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Temporal Arteritis Revealing Antineutrophil Cytoplasmic Antibody–Associated Vasculitides: Case-Control Study of 50 Cases

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Abstract

Background. Temporal arteritis (TA) is a typical manifestation of giant cell arteritis (GCA). Rarely, ANCA-associated vasculitides (AAV) can be revealed by TA, leading to misdiagnoses of GCA and inappropriate treatments.

Methods. We retrospective included patients with TA revealing AAV (TA-AAV), and compared them with classical GCA patients.

Results. Fifty patients with TA-AAV (median age 70 years) were included. Thirty-three (66%) patients presented atypical symptoms for GCA (ENT, renal, pulmonary and neurological involvement in 32%, 26%, 20% and 16%, respectively). ANCA were screened at disease onset in 33 cases, and were positive in 88%, leading to diagnosis of early TA-AAV in 20 cases. AAV diagnosis was delayed in 30 cases after a median interval of 15 months. Compared to GCA, TA-AAV patients were younger (70 vs. 74 years), more frequently men (48 vs. 30%), had high frequency of atypical manifestations and higher CRP levels (10.8 vs. 7.0 mg/dL). Temporal artery biopsy (TAB) from TA-AAV showed fibrinoid necrosis and small branch vasculitis in 23% each, whereas it did not in GCA. Treatment failure-free survival was comparable between early TA-AAV and GCA, whereas those with delayed TA-AAV patients had a significant higher risk of treatment failure compared to GCA [HR 3.85 (1.97-7.51), P<0.0001)].

Conclusion. TA revealing AAV should be considered in case of atypical manifestations for GCA, GCs refractoriness or early relapse. Analysis of TAB for small branch vasculitis and/or fibrinoid necrosis could be useful. Detection of ANCA should be performed in case of suspected GCA with atypical clinical features and/or TAB.

Introduction

The 2012 International Chapel Hill Consensus Conference (CHCC2012) classified vasculitis according to several characteristics, including the size of the affected vessels (1). Giant cell arteritis (GCA) is the most frequent non-necrotizing granulomatous vasculitis involving large vessels (2), whose onset usually occurs after 50 years. In contrast, antineutrophil cytoplasmic antibodies (ANCA)-associated vasculitides (AAV) are a group of necrotizing vasculitis predominantly affecting small vessels (i.e., capillaries, venules, arterioles, and small arteries), associated with myeloperoxidase (MPO) or proteinase 3 (PR3) ANCA (1,3). Temporal artery biopsy (TAB) is frequently performed for the diagnosis of GCA, showing abnormalities in 50 to 80% of cases (4,5). However, in a study on 354 positive TAB, diagnosis of AAV was retained in 3 cases (0.8%) (6). Généreau et al. reported that systemic necrotizing vasculitis was diagnosed based on the TAB in 1.4% of the patients with suspected GCA, and in 4.5% of the inflamed TAB specimens (7). Likewise, rare reports described AAV revealed by temporal arteritis (TA) manifestations, such as granulomatosis with polyangiitis (GPA, Wegener's) (8–10), microscopic polyangiitis (MPA) (11–13) or eosinophilic granulomatosis with polyangiitis (EGPA, Churg-Strauss) (14–16). Nevertheless, therapeutic management and prognosis may strongly differ between GCA and AAV, reason why they should not be misdiagnosed.

In the present study, we aimed to describe the clinical, biological and histological presentation, and outcome of TA revealing AAV, and performed a case-control study to identify features suggestive of AAV in the setting of TA manifestations, especially cephalic manifestations.

Patients and methods

Patient

We conducted a French nationwide retrospective multicenter study including patients from January 2000 to February 2017, supported by the French Vasculitis Study Group (FVSG) and French Study Group for Large Vessel Vasculitis (GEFA), in 19 French and one Belgian departments of Internal Medicine and Rheumatology. Patients with an initial presentation suggestive of TA, i.e. abnormal TAB and/or cephalic manifestations, but a final diagnosis of AAV were included (TA-AAV). Patients without abnormal TAB had to have necessarily cephalic

symptoms suggestive of TA (i.e., headache, scalp tenderness and/or jaw claudication) and fulfilled ACR 1990 criteria of GCA. AAV patients fulfilled American College of Rheumatology (ACR) 1990 criteria (3) and/or the European Medicines Agency (EMA) algorithm (17) and/or the definitions from the 2012 Chapel Hill Consensus Conference (1) for GPA, MPA, or EGPA. This study was conducted in compliance with the Good Clinical Practice protocol and the Declaration of Helsinki principles. The study was approved by local ethics committee, who waived the requirement for informed consent.

Clinical, laboratory, morphological and pathological assessment

For each patient, clinical, biological and pathological data were retrospectively collected from the diagnosis of TA throughout the diagnosis of AAV and until last-follow-up. Clinical and biological assessments included clinical manifestations, serum C-reactive protein (CRP) levels, blood count, ANCA titers and specificity (against PR3 or MPO), TAB findings, and treatment characteristics.

Response to therapy and outcome

Response to therapy was evaluated by physicians in charge of the patients during the routine follow-up of these patients and retrospectively reviewed. Remission was defined as the absence of clinical and morphological manifestations attributable to active disease and normalization of acute-phase reactants.

Control group

Cases (TA-AAV) were compared to controls with TA, i.e. patients with GCA fulfilling the American College of Rheumatology 1990 criteria (2), and without any evidence for AAV. Controls were randomly selected in the GCA databases of two French Vasculitis Centers (Cochin Hospital and Dijon University Hospital) with a ratio of 1 case for 2 controls. We compared clinical, biological and histological features at diagnosis of TA.

Statistical analysis

Data are presented as the mean ± standard deviation (SD) or as the median (interquartile range (IQR)) as appropriate for continuous variables, and frequency (percentage) for qualitative variables. Quantitative variables were compared using Student's *t*-test or the nonparametric Mann-Whitney test, and categorical variables were compared using the chi-square test or the Fisher's exact test. Kaplan–Meier curves were plotted to describe the treatment failure-free survival and the

log-rank test compared both curves. All analyses were performed using the SAS software, version 9.4 and GraphPad Prism version 5.0. All statistical tests were two-sided, and significance was set at the 0.05 level.

Results

Fifty patients with TA-AAV (24 men and 26 women), with a median age of 70 years (IQR 64–75), were included.

Clinical, biological and pathological characteristics of cases at initial presentation suggestive of TA

Clinical, biological and pathological characteristics of TA-AAV cases are summarized in **Table 1**. Clinical manifestations at baseline included cephalic symptoms in 44 (88%) cases, constitutional symptoms in 42 (84%) cases, polymyalgia rheumatica and cough in 15 (30%) each, and visual manifestations in 6 (12%), i.e. visual loss and diplopia in 3 cases each. All TA-AAV cases without cephalic symptoms had inflammation on TAB. Conversely, all cases without positive TAB had cephalic symptoms highly suggestive of TA, associated with constitutional symptoms and increased acute-phase reactants in 70%. Thirty-three (66%) patients presented initially with atypical symptoms for "classical" GCA: ear, nose and throat (ENT) involvement in 16 (32%), renal involvement (renal failure, proteinuria and/or hematuria) in 13 (26%), lung involvement (nodules, intra-alveolar hemorrhage, or consolidation) in 10 (20%), peripheral neuropathy in 9 (18%), abdominal pain and cutaneous manifestations in 5 (10%) cases each, episcleritis in 2 patients and cardiac involvement in 3 patients (i.e. one myocardial infarction and 2 pericarditis). At initial presentation, 17 patients with atypical features were considered as TA-AAV, as well as 3 patients with classical cephalic symptoms but with positive ANCA. Overall, 20 cases as early TA-AAV. For the remaining 30 cases, diagnosis of TA-AAV was delayed, whereas atypical features were present for 16 patients since baseline. ANCA were screened at initial presentation in 33 (66%) cases and were positive in 29 (88%), targeting MPO in 62% and PR3 in 38%, leading to the diagnosis of AAV (early TA-AAV) in 20 cases, while 9 patients were still diagnosed as having GCA because of the absence of symptoms suggestive of AAV (**Figure 1**). TAB was considered abnormal, i.e. with inflammatory infiltrates, in 31/42 (74%) cases, and showed, *a posteriori,* some atypical features for GCA in 13 (42%) cases, i.e. fibrinoid necrosis (**Figure 2**) and small branch vasculitis (**Figure 3**) in 7 (23%) cases each.

Characteristics of cases at diagnosis of AAV

Diagnosis of TA-AAV was made at initial presentation in 20 (40%) cases ("early TA-AAV diagnosis"), and during follow-up in 30 (60%) cases ("delayed TA-AAV diagnosis"), after a median time of 15 months (IQR 9-46). In patients with delayed TA-AAV diagnosis, diagnosis was

made because of a refractory disease in 13 (43%) cases or after vasculitis relapse in 17 (57%). Twenty-six (87%) patients were under glucocorticoids (GCs) at a median dose of 22.5 mg/day (IQR 7-36). Patients' characteristics at AAV diagnosis are summarized in **Table 2**. The delayed TA-AAV diagnosis population presented at baseline constitutional symptoms in 24 (80%) cases and cephalic symptoms in 27 (90%). All 3 patients without cephalic symptoms had inflammation on TAB. Sixteen out the 30 patients (53%) had atypical symptoms for « classical » GCA: ENT involvement in 6, renal involvement in 3, lung involvement in 3, peripherical neuropathy in 3 and cutaneous manifestations in 2 cases. Also, additional features occurred during follow-up before AAV diagnosis: recurrence of constitutional symptoms in 21 (70%) and cephalic symptoms in 11 (37%), ENT involvement in 14 (47%), lung involvement in 12 (40%), peripheral neuropathy in 12 (40%), and renal and cutaneous involvement in 7 (23%) cases each.

In delayed TA-AAV patients, AAV diagnosis was GPA in 67% and MPA in 27%, contrasting with MPO-ANCA specificity in 72% and PR3-ANCA in 24% (including 9 GPA with MPO-ANCA, 6 GPA with PR3-ANCA and 8 MPA patients). In patients with delayed AAV diagnosis, histological evidence of AAV was available in another site than the TAB in 10 (33%). Four of the 5 patients without ANCA had histological evidence of AAV and one had a very suggestive clinical presentation (i.e. ENT involvement, purpura and rapidly progressive glomerulonephritis).

Case-control study of TA-AAV and GCA patients

To identify if TA-AAV patients exhibited peculiar manifestations at initial presentation compared to "classical TA", i.e. GCA, we performed a case-control study between the 50 TA-AAV and 100 GCA patients, and distinguished early TA-AAV (n=20) and delayed TA-AAV (n=30). Comparisons are summarized in **Table 1**. Compared to GCA, patients with early TA-AAV diagnosis were younger and less frequently female, had less headaches, and less visual manifestations but more frequent lung involvement, episcleritis, peripheral arthralgias, renal and ENT involvement, peripheral neuropathy and cutaneous lesions. CRP levels were higher in patients with early TA-AAV diagnosis. TAB showed less frequent granulomatous inflammation and giant cells, and more frequent small branch vasculitis and fibrinoid necrosis in early TA-AAV diagnosis compared to GCA. Patients with delayed TA-AAV diagnosis were more comparable at baseline with GCA patients than those with early TA-AAV. However, extra-cephalic symptoms and findings on TAB were also the main differences with classical GCA patients (**Table 1**). Similar differences were noted when comparing only TA-AAV (n=31) and GCA (n=54) with abnormal TAB, except for sex, age and episcleritis (data not shown).

Therapeutic management of cases and controls

Patient with early TA-AAV were treated with GCs in all cases, in combination with immunosuppressive agents in first-line in 14 cases (including cyclophosphamide in 10 cases, rituximab and methotrexate in 2 cases each). In contrast, patients with delayed TA-AAV received GCs alone in all cases, as in classical GCA patients.

Outcome of cases and controls

To compare the prognosis of TA-AAV compared to GCA, we analyzed treatment failure-free survival in TA-AAV patients with early AAV diagnosis, TA-AAV patients with delayed AAV diagnosis, and GCA patients. Treatment failure-free survival was comparable between early TA-AAV and GCA. In contrast, delayed TA-AAV patients had a significant higher risk of treatment failure compared to GCA patients [Hazard ratio (HR) 3.85 (1.97-7.51), P<0.0001)] (**Figure 4**), the latter being frequently the reason why diagnosis of delayed TA-AAV was made.

Discussion

Besides GCA, temporal arteritis may rarely reveal medium-sized and small-sized vessel vasculitides. Consequences of such misdiagnoses can be detrimental since therapeutic management and outcomes strongly differ between diseases. To early identify TA manifestations revealing AAV, we described presentation and outcome of TA-AAV compared to classical GCA.

Compared to GCA, TA-AAV patients were slightly younger, more frequently men, had a high frequency of atypical manifestations for large vessel vasculitis and had higher CRP levels. At patient-level, because of their lack of specificity, demographical differences and higher CRP levels cannot be used to evoke TA-AAV. On the other hand, two-thirds of TA-AAV patients presented with atypical manifestations for GCA, such as mononeuritis multiplex, lung involvement, ENT or renal involvement. These manifestations were commonly underestimated because cephalic symptoms were at the forefront of initial presentation, while cranial symptoms and headache are not typical of AAV **(18)**, except in the case of pachymeningitis which remains a rare manifestation of the disease (10,13). For these reasons, diagnosis of TA-AAV was more challenging than it looks like.

Detection of ANCA using antigen-specific immunoassays was the most frequent abnormality leading to the final diagnosis of TA-AAV. Majority of TA-AAV patients presented with a GPA phenotype whereas majority of ANCA were directed against MPO. There is a large variability for

ANCA detection using indirect immunofluorescence in older patients what could lead to false positive, contrasting with the high diagnostic performance of immunoassays for PR3-ANCA and MPO-ANCA to discriminate AAV from disease controls **(19)**. Recently, a revised international consensus on testing of ANCA proposed that ANCA measurement should use antigen-specific immunoassays as the primary screening method **(20)**, and especially to all patients with suspected GCA to avoid false positive and false negative.

Temporal artery biopsy could be useful in challenging situations. TAB was frequently abnormal in case of cephalic symptoms, either in GCA or AAV, suggesting that TAB could be contributive for the diagnosis of systemic vasculitides whatever the underlying diagnosis (7). Some cases did not have abnormality in TAB, but all of them had cephalic symptoms and clinical presentation suggestive of GCA. In our study, histological findings that could be highly suggestive of small vessels vasculitis were the presence of necrotizing vasculitis or small branch vasculitis **(21)**, contrasting with the absence of granulomatous inflammation and/or giant cells, but these abnormalities lacked sensitivity. In contrast, no small branch vasculitis and/or fibrinoid necrosis were noted in any biopsy from GCA patients, showing that it could represent a major red flag when analyzing TAB. Indeed, in the study by Cavazza et al.**(6)**, a SVV pattern without positive ANCA was reported in 9% of patients. Nevertheless, in our study, the patients that were considered as TA-AAV all met criteria for AAV and not for other SVV, including immune complex small vessel vasculitis. However, the absence of centralized review of TAB represents a limitation of our study, that could have underestimated the number of histological abnormalities consistent with AAV. Overall, atypical manifestations and TAB findings in case of suspected GCA should alert physicians to the possibility of TA-AAV diagnosis, for which management would be different.

Based on the initial presentation and follow-up of patients, we could distinguish patients with early diagnosis of TA-AAV and those with delayed diagnosis of TA-AAV. Diagnosis of delayed TA-AAV was made after a median time of 15 months, because of a refractory disease or vasculitis relapse, these patients having been managed as classical GCA, while early TA-AAV had a similar failure-free survival than GCA. These findings show that the prognosis of TA-AAV is poor when initial treatment is not appropriate and suggest considering TA-AAV in case of any GCA with GCs refractoriness or early relapse. Such distinction is of major importance since cyclophosphamide or rituximab would be preferentially used to treat TA-AAV **(22,23)**, whereas tocilizumab or methotrexate would be preferentially considered as second-line therapies in GCA

(24–26). To illustrate the diagnostic and therapeutic challenge of TA-AAV and GCA with positive ANCA, a small study previously analyzed the relevance of ANCA during GCA, especially to estimate ANCA frequency and their impact on disease outcome. Thirty percent of GCA patients had positive ANCA, but the majority had positive indirect immunofluorescence without any positive antigen-specific immunoassays. Also, positive ANCA seemed predictive of premature relapse (mean interval 15.8 vs. 28.5 months) **(27)**.

Fourteen out of the 30 patients with delayed TA-AAV did not have any extracranial feature suggestive of AAV at initial presentation. For those patients, close monitoring during follow-up is necessary, and reconsidering initial diagnosis should be mentioned in case of lack of response. Some patients with atypical features for GCA at baseline were still considered as GCA because of the predominance of cephalic manifestations and inflammation on TAB, with a diagnosis of AAV only during follow-up. It is therefore very important to consider any atypical features as red flags for the diagnosis of GCA and immediately raise some concerns and discuss an alternative diagnosis. To help physicians diagnose TA-AAV, we identified some clinical and biologic red flags from our study, including the screening for atypical manifestations and in these patients screening for ANCA, and careful reading of TAB in all patients with temporal arteritis. The presence of features that are atypical for GCA should prompt careful consideration for an alternative diagnosis and prompt screening for ANCA and further careful review of the TAB.

Finally, despite its inherent limitations related to the small number of patients and its retrospective design, our study represents a large compilation of AAV patients presenting with cephalic manifestations. As a limitation, data of GCA controls were taken from two centers and not in each center were the TA-AAV were recruited. Also, controls were not matched on age and gender, but this choice was made voluntarily in this hypothesis of demographical differences between groups. Furthermore, TAB centralized review was not possible and could be a limitation due to the difficulty in distinction between fibrinoid necrosis and laminar necrosis **(6)**. Given the aim of this work, and since ANCA testing is performed in patients with suspected GCA, we considered mandatory to be ANCA-negative to get a diagnosis of GCA. Lastly, diagnosis of AAV was based on robust features, especially typical manifestations of AAV, positive PR3- or MPO-ANCA and/or histological evidence of AAV in another site than the TAB, and one of the main outcome we used was the relapse of the disease requiring the initiation of new treatment lines.

In conclusion, TA revealing AAV should be considered in case of atypical manifestations for GCA and in case of any GCA with GCs refractoriness or early relapse. In these cases, TAB could be useful, especially when showing small branch vasculitis and/or fibrinoid necrosis. Detection of ANCA using antigen-specific immunoassays should be performed in case of suspected GCA with clinical atypical features and atypical TAB.

Authors contribution

Study conception and design: Delaval, Terrier.

Acquisition of data: Delaval, Samson, Schein, Agard, Tréfond, Deroux, Dupuy, Garrouste, Godmer, Landron, Maurier, Le Guenno, Rieu, Desblache, Durel, Jousselin-Mahr, Kassem, Pugnet, Queyrel, Swiader, Blockmans, Sacré, Lazaro, Mouthon, Aumaître, Cathébras, Guillevin, Terrier.

Analysis and interpretation of data: Delaval, Terrier.

Drafting and writing of the manuscript: Delaval, Terrier.

All authors were involved in revising the manuscript, and all authors approved the final version to be published. Dr Terrier has full access to all the data and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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Figure legends

Figure 1. Flow chart of patient with temporal arteritis revealing ANCA-associated vasculitis

Figure 2. Temporal artery biopsy (TAB) with fibrinoid necrosis from a patient with temporal arteritis revealing ANCA-associated vasculitis. TAB showing necrotizing panarteritis with inflammatory infiltrate rich in macrophages, lymphocytes, epithelioid cells and some eosinophils, in contact with a band of fibrinoid necrosis (*) with pycnotic debris (Courtesy Dr Claire Toquet).

Figure 3. Temporal artery biopsy (TAB) with small branch vasculitis from a patient with temporal arteritis revealing ANCA-associated vasculitis. TAB showing the absence of intimal or medial inflammatory infiltrate (**A**, magnification x 4), with small branch necrotizing vasculitis on HES staining (**B**, magnification x 10; **C**, magnification x 40) and orcein staining (D, magnification x 40) (Courtesy Pr Jean-Louis Kemeny for the picture).

Figure 4. Treatment failure-free survival in TA-AAV patients with early AAV diagnosis, TA-AAV patients with delayed AAV diagnosis. and GCA diagnosis. Delayed TA-AAV patients had a significant higher risk of treatment failure compared to GCA patients [HR 3.85 (1.97-7.51), P<0.0001). (TA: Temporal Arteritis; AAV: ANCA-Associated Vasculitis, GCA: Giant Cell Arteritis; HR: hazard ratio)

Tables

Table 1. Baseline clinical, biological and pathological features of 50 TA-AAV patients compared to 100 GCA patients.

Characteristics	TA-AAV (n=50)	Early diagnosis (n=20)	Delayed diagnosis (n=30)	GCA (n=100)	P-value Early vs. GCA	P-value Delayed vs. GCA
Demography						
Age (years), median (IQR)	70 (64–75)	66.5 (63-71)	71.5 (65-78)	74 (66-82)	**0.008**	0.22
Female	26 (52)	9 (45)	17 (57)	70 (70)	**0.04**	0.19
Clinical manifestations						
Constitutional symptoms	42 (84)	18 (90)	24 (80)	82 (82)	0.52	0.79
Asthenia	*39 (78)*	*16 (80)*	*23 (77)*	*79 (79)*	1.00	0.80
Fever	*27 (54)*	*11 (55)*	*16 (53)*	*45 (45)*	0.47	0.53
Weight loss	*23 (46)*	*10 (50)*	*13 (43)*	*55 (55)*	0.81	0.30
Night sweats	*11 (22)*	*6 (30)*	*5 (17)*	*21 (21)*	0.39	0.80
Cephalic symptoms	44 (88)	17 (85)	27 (90)	97 (97)	0.06	0.14
Headache	*34 (68)*	*12 (60)*	*22 (73)*	*82 (82)*	**0.04**	0.30
Jaw claudication	*22 (44)*	*7 (35)*	*15 (50)*	*33 (33)*	1.00	0.13
Scalp tenderness	*22(44)*	*9 (45)*	*13 (43)*	*45 (45)*	1.00	1.00
No temporal pulse	*8 (16)*	*3 (15)*	*5 (17)*	*17 (17)*	1.00	1.00
Lung involvement	10 (20)	6 (30)	4 (13)	0 (0)	**<0.0001**	**0.002**
Visual manifestation	6 (12)	0 (0)	6 (20)	23 (23)	**0.01**	0.80
Episcleritis	2 (4)	2 (10)	0	1(1)	**0.01**	1.00
Polymyalgia rheumatica	15 (30)	5 (25)	10 (33)	32 (32)	0.11	1.00
Peripheral arthralgias	17 (34)	7 (35)	10 (33)	15 (15)	**0.05**	**0.03**
Renal involvement	13 (26)	8 (40)	5 (17)	0 (0)	**<0.0001**	**0.0005**
ENT involvement	16 (32)	10 (50)	6 (20)	0 (0)	**<0.0001**	**<0.0001**
Peripheral neuropathy	9 (18)	6 (30)	3 (10)	0 (0)	**<0.0001**	**0.01**
Cutaneous lesions	5 (10)	3 (15)	2 (7)	0 (0)	**0.004**	**0.05**
GI involvement	5 (10)	3 (15)	2 (7)	3 (3)	0.06	0.33
Cardiac involvement	3 (6)	2 (10)	1 (3)	2 (2)	0.13	0.55
CNS involvement	2 (4)	1 (5)	1 (3)	3 (3)	0.52	1.00
Pachymeningitis	*1 (2)*	1 (5)	0	*0 (0)*	0.17	1.00
C-reactive protein (mg/dl), median (IQR)	10.8 (6.5-16.4)	13.9 (8.3-17)	9.8 (6-15.2)	7.0 (4.4-12.6)	**0.02**	0.46

Abnormal temporal artery biopsy*	31/42 (74)	11/16 (69)	20/24 (83)	56/94 (60)	0.59	**0.03**
Mononuclear cell infiltrates	22 (71)	6 (55)	16 (80)	44 (79)	0.13	1.00
Granulomatous inflammation	4 (13)	0 (0)	4 (20)	21 (38)	**0.01**	0.18
Disruption of the internal elastic lamina	14 (45)	4 (36)	10 (50)	36 (64)	0.10	0.30
Giant cells	9 (29)	1 (9)	8 (40)	31 (55)	**0.007**	0.30
Small branch vasculitis	7 (23)	3 (27)	4 (20)	0 (0)	**0.003**	**0.004**
Fibrinoid necrosis	7 (23)	3 (27)	4 (20)	0 (0)	**0.003**	**0.004**

* Temporal artery biopsy was performed in 42/50 cases in TA-AAV and in 94/100 cases in control GCA.
Values are expressed as n (%) of patients or median (interquartile range).
IQR: interquartile range; AAV: antineutrophil cytoplasmic antibody–associated vasculitis; GCA: giant cell arteritis. Fisher's exact test was used for statistical analysis.

Table 2. Characteristics of the patients at the diagnosis of AAV.

Characteristics	**Early TA-AAV (n=20)**	**Delayed TA-AAV (n=30)**
Median delay between diagnosis of TA and AAV (months), median (IQR)	-	15 (9-46)
Type of AAV		
GPA	11 (55)	20 (67)
MPA	8 (4)	8 (27)
EGPA	1 (5)	2 (7)
Clinical manifestations		
Constitutional symptoms	18 (90)	21 (7)
Cephalic symptoms	17 (85)	11 (37)
ENT involvement	10 (50)	14 (47)
Lung involvement	6 (30)	12 (40)
Ocular manifestations	3 (15)	7 (23)
Peripheral neuropathy	6 (30)	12 (40)

Renal involvement	8 (40)	7 (23)
Cutaneous lesions	3 (15)	7 (23)
Gastrointestinal involvement	3 (15)	2 (7)
Pachymeningitis	1 (5)	3 (10)
C-reactive protein (mg/dL), median (IQR)	13.9 (8.3-17)	3.7 (1.9-8.4)
ANCA measurement		
Positive	19 (95)	25 (83)
MPO-ANCA	10 (53)	18 (72)
PR3-ANCA	9 (47)	6 (24)
Prednisone at AAV diagnosis		
Patients under prednisone	-	26 (87)
Prednisone dose, median (IQR), mg/day	-	22.5 (7-36)

Values are expressed as n (%) of patients or median (IQR).

AAV: ANCA-associated vasculitis; ANCA: antineutrophil cytoplasmic antibodies; EGPA: eosinophilic granulomatosis with polyangiitis; ENT: ear nose and throat; GPA: granulomatosis with polyangiitis; MPA: microscopic polyangiitis; MPO: myeloperoxyase; PR3: proteinase 3; TA: temporal arteritis

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Fever	*27 (54)*	*11 (55)*	*16 (53)*	*45 (45)*	0.47	0.53
Weight loss	*23 (46)*	*10 (50)*	*13 (43)*	*55 (55)*	0.81	0.30
Night sweats	*11 (22)*	*6 (30)*	*5 (17)*	*21 (21)*	0.39	0.80
Cephalic symptoms	44 (88)	17 (85)	27 (90)	97 (97)	0.06	0.14
Headache	*34 (68)*	*12 (60)*	*22 (73)*	*82 (82)*	**0.04**	0.30
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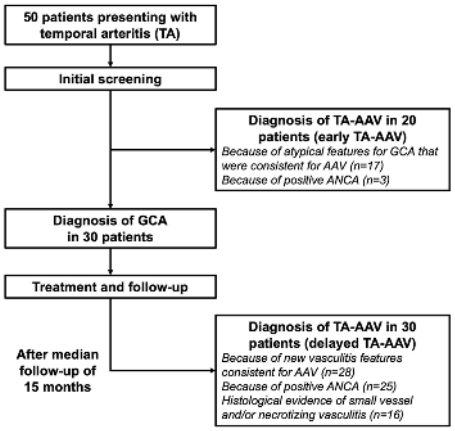

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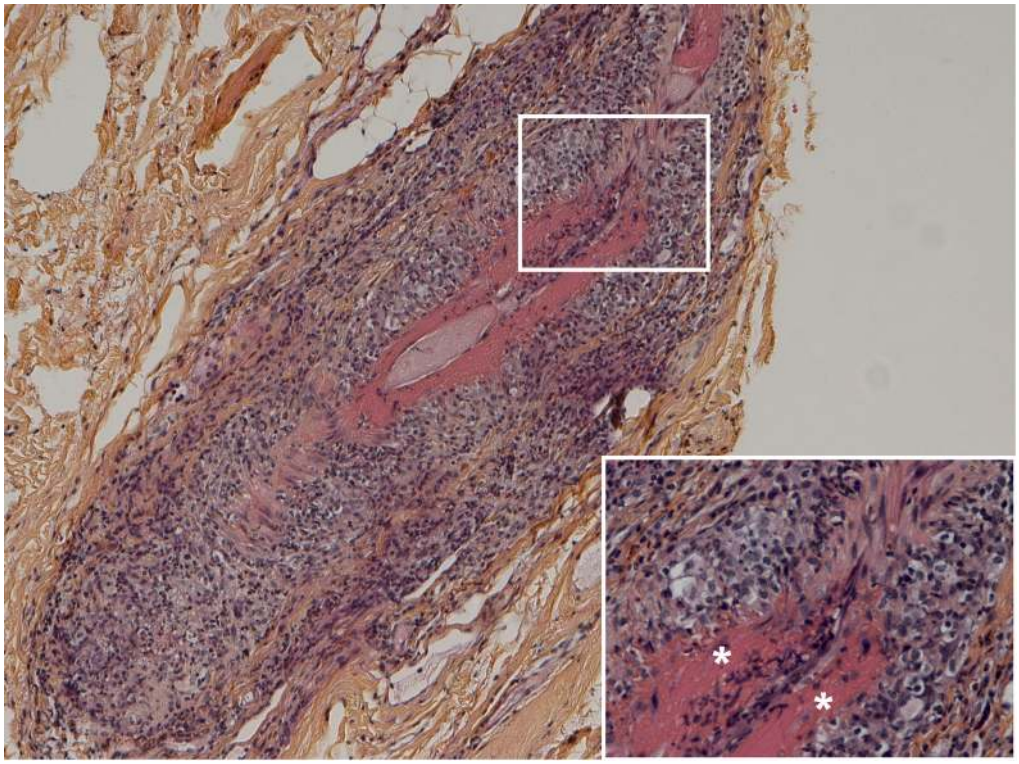

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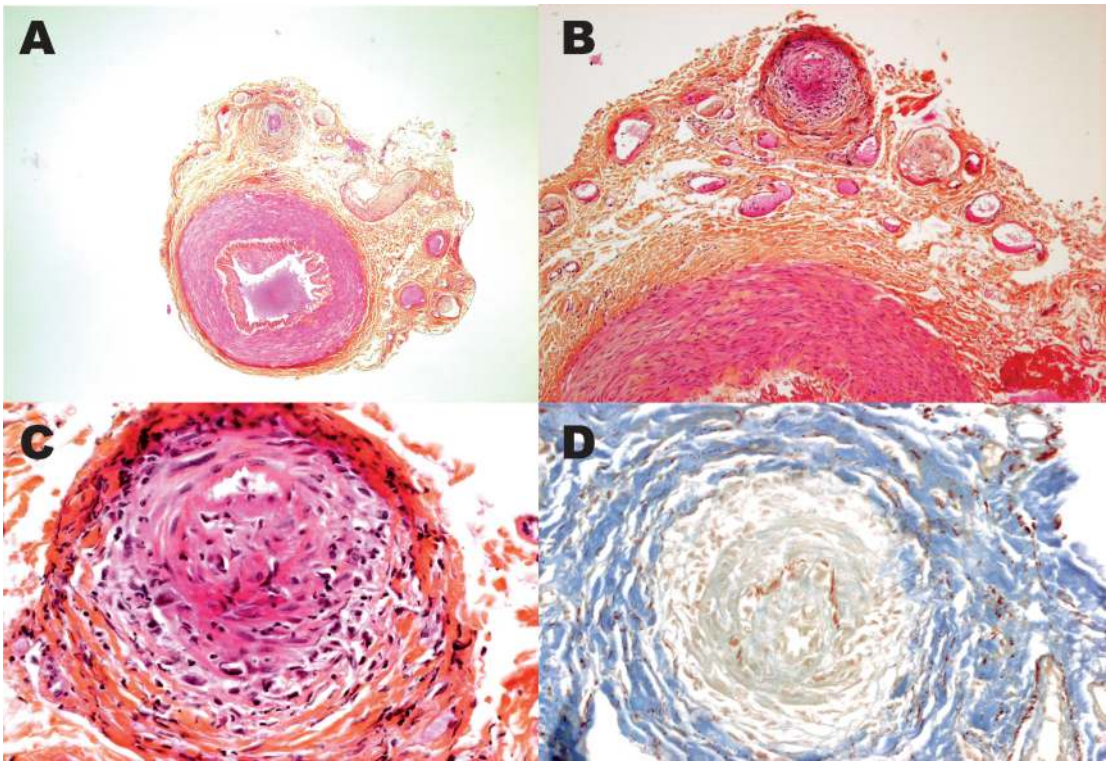

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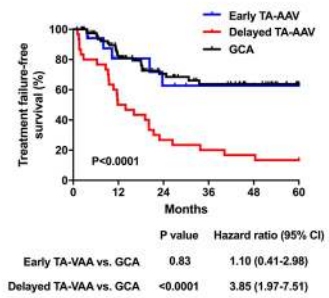

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