Cutaneous involvement might be associated with gastrointestinal involvement and better renal outcomes in patients with ANCA-associated vasculitis

Sir,

Antineutrophilic cytoplasmic antibody (ANCA)-associated vasculitides (AAV) are a group of diseases that affect many organs. Skin is one of the most prevalent areas of involvement and may serve as the initial manifestation. The purpose of this study was to evaluate the characteristics of patients with cutaneous involvements and investigate potential associations between cutaneous involvements and other organ/system diseases at the diagnosis. Additionally, this study aimed to compare the features and outcomes of patients with cutaneous involvement and those of patients without cutaneous involvement.

This is a retrospective, single-centre study. The investigation encompassed patients diagnosed with AAV between 2010 and 2024 according to the 2012 Chapel Hill consensus nomenclature. Individuals diagnosed with renal-limited vasculitis (RLV) were included, but eosinophilic granulomatosis with polyangiitis (EGPA) was excluded because of the very few patients. The British Vasculitis Activity Score (BVAS) definitions for cutaneous involvement were met by patients with AAV-related cutaneous involvement, as indicated by their clinic notes. Univariate and multivariate analyses were conducted to determine the factors associated with cutaneous disease in AAV patients. This study was approved by the ethics committee of Izmir Katip Celebi University (approval number of 2025-0162).

Of the 158 patients included in the study, 59% were male, and the median age at diagnosis (IQR) was 54 (44-65) years. Thirty-eight (24%) patients exhibited cutaneous involvement, whereas 120 (76%) did not. Thirty-three (87%) had purpura, 1 (3%) had an ulcer on his leg, 1 (3%) had gangrene, and 3 (8%) had other skin vasculitis. In patients with cutaneous involvement, 57% were male, and the median age at diagnosis (IQR) was 53 (39-61) years. Twenty-four patients (75% c/PR3-ANCA positive, 25% p/MPO-ANCA positive) had positive ANCA test results at the time of diagnosis. Eye (22% *vs*. 9%; p=0.04), gastrointestinal (16% *vs*. 1%; p=0.001), and musculoskeletal involvements (58% *vs*. 27%; p<0.001) were more common in patients with cutaneous involvement than patients without cutaneous involvement. Other organ involvements (renal, pulmonary, ear, nose, throat, cardiac, neurologic, and venous thromboembolism) were not different between groups (p>0.05). Median serum CRP level was higher in patients with cutaneous involvement (p=0.031). Although the frequency of renal involvement was not statistically different between groups, median serum creatinine level and eGFR were lower in patients with cutaneous involvement. Furthermore, patients with cutaneous involvement required less acute haemodialysis and exhibited a lower prevalence of end-stage renal disease (ESRD) as a result (Table I). We conducted a multivariate analysis to identify the factors related to cutaneous involvement and found that baseline eGFR (B:1.019, 95%CI: [1.005-1.032]; p=0.005), the presence of gastrointestinal involvement (B:39.325, 95%CI: [3.697-418.271]; p=0.002), and serum CRP level (B:1.009, 95%CI: [1.001-1.018]; p=0.038) were independent factors associated with cutaneous involvement at diagnosis.

Table I. Cutaneous involvement in ANCA-associated vasculitis.

	Patients without cutaneous involvement (n=120)	Patients with cutaneous involvement (n=38)	p-value
Age at diagnosis, median (IQR), years	55 (45-66)	53 (39-61)	0.24
Male sex, n (%)	68 (66)	25 (57)	0.32
c-ANCA/PR3-ANCA, n (%)	50 (57)	18 (75)	
0.11			
p-ANCA/MPO-ANCA, n (%)	38 (43)	6 (25)	
ANCA-negative, n (%)	25 (22)	13 (35)	0.10
Organ involvement, n (%)			
Renal	100 (83)	32 (84)	0.90
Pulmonary	77 (64)	22 (60)	0.60
Alveolar haemorrhage	12 (26)	5 (39)	0.49
Eye	10 (9)	8 (22)	**0.04**
Ear, nose, throat	36 (30)	16 (42)	0.18
Cardiac	3 (3)	1 (3)	1.0
Gastrointestinal	1 (1)	6 (16)	**0.001**
Musculoskeletal	32 (27)	22 (58)	**<0.001**
Neurologic	4 (3)	2 (5)	0.63
Venous thromboembolism (n=147)	4 (4)	3 (8)	0.36
Laboratory Findings			
Serum creatinine level, median (IQR)	3.7 (1.8-6.6)	1.9 (1.1-4.1)	**0.003**
eGFR, median (IQR) ml/min/1.73 m^2	14 (8-35)	36 (13-88)	**0.001**
Proteinuria (n=154), n (%)	94 (81)	30 (79)	0.78
Haematuria (n=143), n (%)	89 (82)	27 (79)	0.77
C-reactive protein, median (IQR) mg/L	15 (6-28)	20 (10-92)	**0.031**
BVAS (n=87), median (IQR)	15 (12-19.5)	18 (14-25)	**0.026**
Treatment modalities			
Cyclophosphamide (n=105) , n (%)	72 (88)	19 (83)	0.50
Rituximab (n=105), n(%)	10 (12)	4 (17)	
Plasmapheresis (n=152), n (%)	45 (39)	9 (24)	0.10
Acute haemodialysis (n=153), n (%)	56 (48)	7 (19)	**0.002**
Outcomes			
End-stage renal disease, n (%)	40 (36)/115	6 (17)/34	**0.036**
12-month mortality (n=96), n (%)	13 (18)	3 (13)	0.75

eGFR: estimated glomerular filtration rate; BVAS: Birmingham Vasculitis Activity Score.
*Acute haemodialysis: haemodialysis required during initial hospitalisation.
**End-stage renal disease: defined as eGFR <15 mL/min/1.73 m^2 for ≥3 months or the need for long-term dialysis.

AAV are necrotizing small and medium size vessels vasculitis affecting the skin and other organs. Cutaneous involvement was observed in 43% of patients in a previous study (1) A cross-sectional analysis of patients with ANCA-associated vasculitis, cutaneous manifestations were common across subtypes: affecting 34% of GPA, 28% of MPA, and 47% of EGPA cases and revealed that the predominant skin lesion was petechiae/purpura. Patients exhibiting cutaneous involvement, particularly those with GPA or EGPA and either PR3-ANCA or ANCA-negative status, demonstrated a higher likelihood of experiencing severe systemic manifestations, including glomerulonephritis and alveolar haemorrhage (hazard ratio >1.9) (2).

In our analysis, we observed a lower prevalence of cutaneous involvement, most probably due to the inclusion of patients with RLV and the exclusion of those with EGPA. Although serum CRP levels were elevated in patients with cutaneous involvement, renal involvement might be less severe, and the outcome could be better in those patients. In a recently published multicentre study that included GPA and MPA patients, cluster analysis was conducted to establish seven clusters. The group with the least cutaneous involvement exhibited the highest rate of ESRD (3). This observation may be explained by the possibility that cutaneous involvement leads to an early diagnosis of AAV.

Our study has some limitations. First, the study was a cross-sectional single-centre study, which prevented us from generalising our findings to other patient populations. Second, we were unable to incorporate the histological characteristics of skin biopsies.

In conclusion, cutaneous involvement in patients with AAV may be a predictor of improved renal outcomes, and increased inflammation may not always be a poor

prognostic factor. Furthermore, clinicians should be careful when considering AAV patients with cutaneous involvement due to the increased likelihood of gastrointestinal involvement.

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