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Temporal Arteritis Revealing Antineutrophil Cytoplasmic Antibody–Associated Vasculitides: A Case–Control Study

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志水　隼人

膠原病Journal Club　2021年1月20日

はじめに

- 側頭動脈生検 (Temporal artery biopsy; TAB) は
  巨細胞性動脈炎 (GCA) を診断するためにしばしば
  施行される。

- GCAの典型的病理：リンパ球とマクロファージ浸潤を
  主体とした、血管の中膜から内膜を中心とする全層性炎症で、
  内膜肥厚と内弾性板の断裂が見られる。
  約75%で多核巨細胞を認める一方、フィブリノイド壊死は
  通常見られない。

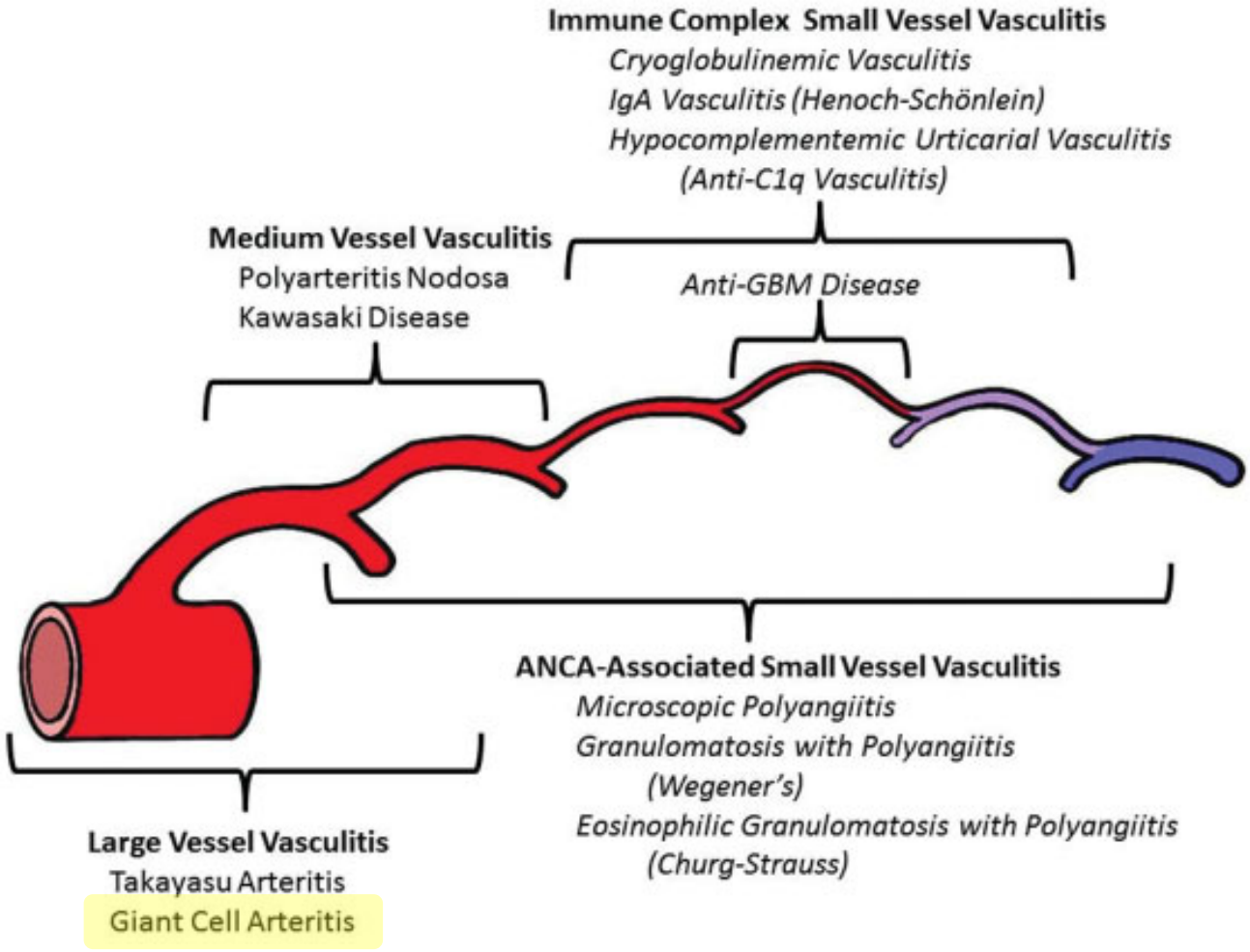
Arthritis Rheumatol 2012;64:549-556
Rheumatology 7th ed

ANCA関連血管炎 (AAV) , 結節性多発動脈炎 (PAN) でも、
側頭動脈生検の検体で血管炎を認める報告がある

Arthritis Rheumatol 2001;44:1387-1395

J Rheumatol 2003;30:3165-9

Am J Sur Pathol 2014;38:1360-1370



Arthritis Rheumatol 2013;65:1-11

目的

古典的GCAと比較して、
側頭動脈の炎症をきたしているAAV (TA-AAV) の症例の臨床的・生物学的・組織学的所見およびアウトカムを明らかにする。

研究デザイン

フランスの全国的な多施設後方視的研究

期間：2000年1月から2017年2月

対象：フランスの19施設とベルギーの1施設

患者：TA-AAV

TAB異常所見や頭部症状 (頭痛、頭皮痛、顎跛行) があり
初期評価で側頭動脈炎 (TA) を疑ったが、
最終的にAAVと診断された患者

- TAB異常所見はないが、頭部症状と1990年 ACR GCA分類基準を満たす患者も含まれた
- AAVの診断：以下のいずれかを満たす
  - ACR1990年血管炎 (GPA, EGPA) 分類基準
  - European Medicines Agency algorithm (Wattsのアルゴリズム)
  - 2012年CHCCの定義

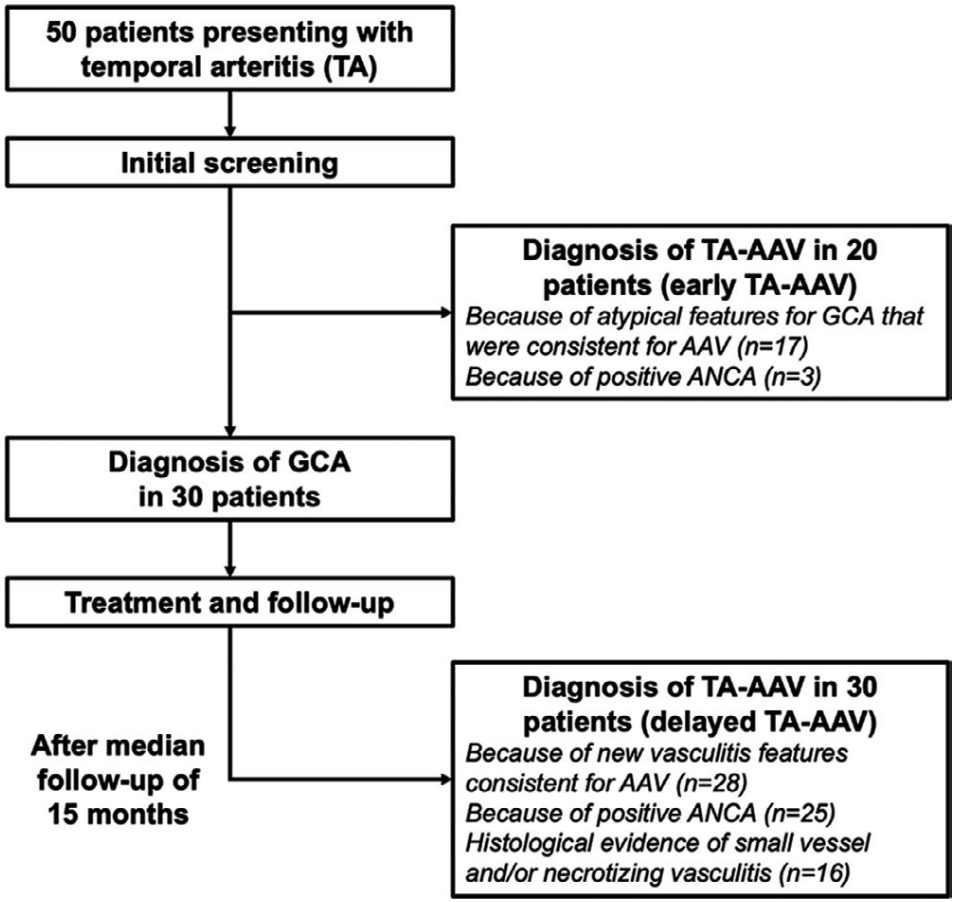


Figure 1. Flow chart of study distribution of patients with temporal arteritis revealing antineutrophil cytoplasmic antibody (ANCA)–associated vasculitis (TA-AAV). GCA = giant cell arteritis.

- **Early TA-AAV**
  初期評価でAAVと診断
- **Delayed TA-AAV**
  GCAとしてフォローされ、
  最終的にAAVと診断

対照患者

ACR1990年GCA分類基準を満たして AAVではなかったGCA患者

・対照患者は、2つのフランス血管炎センターのデータベースから、
1患者ごとに2人の対照患者の割合となるようにランダムに選ばれた

結　果

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

	Early TA-AAV (n = 20)	Delayed TA-AAV (n = 30)
Delay from TA to AAV diagnosis, median (IQR) months	–	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, median (IQR) mg/dl	13.9 (8.3–17)	3.7 (1.9–8.4)
ANCA positive		
All ANCAs	19 (95)	25 (83)
MPO-ANCAs	10 (53)	18 (72)
PR3-ANCAs	9 (47)	6 (24)
Prednisone at AAV diagnosis		
Taking prednisone	–	26 (87)
Dose, median (IQR) mg/day	–	22.5 (7–36)

- **Early TA-AAV： 20名**
- **Delayed TA-AAV ： 30名**
- **GCA control： 100名**

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TA-AAV 50名のうち

33名（66%）で
GCAに非典型的な症状を
初期評価時に認めた

Table 1. Baseline clinical, biologic, and pathologic features of the patients with TA-AAV compared to controls with GCA*

	TA-AAV cases				*P*†	
	All (n = 50)	Early diagnosis (n = 20)	Delayed diagnosis (n = 30)	GCA controls (n = 100)	Early diagnosis vs. controls	Delayed diagnosis vs. controls
Demographics						
Age, median (IQR) years	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
CRP, median (IQR) mg/dl	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
Abnormalities on TAB‡	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

* Except where indicated otherwise, values are the number (%) of the patients or the number of patients/total number assessed (%). IQR = interquartile range; ENT = ear, nose, and throat; GI = gastrointestinal; CNS = central nervous system; CRP = C-reactive protein.
† By Fisher's exact test.
‡ Temporal artery biopsy (TAB) was performed in 42 of 50 patients with temporal arteritis revealing antineutrophil cytoplasmic antibody–associated vasculitis (TA-AAV) and in 94 of 100 controls with giant cell arteritis (GCA).

TA-AAV vs. GCA (症状)

TA-AAVで多い：

肺, 末梢関節炎, 腎, 皮膚

ENT, 末梢神経障害

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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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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
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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
CRP, median (IQR) mg/dl	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
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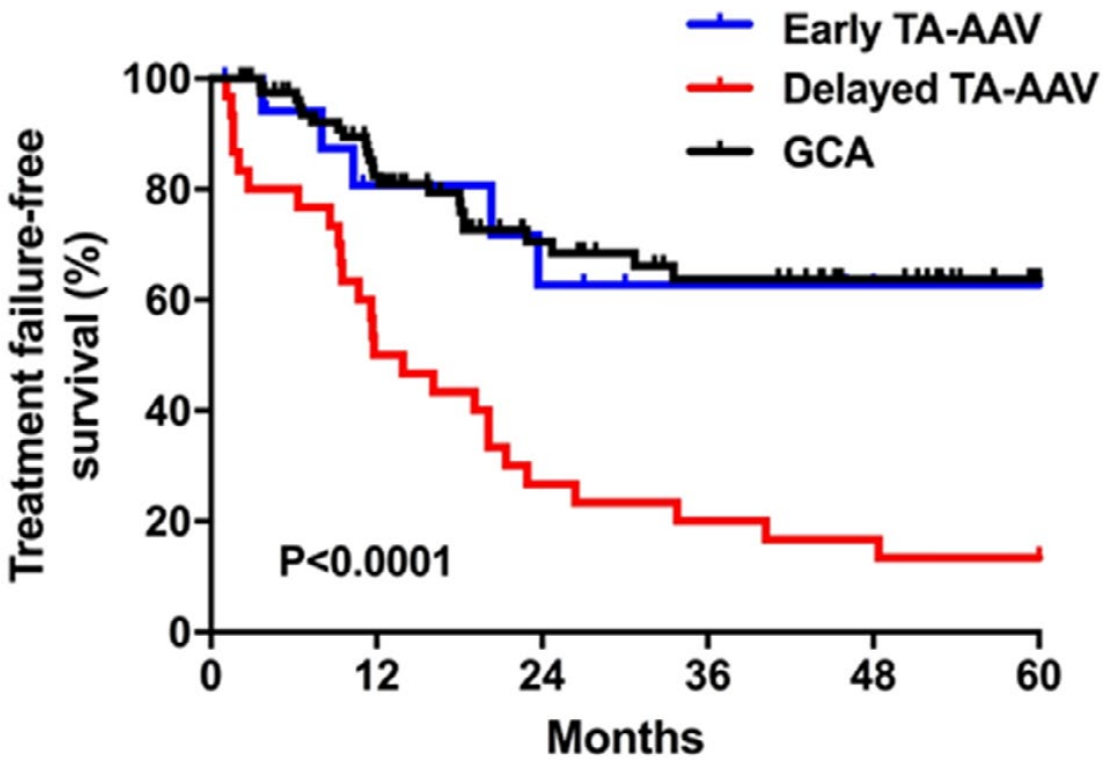
‡ Temporal artery biopsy (TAB) was performed in 42 of 50 patients with temporal arteritis revealing antineutrophil cytoplasmic antibody–associated vasculitis (TA-AAV) and in 94 of 100 controls with giant cell arteritis (GCA).

TA-AAV vs. GCA (病理)

TA-AAVで多い：
- 小血管炎
- フィブリノイド壊死

Early TA-AAVで少ない：
- 肉芽腫, 巨細胞



	P value	Hazard ratio (95% CI)
Early TA-VAA vs. GCA	0.83	1.10 (0.41-2.98)
Delayed TA-VAA vs. GCA	<0.0001	3.85 (1.97-7.51)

Limitation

- 患者数が少なく、後方視的研究であること
- GCA controlはフランス2施設のみからの患者であり、また年齢や性別をマッチさせていないこと
- TABの病理評価を一極化できていないこと

まとめ

- AAVでも側頭動脈炎の症状を伴うことがあり、
  初発時にGCAとしては非典型的な症状を伴うことが多い

- TA-AAVの多くはANCA (特にMPO-ANCA) 陽性だが、
  陰性の場合もある

- AAVでもTABで異常所見を見ることがあり、
  GCAには非典型的であるフィブリノイド壊死や小血管炎を
  認めた場合は、よりTA-AAVの可能性を考える必要がある