Application of the 2019 classification criteria for systemic lupus erythematosus to patients with established ANCA-associated vasculitis

Sirs,

Antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) is a group of systemic vasculitides based on the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides (1). Based on the clinical manifestations and histological features, AAV consists of three variants, which are microscopic polyangiitis (MPA), granulomatosis with polyangiitis (GPA) and eosinophilic GPA (EGPA) (1-3). Systemic lupus erythematosus (SLE) is a systemic autoimmune disease. Recently, the 2019 classification criteria for SLE were proposed by European League Against Rheumatism/American College of Rheumatology (EULAR/ACR 2019 criteria for SLE) (4). AAV and SLE often exhibit notably distinct differences in the pathogenesis of pauci-immune *vs*. immune-complex mediated vasculitis. However, they may also share similar clinical symptoms that are not easily differentiated at the time of diagnosis. Hence, in this study, we applied the 2019 criteria for SLE to immunosuppressive drug-naïve patients in a retrospective cohort of AAV and determined the clinical factors at diagnosis which are useful for the differentiation between AAV and SLE.

We retrospectively reviewed the medical records of 214 immunosuppressive drug-naïve patients with AAV from the retrospective cohort. Patients, who were concomitantly classified as malignancies, serious infection and autoimmune diseases other than AAV, were excluded from this study. Prior to diagnosis, they had never received immunosuppressive drugs for AAV or drugs inducing or mimicking AAV. Based on the documented clinical, laboratory and histological data such as antinuclear antibody (ANA), autoantibodies and biopsy reports, all AAV patients were reclassified by the 2019 criteria for SLE. This study was approved by the Institutional Review Board of Severance Hospital (4-2017-0673 and 4-2016-0901), who waived the need for patient written informed consent as this was a retrospective study.

The median age of the AAV patients was 58.8 years and 69 of them were men (32.2%). ANA was detected in 51 AAV patients (23.8%) at diagnosis. Ten of the 214 AAV patients (4.7%) or 10 out of 51 ANA-positive AAV patients (19.6%), fulfilled the 2019 criteria for SLE. Among clinical domains, a criterion of proteinuria >0.5g/24h (41.2%) was most frequently fulfilled, and among immunology domains, a criterion of antiphospholipid antibodies (11.8%) was most frequently observed. Myeloperoxidase (MPO)-ANCA (or perinuclear (P)-ANCA) and proteinuria >0.5g/24h were detected in all 10 ANA-positive AAV patients fulfilling the 2019 criteria for SLE. They all underwent renal biopsy, which revealed pauci-immune glomerulonephritis associated with ANCA (Table I). With these results, we can infer three facts. Firstly, either ANCA positivity or surrogate markers suggesting GPA cannot be an indicator for the differentiation between AAV and SLE at diagnosis. Secondly, SLE-specific antibodies cannot be an absolute indicator of disease type. Thirdly, only a histological confirmation of pauci-immune vasculitis can be an indicator for it. Therefore, we conclude that tissue-biopsy should be recommended to patients suspected of both AAV and SLE.

The merit of this study is that to our knowledge, for the first time, we applied the 2019 criteria for SLE to immunosuppressive drug-naïve patients with established AAV and determined that the histological confirmation is the best way to differentiate AAV from SLE in patients suspected of both diseases. However, our study several issues: We could not evaluate how many AAV patients were suspected of SLE at the time of diagnosis due to a retrospective study design. Also, the number of AAV patients fulfilling the 2019 criteria for SLE was not large enough to draw a powerful consequence and apply the result of this study to most AAV patients in the daily clinical practice. In conclusion, 10 of 214 AAV patients (4.7%) fulfilled the 2019 criteria for SLE. The histological confirmation was the key indicator for differentiating AAV from SLE.

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Table I. ANA-positive AAV patients who fulfilled the 2019 criteria for SLE.

Patients number	AAV variants	Gender/ Age	ANCA	Fever	Leukopenia	Thrombo-cytopenia	Auto-immune haemolysis	Delirium	Psychosis	Seizure	Non-scarring alopecia	Oral ulcer	Subacute cutaneous OR discoid lupus	Acute cutaneous lupus	Pleural or pericardial effusion
1	MPA	F/76	MPO(P)												YES
2	MPA	M/71	MPO(P)	YES											
3	MPA	F/56	MPO(P)	YES											YES
4	MPA	F/36	MPO(P)	YES											
5	MPA	M/70	MPO(P)	YES	YES	YES								YES	
6	MPA	M/51	MPO(P)												
7	MPA	F/62	MPO(P)												
8	GPA	F/73	MPO(P)	YES											YES
9	GPA	M/61	MPO(P)		YES	YES									
10	EGPA	F/73	MPO(P)												

Patients number	Acute peri-carditis	Joint involve-ment	Proteinuria II or V LN	CLASS or IV LN	CLASS III IgM	ACA IgG	ACA IgM	Aβ2GP1 IgG	Aβ2GP1	LAC OR low	Low C3 and low C4	Low C3 dsDNA C4	Anti-	Anti-Sm POINTS	TOTAL
1		YES	YES								YES				18
2			YES				YES							YES	14
3			YES			YES									13
4		YES	YES												12
5			YES							YES					12
6			YES							YES			YES		12
7		YES	YES												10
8			YES								YES				14
9			YES					YES							10
10		YES	YES												10

ANA: antinuclear antibody; AAV: antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis; ANCA: antineutrophil cytoplasmic antibody; SLE: systemic lupus erythematosus; MPA: microscopic polyangiitis; GPA: granulomatosis with polyangiitis; EGPA: eosinophilic granulomatosis with polyangiitis; MPO: myeloperoxidase; P: perinuclear; ACA: anticardiolipin; Aβ2GP1: anti-beta2 glycoprotein1; LAC: lupus coagulant; C3: complement 3; C4: complement 4.

Letters to the Editors

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