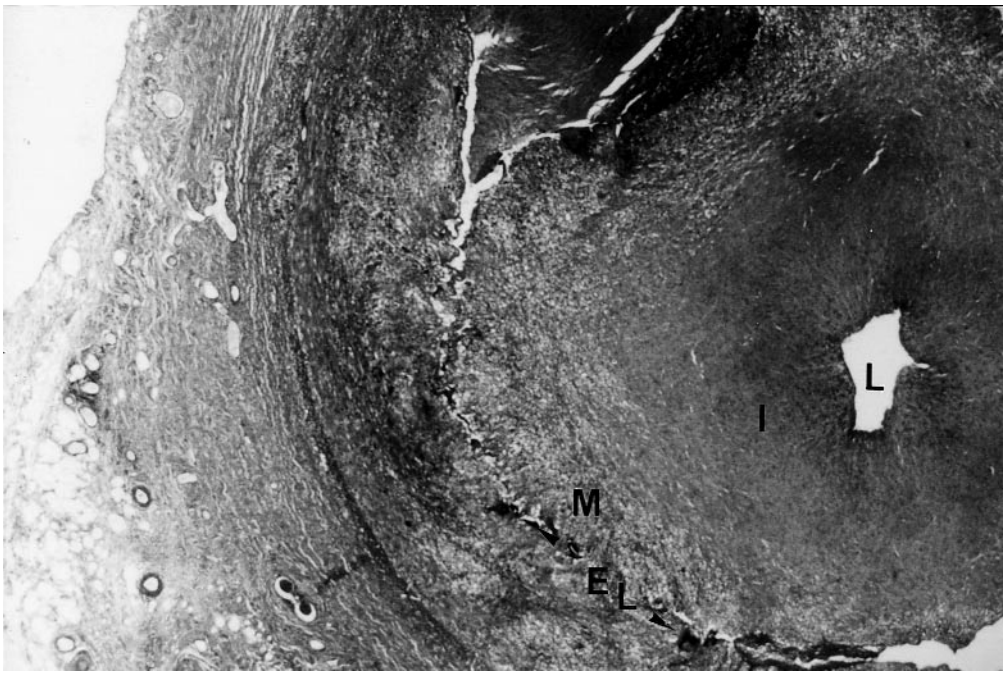

Figure 3. Patient 3. Histology of a superficial femoral artery (H&E-safran × 8.3). L: narrow lumen, I: thickened intima, M: thickened media, EL: disruption of the elastic lamina with giant cells (arrowheads) and granulomas.

pulses of methylprednisolone followed by oral prednisone (1 mg/kg/day) (Table 3). Heparin was initially administered and replaced by an oral anticoagulant or platelet inhibitor. Patient 1 died of a stroke a few days after initiation of CS; cerebral GCA was found at autopsy. Patient 5 was lost to followup after 29 months, when she was asymptomatic while receiving prednisone (10 mg/day). Mean followup for the 6 others was 74.9 months (range 37–105); mean duration of CS treatment was 50.6 months (range 24–100). Patients 2, 3, and 6 remained asymptomatic 105, 60, and 71 months, respectively, after initiation of CS, which were discontinued after 49, 28, and 66 months. Patient 8 is asymptomatic under CS therapy, which has lasted 37 months and is still being tapered regularly. Patient 7 required unilateral amputation and remains asymptomatic and was receiving prednisone (8 mg/day) 101 months after starting CS. Patient 4 still experiences claudication upon walking 300 m, 75 months after initiation of treatment; CS were discontinued after 24 months. Revascularization (bypass and/or endarterectomy) was performed in 3 patients. Patient 2 had been taking prednisone for 11 months to treat GCA when he experienced acute ischemia of the legs. A right femoropopliteal bypass was performed because of uncertain etiology for leg ischemia: lower limb GCA was proven histologically. Patient 4 received CS just after right femorofemoral bypass and left superficial femoral endarterectomy. The diagnosis of TA had not been established for Patient 7 when she experienced bilateral acute ischemia: bilateral femoropopliteal bypasses were performed without biopsy. CS were started one month later when GCA diagnosis was considered because of upper limb ischemia with bilateral axillary smooth stenoses on angiograms. Functional results of revascularization remained poor: 3 of the 4 bypasses were occluded after 3 months (Patient 7) and after 3 years (Patient 2). Similarly, the endarterectomy rapidly became occluded (Patient 4). During CS treatment, classical signs of TA disappeared within 24–48 hours, whereas function of the affected extremities improved within 3–4 weeks. However, pulses did not reappear each time. Doppler ultrasonography and walking distance played a useful role in evaluating evolution of peripheral blood flow. Ischemia recurred during CS tapering for Patients 4, 7, and 8 at doses of 30–35 mg/day. Each time, vascular symptoms disappeared more slowly after increasing the CS dose.

Table 3. Treatment and followup.

Patient	Followup, mo	CS Duration, mo	CS Dose Now	Surgery	Other Drugs	Outcome
1		< 1				Died
2	105	49	0	M11: bypass	OA + PI	Recovered
3	60	28	0		PI	Recovered
4	75	24	0	M0: bypass + Endarterectomy	OA	Symptomatic
5	29	lost M29	?		?	?
6	71	66	0		PI, then OA	Recovered
7	101	100	8	M –1: 2 bypasses M0: amputation	PI	Recovered
8	37	37	2		PI	Recovered

M: month of diagnosis, OA: oral anticoagulant, PI: platelet inhibitor.

DISCUSSION

Other than being occasionally associated, a lower limb localization has rarely been reported in TA or GCA. The general characteristics of our 8 patients are similar to those of the 18 living patients with documented lower limb histological findings[10-27]. These 18 cases showed a female predominance (15 female, 3 male) with a mean age of 52.3 (range 48–75) years; only 3 patients had headaches[10,13,26] and the ESR was under 50 mm/h for 3 patients[12,14,17]. Ten patients underwent a temporal artery biopsy, which was positive for 3[15,22,26]. Two temporal artery biopsies were negative for patients who had headaches[10,13].

Lower limb GCA must not be excluded for patients with clinical manifestations of peripheral vascular disease without classical symptoms of GCA or with a silent biological inflammatory syndrome or negative temporal artery biopsy findings, as seen with our patients and in the literature. The most striking sign of vascular involvement in this localization is the recent onset of bilateral and rapidly progressive claudication with total or near total abolition of peripheral pulses. All patients experienced claudication, which was the first sign of illness for 10 of these 18 patients, and distal necrosis was observed in 7[10-17,24,26].

Among the 18 patients, 14 had angiograms showing long segments of smooth arterial stenoses or smooth tapered occlusions alternating with areas of normal caliber, or thromboses, or both[10-15,18-22,25-27]. Conclusions regarding clinical findings and angiograms were similar in our study and in the literature. GCA was found in 11 patients following biopsy or vascular surgery on lower limb arteries[10-12,18-21,24-27] and following histological examination of amputation specimens of 7 patients[13–17,22,23]. The major diagnostic difficulty is distinguishing between inflammatory and atherosclerotic lesions, which are common in this age group. Only biopsy of the involved arterial segment can provide a definitive answer. When tissue specimens are not available, this diagnosis can be considered when vascular risk factors are limited, angiographic lesions are typical of an inflammatory etiology, and symptoms regress dramatically under CS. The second differential diagnosis is Takayasu's disease, but patients are younger, lower limbs are usually spared, and criteria are different[30]. Claudication regressed progressively for 11 of the 18 patients[10-12,18-21,24-27] and for 5 of our 7 patients. Recurrence was noted during tapering of CS for 3[22,23,26] and 3 of our patients. However, symptoms again disappeared after CS therapy was intensified. Seven amputations[13-17,22,23] including our Patient 7 were necessary, clearly showing the severity of disease in this localization, with bilateral amputation 6 times. Four patients[13,17,23] and one of ours were taking different CS doses when these amputations were necessary. Revascularization procedures should also be avoided, especially during the inflammatory period. When necessary, vascular surgery in these patients should be performed once the inflammatory syndrome has been controlled. Bypass grafts tend to occlude when put in place during the active phase of the disease[32]. When emergency surgery is necessary during the acute inflammatory phase, grafts should be attached to adjacent healthy artery and CS initiated without delay, but revascularization may be dangerous. This risk is particularly true for endarterectomy, patch angioplasty, or bypass surgery[33]. It is necessary to add an anti-platelet-aggregating agent[34]. For the 5 patients observed over a certain time, the longest followup in the literature never exceeded 48 months[12,21,24-26]: the evolution was favorable but few details were given. One patient had a relapse, which regressed after intensification of CS treatment[26], as for 3 of our 8 patients.

GCA involvement of the lower limbs is rare and seldom proven. Furthermore, post mortem studies indicate that this entity is more frequent than previously reported. CS and anti-platelet-aggregating agents should be started immediately because of the poor prognosis. When revascularization is necessary, CS should be systematically used. GCA should be included in the differential diagnosis of any unexplained case of peripheral vascular disease occurring in middle aged or elderly patients when the typical symptoms of TA are slight or absent. It is also important to biopsy a lower limb artery when arterial disease etiology is not evident.

REFERENCES

1. Horton BT, Magath TB, Brown GE. Arteritis of the temporal vessels, a previously undescribed form. Arch Intern Med 1934;53:400-9.
2. Jennings GH, Camb MB. Arteritis of the temporal vessels. Lancet 1938;i:424-8.
3. Hamrin B, Jonsson N, Landberg T. Involvement of large vessels in polymyalgia arteritica. Lancet 1965;i:1193-6.
4. Bruk MI. Articular and vascular manifestations of polymyalgia rheumatica. Ann Rheum Dis 1967;26:103-16.
5. Cardell BS, Hanley T. A fatal case of giant-cell or temporal arteritis. J Pathol Bacteriol 1951;63:587-97.
6. Östberg G. On arteritis with special reference to polymyalgia arteritica. Acta Pathol Microbiol Scand 1973;237:1-59.
7. Heptinstall RH, Porter KA, Barkley H. Giant-cell (temporal) arteritis. J Pathol Bacteriol 1954;67:507-19.
8. Östberg G. Temporal arteritis in a large necropsy series. Ann Rheum Dis 1971;30:224-35.
9. Klein RG, Hunder GG, Stanson AW, Sheps SG. Large artery involvement in giant cell (temporal) arteritis. Ann Intern Med 1975;83:806-12.
10. Sériès C, Chéradame I, Baste JC, Midy D. Maladie de Horton révélée par une atteinte des membres inférieurs. Rev Méd Interne 1993;14:317-9.
11. O'Brien PK, Pudden AJD. Peripheral arterial insufficiency due to giant cell arteritis. Can J Surg 1978;21:441-2.
12. Stautner-Bruckmann C, Haschka C, Baumann G, Bogner J, Spengel FA. Giant-cell arteritis limited to the femoral arteries. Dtsch Med Wochenschr 1992;117:974-7.
13. Greene GM, Lain D, Sherwin RM, Wilson JE, McManus BM. Giant cell arteritis of the legs. Clinical isolation of severe disease with gangrene and amputations. Am J Med 1986;81:727-33.
14. McCain GA, Thompson JM. Isolated giant cell arteritis. J Rheumatol 1978;5:474-6.
15. Lie JT, Tokugawa DA. Bilateral lower limb gangrene and stroke as initial manifestations of systemic giant cell arteritis in an African-

American. J Rheumatol 1995;22:363-5.
16. Atlas LN. A case of Buerger's disease in an old woman. Am Heart J 1943;26:120-3.
17. Finlayson R, Robinson JO. Giant-cell arteritis of the legs. BMJ 1955;2:1595-7.
18. Jouquan J, Volant A, Balouet G, Le Goff P. Artériopathie des membres inférieurs et artérite giganto-cellulaire. Démonstration artériographique et histologique. Semin Hôp Paris 1982;58:1611-6.
19. Hunder GG, Sheps SG. Intermittent claudication and polymyalgia rheumatica. Arch Intern Med 1967;119:638-43.
20. Bourgeois J, Bréger PR, Cosset HB, Renaut-Hovasse H. Une forme rare de maladie de Horton. Ouest Méd 1984;37:831-5.
21. Tazi Z, Cacoub P, Cheysson D, Godeau P, Piette JC. Maladie de Horton démasquée par une artériopathie inflammatoire spécifique des membres inférieurs. Rev Méd Interne 1997;18:638-41.
22. Helfgott SM, Bauer MR. Pedal gangrene caused by giant cell arteritis. Arthritis Rheum 1987;30:1078-9.
23. Bastin R, Godeau P, Lavernhe J, Léger L, Lemaigre G. Pseudo-polyarthrite rhizomélique de l'artérite temporale à l'artérite des membres inférieurs. Presse Méd 1969;77:1649-51.
24. Amatucci G, Del Mastro G, Iandoli R. Horton giant cell arteritis of the legs. Report of a case. J Cardiovasc Surg 1997;38:309-12.
25. Dupuy R, Mercié P, Neau D, Longy-Boursier M, Conri C. Giant cell arteritis involving the lower limbs. Rev Rhum (Engl Ed) 1997;64:500-3.
26. Garcia Vazquez JM, Carreira JM, Seoane C, Vidal JJ. Superior and inferior limb ischaemia in giant cell arteritis: angiography follow-up. Clin Rheumatol 1999;18:61-5.
27. Viallard JF, Fach J, Neau D, et al. Giant cell arteritis of the lower limbs in rhizomelic pseudopolyarthritis. Ann Méd Interne (Paris) 1996;147:225-7.
28. Cailleux N, Lévesque H, Borg JY, Clavier E, Courtois H. Maladie de Horton avec atteinte des troncs artériels des membres supérieurs. Rôle pathogène des anticorps anticardiolipine? A propos de deux observations. J Mal Vasc 1992;17:157-9.
29. Hunder GG, Bloch DA, Michel BA, et al. The American College of Rheumatology 1990 criteria for the classification of giant cell arteritis. Arthritis Rheum 1990;33:1122-8.
30. Arend WP, Michel BA, Bloch DA, et al. The American College of Rheumatology 1990 criteria for the classification of Takayasu arteritis. Arthritis Rheum 1990;33:1129-34.
31. Ninet JP, Bachet P, Dumontet CM, Du Colombier PB, Stewart MD, Pasquier JH. Subclavian and axillary involvement in temporal arteritis and polymyalgia rheumatica. Am J Med 1990;88:13-20.
32. Joyce JW. The giant cell arteritides: diagnosis and the role of surgery. J Vasc Surg 1986;3:827-31.
33. Rivers SP, Bauer GM, Inahara T, Porter JM. Arm ischemia secondary to giant cell arteritis. Am J Surg 1982;143:554-8.
34. Weyand CM, Goronzy JJ. Arterial wall injury in giant cell arteritis. Arthritis Rheum 1999;42:844-53.