Cutaneous vasculitis in SLE

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ABSTRACT

Objectives We determined the temporal association between clinical and serological disease manifestations and development of cutaneous small vessel vasculitis in a large prospective multiethnic cohort.

Methods Patients with SLE diagnosed according to the Systemic Lupus International Collaborating Clinics (SLICC) classification criteria or the revised classification criteria as defined by the American College of Rheumatology (ACR) were enrolled in the Hopkins Lupus Cohort. Cutaneous small vessel vasculitis was determined as a component of the Systemic Lupus Erythematosus Disease Activity Index. SLE-associated cutaneous small vessel vasculitis lesions were reported clinically. They presented as punctate lesions, palpable purpura, tender erythematous plaques or macules with or without necrosis. No histopathological diagnosis was pursued to confirm the diagnosis of vasculitis or to differentiate it from other causes of digital lesions in patients with SLE. Disease manifestations that preceded the first occurrence of cutaneous small vessel vasculitis lesions were analysed using Kaplan-Meier. Cox regression analysis was used to assess the relationship between baseline clinical and immunological manifestations and the development of cutaneous small vessel vasculitis. We adjusted for gender, race and age at SLE diagnosis.

Results A total of 2580 patients were studied: 52.4% were Caucasian and 39.4% were African-American. The mean age of the cohort was 45.5±14.5 years. The mean years of cohort follow-up was 7.9±7.6. Cutaneous small vessel vasculitis was observed in 449 (17.3%). The mean time to cutaneous vasculitis after SLE diagnosis was 4.78 years (95% CI 3.96 to 5.60). At least 159 (35%) patients had recurrences of cutaneous vasculitis lesions. Discoid rash, Raynaud's phenomenon, myositis, anaemia, Coombs' positivity, leucopenia, anti-Smith and anti-RNP (Ribonucleoprotein) were significantly associated with the development of cutaneous vasculitis. The SLICC/ACR Damage Index score was higher in patients with cutaneous vasculitis compared with those without cutaneous vasculitis.

Conclusions Cutaneous vasculitis is frequent (17.3%) and often recurrent (35%). African-Americans are at higher risk of developing cutaneous small vessel vasculitis than Caucasians. Clinical presentations such as myositis and haematological manifestations are predictors of cutaneous vasculitis development. The presence of cutaneous vasculitis is associated with increased organ damage.

I- INTRODUCTION

Lupus-specific cutaneous manifestations are important in relation to the development of systemic involvement and ultimate

prognosis.^{1–3} Among juvenile patients with SLE, those with acute cutaneous lupus erythematosus or non-scarring alopecia were more likely to develop arthralgia, while mucosal ulcers were associated with a higher risk of leucopenia.¹ In adult patients with SLE, the presence of malar rash was indicative of more severe systemic disease, while discoid lupus appeared to be associated with a decreased incidence of renal disease^{2,3} but an increased Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SLICC/ACR DI).³

Cutaneous small vessel vasculitis is a non-specific cutaneous manifestation and is the most frequent type of vasculitis among patients with SLE.^{4,5} It is mostly skin limited and is infrequently associated with systemic vasculitis.^{5,6} It is seen in up to 20%.^{4,5,7} Cutaneous small vessel vasculitis mostly presents as punctate lesions, palpable purpura, ulcers, erythematous plaques or macules and erythema with necrosis that may occur once or may be relapsing.⁵

In the setting of Sjögren's syndrome, development of cutaneous vasculitis signified more severe disease, including higher rates of joint disease, peripheral neuropathy, renal involvement, lymphoma, hospitalisation and even death.⁸ In the setting of rheumatoid arthritis, leucocytoclastic vasculitis had an unfavourable prognosis with associations with mononeuritis multiplex and bowel involvement.⁹

In SLE, past studies evaluated the clinical and serological characteristics of patients with combined cutaneous and visceral vasculitis.^{4,5,10–12} In these studies, SLE patients with vasculitis were found to be mostly men, were younger at SLE onset,¹³ had longer disease duration, livedo reticularis, haematological parameters (anemia and high Erythrocyte Sedimentation Rate),¹⁰ anti-dsDNA,⁴ anti-SSA,¹¹ anti-SSB⁵ and anti-Smith.¹² However, only 2% of patients with SLE have concomitant visceral and cutaneous vasculitis.^{5,6} Moreover, as detailed in the Dermatologic Addendum to the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides, the presentation of cutaneous vasculitis occurring

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in patients with SLE is heterogeneous but is mostly small vessel vasculitis rather than medium vessel.¹⁴ Therefore, studies of cutaneous small vessel vasculitis are more relevant to clinical practice.

One study of juvenile SLE patients with cutaneous vasculitis alone found that it was associated with more seizures and granular casts.¹ In adult patients with SLE, having cutaneous vasculitis was associated with Raynaud's phenomenon,¹⁵ mucocutaneous and musculoskeletal manifestations,⁷ myositis¹ or no major organ involvement.¹⁵ Cutaneous vasculitis was also found to correlate with disease activity^{1 5 7 16} and poor prognosis with renal system and central nervous system (CNS) deterioration.¹⁶ Patients with cutaneous vasculitis were more likely to have antiribosomal P antibodies,¹⁵ anti-Ro antibody¹¹ and cryoglobulins.¹⁷ One study of patients with SLE reported an association with hypocomplementaemia and antiphospholipid syndrome.⁷

The aim of this study was to determine the association between clinical and serological manifestations of SLE and development of future cutaneous small vessel vasculitis, as well as the association between the presence of cutaneous vasculitis and organ damage in a large prospective multiethnic cohort.

PATIENTS AND METHODS

The Hopkins Lupus Cohort is a longitudinal cohort of patients diagnosed with SLE at the Hopkins Lupus Center. All patients gave written informed consent to participate. Patients were followed up by protocol quarterly or more often as clinically indicated. A total of 2580 patients with SLE diagnosed according to the SLICC classification criteria¹⁸ or the revised classification criteria as defined by the ACR.^{19 20}

Variables

Cutaneous vasculitis was defined clinically by the presence of cutaneous small vessel vasculitis lesions documented on the Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) score by one rheumatologist (MAP) during physical examination. Cutaneous small vessel vasculitis lesions were reported as part of the SLEDAI score in our cohort. They presented as punctate lesions, palpable purpura, tender erythematous plaques or macules with or without necrosis. In our patients presenting with these lesions, the diagnosis was made clinically, and no histopathological diagnosis was pursued. We used the date of first appearance of the cutaneous vasculitis in our analysis. We excluded patient who developed cutaneous vasculitis before SLE diagnosis as the baseline variables were recorded at the time of SLE diagnosis.

The clinical data included cutaneous, musculoskeletal, serositis, renal, neuropsychiatric, haematological, cardiac, pulmonary and gastrointestinal manifestations of SLE. The date of first appearance of each manifestation was used. The cutaneous manifestations included malar rash, discoid lupus, oral ulcers, photosensitivity,

livedo and Raynaud's phenomenon. The musculoskeletal manifestations included arthralgias and arthritis. The renal data included proteinuria, haematuria, renal insufficiency and renal failure. The neuropsychiatric manifestations included seizure, psychosis, meningitis, stroke, lupus headaches, depression, mononeuritis multiplex, cognitive impairment, optic neuritis, cranial neuropathy, peripheral neuropathy, longitudinal myelitis or brain CT/MRI abnormalities. The haematological data included anaemia defined as haemoglobin less than 11.0g/dL in a woman and less than 12.0g/dL in men, haemolytic anaemia, leucopenia defined as white blood cell count (WBC) <4000 documented two or more times when the patient was not on drugs known to cause bone marrow suppression and thrombocytopenia defined as platelets <100 000, which was not due to medications. Cardiac manifestations included myocarditis, Libman-Sacks and cardiac murmur. Pulmonary manifestations included fibrosis and pulmonary hypertension. Gastrointestinal manifestations included hepatomegaly, increased liver function tests, splenomegaly, gastrointestinal lupus and pancreatitis. Sjögren's syndrome was diagnosed in the presence of dry eyes confirmed by an abnormal Schirmer test and/or low ocular surface staining not due to medications or dry eyes and dry mouth in the presence of anti-Ro and/or La antibodies. We also included venous and arterial thrombosis.

The immunological data included anti-dsDNA, anti-Smith, anti-RNP, anti-SSA, anti-SSB, lupus anticoagulant (by International Society on Thrombosis and Haemostasis definitions), anticardiolipin IgG and IgM, anti-beta-2 glycoprotein IgG and IgM, C3 and C4 level and CH50.

The SLICC/ACR DI was used to measure damage, defined as irreversible organ dysfunction, present for 6 months or longer, regardless of aetiology, in all organ systems.²¹ The SLICC/ACR DI was calculated based on organ damage accumulated since the onset of SLE until the last visit.

The socioeconomic-demographic factors included gender (female or male), race (Caucasian, African-American, Asian, Hispanic or others), age at last visit as a continuous variable, education (categorised into less or equal to 12 years and more than 12 years) and annual household income as a continuous variable.

Statistical analysis

SLE manifestations that preceded the first occurrence of cutaneous vasculitis were analysed using Kaplan-Meier. To assess the temporal relationship between clinical/immunological manifestations and development of cutaneous vasculitis, Cox regression analysis was done and adjusted for gender, race and age at SLE diagnosis. The relationship between socioeconomic-demographic variables was examined by Student's t-test or Fisher's t-tests as appropriate. A p value of less than 0.05 was used to determine significance. All analyses were performed using JMP, V.13.0.

Table 1 Demographics and socioeconomic status of SLE patients with and without cutaneous vasculitis

Factor	With cutaneous vasculitis (n=449)	Without cutaneous vasculitis (n=2131)	OR (95% CI)	P value
Gender (male)	6.7%	8.1%	0.82 (0.55 to 1.22)	0.3840
Race (African-American)	46.3%	42.2%	1.18 (0.95 to 1.46)	0.1404
Smoking ever	39.5%	34.7%	1.23 (0.997 to 1.52)	0.0573
Alcohol abuse ever	6.9%	6.6%	1.05 (0.71 to 1.58)	0.8346
Drug abuse ever	7.1%	5.8%	1.24 (0.83 to 1.86)	0.3264
Age at cohort entry	41.6±13.0	41.2±12.4		0.6974
Age at SLE diagnosis	30.4±12.8	32.6±13.0		0.0020

Values are expressed as mean±SD or percentage.

III- RESULTS

From 1987 to 2019, there were 2580 patients with SLE. The cumulative classification criteria were 48.2% malar rash, 19.1% discoid rash, 51.5% photosensitivity, 52.5% oral ulcer, 71.6% arthritis, 42.9% serositis, 45.2% proteinuria, 47.2% leucopenia, 20.2% thrombocytopenia and 96.5% ANA positivity based on revised ACR classification criteria.²² Additional SLICC classification criteria included 20.8% direct Coombs' test, 54.8% low C3, 47.6% low C4 and 16.2% low CH50.¹⁸ Among the 2580 patients, there were 92.2% female, 7.8% males, 52.4% Caucasian and 39.4% African-American. The mean age of the cohort was 45.5±14.5 years. The mean years of cohort follow-up was 7.9±7.6 (range 0–32.2 years), and the mean years of follow-up after SLE diagnosis was 13.2±9.7 (range 0–57 years). We excluded 61 patients in whom cutaneous vasculitis occurred prior to SLE diagnosis.

Cutaneous vasculitis was observed in 17.3% of patients with SLE. The mean time to cutaneous vasculitis after SLE diagnosis was 4.78 years (95% CI 3.96 to 5.60). Among patients who developed cutaneous vasculitis, 50% had the onset by 2 years after their SLE diagnosis and 75% by 10 years after their diagnosis. At least 159 out of 449 (35%) patients had two or more cutaneous vasculitis events.

Table 1 shows the socioeconomic-demographic features in patients with SLE included in this analysis. There were no significant differences observed for gender, race, socioeconomic status (defined by income and years of education), smoking or alcohol abuse. The age at SLE diagnosis was younger in those with cutaneous vasculitis compared with those without cutaneous vasculitis (30.4 vs 32.6 with a p value of 0.002).

Table 2 outlines the clinical and immunological manifestations as predictors of development of cutaneous vasculitis before and after adjustment for gender, race and age at SLE diagnosis. Discoid rash, Raynaud's phenomenon, myositis, anaemia, Coombs' positivity, leucopenia, anti-Smith and anti-RNP were significantly associated with the development of cutaneous vasculitis. African-American patients had a 25% higher likelihood of developing cutaneous vasculitis compared with Caucasian patients (HR 1.26, 95% CI 1.02 to 1.55). There was no association with anti-Ro or anti-La positivity and the development of

cutaneous small vessel vasculitis. Only 13% (253/1991) and 5% (111/2256) of patients with anti-Ro and anti-La, respectively, developed vasculitic lesions. Moreover, only a minority of patients with low C3 (9%, 245/2746) or low C4 (18%, 321/1809) developed cutaneous small vessel vasculitis.

The SLICC/ACR DI score was higher in patients with cutaneous vasculitis compared with those without cutaneous vasculitis. Patients with cutaneous vasculitis had a SLICC/ACR DI score of 3.53±3.25 compared with 2.19±2.5 in patients without cutaneous vasculitis (p value <0.0001).

IV- DISCUSSION

In this study, we found that presence of cutaneous small vessel vasculitis was associated with both mild and severe disease manifestations. Mucocutaneous and haematological manifestations, myositis, Raynaud's phenomenon, anti-Smith and anti-RNP were predictors of the development of later cutaneous small vessel vasculitis. In addition, SLE patients with cutaneous vasculitis were found to have an increased risk of organ damage overall.

First, the prevalence of cutaneous vasculitis in our cohort was around 18%. In a cohort of 667 patients with SLE of Hispanic decent, the prevalence of cutaneous vasculitis was similar at 23%.⁴ In a cohort of 670 patients with SLE of European decent, 76 (11%) patients were reported to have vasculitis (either visceral or cutaneous).⁵ The increased risk of cutaneous vasculitis in African-American patients is a novel finding that has not been previously reported. African-American patients had a 20% higher likelihood of developing cutaneous vasculitis compared with Caucasian patients in our analysis. This supports the role of race and hence genetic factors in determining disease manifestations in SLE. Few studies have looked at the rate of recurrence of cutaneous vasculitis in patients with SLE. We report that at least 35% of patient with cutaneous vasculitis had a recurrent episode during their disease course. A study by Drenkard *et al*⁴ reported that, among 194 patients with either cutaneous or visceral vasculitis, 75 (38%) had two or more vasculitis events.

Table 2 Clinical and immunological manifestations as predictors of development of cutaneous vasculitis

Factor	HR (95% CI)	P value	HR (95% CI) adjusted*	P value adjusted*
Gender (male)	0.74 (0.47 to 1.10)	0.1452		
Race (African-American)	1.26 (1.02 to 1.55)	0.0315		
Age at SLE diagnosis	0.99 (0.98 to 1.00)	0.0996		
Post-high school education (>12 years)	0.76 (0.62 to 0.94)	0.0099	0.76 (0.61 to 0.94)	0.0125
Malar rash	1.04 (0.84 to 1.28)	0.7077	1.03 (0.83 to 1.28)	0.7801
Discoid rash	1.38 (1.04 to 1.81)	0.0274	1.27 (0.94 to 1.70)	0.1202
Photosensitivity	0.90 (0.72 to 1.10)	0.2996	0.90 (0.72 to 1.13)	0.3815
Mouth ulcer	1.22 (0.98 to 1.51)	0.0732	1.22 (0.97 to 1.53)	0.0898
Alopecia	1.18 (0.95 to 1.47)	0.1336	1.09 (0.87 to 1.38)	0.4361
Raynaud's phenomenon	1.35 (1.10 to 1.67)	0.0049	1.35 (1.09 to 1.68)	0.0075
Arthritis	1.04 (0.85 to 1.27)	0.7361	1.07 (0.87 to 1.32)	0.5206
Myositis	2.18 (1.12 to 3.77)	0.0236	2.13 (1.05 to 2.80)	0.0366
Pleuritis	1.17 (0.91 to 1.49)	0.2219	1.16 (0.90 to 1.50)	0.2487
Pericarditis	1.25 (0.89 to 1.72)	0.1880	1.24 (0.87 to 1.71)	0.2321
Proteinuria	1.09 (0.85 to 1.40)	0.4851	1.15 (0.88 to 1.49)	0.3050
Anaemia	1.35 (1.08 to 1.68)	0.0090	1.39 (1.10 to 1.75)	0.0063
Haemolytic anaemia	1.35 (0.80 to 2.13)	0.2478	1.40 (0.82 to 2.20)	0.2022
Coombs ever	1.57 (1.07 to 2.24)	0.0212	1.53 (1.03 to 2.20)	0.0366
Leucopenia	1.38 (1.09 to 1.73)	0.0078	1.39 (1.09 to 1.77)	0.0089
Thrombocytopaenia	0.81 (0.55 to 1.15)	0.2418	0.84 (0.56 to 1.22)	0.3787
Anti-dsDNA ever	1.19 (0.95 to 1.49)	0.1227	1.23 (0.97 to 1.55)	0.0868
Anti-Sm ever	1.53 (1.10 to 2.06)	0.0112	1.59 (1.14 to 2.17)	0.0076
Anti-Ro ever	1.31 (0.93 to 1.79)	0.1223	1.24 (0.85 to 1.74)	0.2485
Anti-La ever	1.29 (0.79 to 1.99)	0.2947	1.31 (0.77 to 2.07)	0.2964
Anti-RNP ever	1.65 (1.19 to 2.25)	0.0033	1.56 (1.09 to 2.17)	0.0151
Low C3 ever	1.19 (0.87 to 1.61)	0.2716	1.26 (0.90 to 1.73)	0.1743
Low C4 ever	1.13 (0.81 to 1.55)	0.4609	1.21 (0.85 to 1.69)	0.2781
Russell Viper Venom Time (RVVT) ever	0.85 (0.48 to 1.37)	0.5269	0.85 (0.46 to 1.43)	0.5714
Anti-cardiolipin ever	1.09 (0.77 to 1.48)	0.6271	1.18 (0.83 to 1.64)	0.3406
Anti-beta 2 GPI ever	0.35 (0.06 to 1.11)	0.0797	0.24 (0.01 to 1.06)	0.0630

*Adjusted for gender, race and age at SLE diagnosis.

Second, our study showed that the presence of discoid rash predicted an increased risk of development of cutaneous vasculitis. The association between discoid rash and vasculitis has been reported by Santiago-Casas *et al*⁸ in a large multiethnic, multicentre cohort of patients with SLE. A large cross-sectional study of childhood SLE determined an association between cutaneous vasculitis and other mucocutaneous manifestations including discoid rash, acute cutaneous rash and photosensitivity.²³ In addition, Gomes *et al*²⁴ reported that acute cutaneous rash, alopecia and oral ulcers were associated with cutaneous vasculitis. A small retrospective study of 50 patients with SLE in Egypt found an association between combined mucocutaneous manifestations and cutaneous vasculitis.⁷

Haematological manifestations such as anaemia, direct Coombs' positivity and leucopenia were found to be risk factors for developing cutaneous vasculitis in our study. Gheita *et al*⁷ had also reported an association between anaemia and cutaneous vasculitis. In Ramos-Casals *et al*'s⁵ study, 67% of patients with vasculitis (visceral or cutaneous) were reported to be anaemic compared with 17% of patients with no vasculitis. Looking at the SLEDAI parameters, Gomes *et al*²⁴ reported an association with leucopenia but not thrombocytopaenia.

A more serious manifestation, myositis, was shown in our study as predicting later cutaneous vasculitis. A retrospective study of 206 adult and 171 juvenile patients with SLE of Southeast Asian descent, with a mean follow-up of 8

years, had reported the association of cutaneous vasculitis and myositis only in adult patients.¹ Cutaneous vasculitic features in adult inflammatory myopathies without SLE have been reported. In a retrospective study of 76 patients with polymyositis and dermatomyositis followed-up over an 11-year period, 9% had cutaneous vasculitis.²⁵ In addition, two studies found cutaneous vasculitis in patients with myositis to be a predictor of malignancy.^{25 26} Interestingly, one study showed that vasculitic skin lesions were associated with muscle vasculitis on muscle biopsy.²⁶

We did not find an association between other major organ involvement and cutaneous vasculitis. All clinical manifestations including renal and CNS involvements were similar in SLE patients with or without cutaneous vasculitis in two cross-sectional studies from Brazil evaluating both adult (comparing 91 patients with cutaneous vasculitis to 163 patients without cutaneous vasculitis¹⁵) and juvenile patients with SLE (a cohort of 852 patients, of which 25 had cutaneous vasculitis²³). A study that examined the association between digital vasculitis as defined by the SELENA-SLEDAI score and lupus severity in 168 patients with SLE determined that digital vasculitis was not associated with severe lupus manifestations, particularly renal and CNS.²⁴ However, Callen *et al*¹⁶ had reported in 1983 that cutaneous vasculitis correlated with active systemic lupus and portended a poor prognosis. A patient with several vasculitic changes on the fingers died of progressive renal and CNS deterioration.¹⁶ A retrospective analysis of 171 juvenile patients with SLE of Asian descent found an increased risk of renal and neuropsychiatric manifestations in patients who have cutaneous vasculitis compared with those who did not.¹ Gheita *et al*⁷ had reported an association between cutaneous vasculitis and lupus nephritis in a small retrospective study from Egypt evaluating 50 adult patients with SLE. Our study, the largest overall and the only one with long follow-up, did not show any association between cutaneous vasculitis and CNS or renal lupus.

Third, considering the possibility of vasculopathy in patients with SLE, our study showed that only Raynaud's phenomenon predicted the development of cutaneous vasculitis. We found no association between cutaneous vasculitis and antiphospholipid antibodies, livedo reticularis, arterial or venous thrombosis. This is in accordance with a study of 852 patients with childhood SLE in which none of the patients with cutaneous vasculitis had antiphospholipid syndrome or thrombotic thrombocytopenic purpura.²³ Two other studies, though, suggested antiphospholipid antibodies and vasculopathy as players in the mechanism for cutaneous vasculitis in patients with SLE.^{4 7} It is important to note that non-vasculitic occlusive vasculopathy might mimic vasculitis lesions.²⁷ Vasculitis is characterised by an inflammatory process involving infiltration of the vessel walls by leucocytes with subsequent endothelial damage and fibrinoid necrosis.²⁸ Vasculopathy is characterised by non-inflammatory lesions due to coagulopathy (such as the presence of antiphospholipid

antibodies) that result in occlusion of dermal blood vessels with fibrin thrombi.²⁹

Fourth, in terms of autoantibody associations, anti-Smith and anti-RNP were found to be significant risk factors for cutaneous vasculitis. Anti-RNP is a novel finding that has not been previously reported. Only one small retrospective study (evaluating 34 patients), in 1983, found an association between anti-Smith and cutaneous vasculitis.¹² An association between anti-P antibodies¹⁵ and cutaneous vasculitis but not the other autoantibodies^{15 23} has been reported. Although some studies suggested an association between cutaneous vasculitis and Sjögren's syndrome or anti-SSA/SSB antibodies,^{7 8 11} our study did not find an association with secondary Sjögren's syndrome in SLE. No patients with primary Sjögren's syndrome and hypergammaglobulinaemia were included.

Fifth, we did not find an association between hypocomplementaemia or anti-dsDNA and cutaneous vasculitis. Hypocomplementaemia and high disease activity⁵ have been reported to be associated with cutaneous vasculitis.^{4 7 17} A higher mean European Consensus Lupus Activity Measurement (ECLAM) score was reported in patients with vasculitis, 90% of which were cutaneous. The mean ECLAM score was 5.86 in patients with vasculitis compared with 3.87 in those without vasculitis.⁵ This was not confirmed in a study that looked at childhood SLE patients with digital vasculitis. The SLEDAI median, after excluding the vasculitis descriptor, was significantly lower in patients with digital vasculitis compared with those without this manifestation (10 vs 14, $p=0.004$).²³ Moreover, Gomes *et al*, who specifically looked at SLEDAI parameters associated with digital vasculitis, did not find low complement levels or high anti-dsDNA in patients who presented with digital vasculitis.²⁴ This study suggested that the high weight attributed to cutaneous vasculitis in the SLEDAI score should be reevaluated.²⁴

Sixth, patients with cutaneous vasculitis had higher SLICC/ACR DI scores compared with those without. In fact, in a study of childhood SLE, the presence of cutaneous vasculitis was associated with permanent damage in 20% of the patients.²³ In a study looking at both cutaneous and visceral vasculitis, patients with visceral but not cutaneous vasculitis had a higher mortality compared with patients without vasculitis.⁴

We did not subdivide into subtypes such as palpable purpura, ulcers and erythema with or without necrosis. Biopsies are not done as part of routine practice. Patients were treated at presentation with a clinical diagnosis of small vessel vasculitis. Small vessel vasculitis may be overestimated based on clinical presentation alone.³⁰ The differential diagnosis of digital cutaneous lesions includes discoid lupus erythematosus and non-occlusive vasculopathy, among others. As we found no association with antiphospholipid antibodies, it is unlikely that non-occlusive vasculopathy was a major limitation. Biopsies can differentiate between the different types of cutaneous vasculitis that can be seen in patients with SLE.¹⁴ Despite these limitations, all diagnoses were made by

one rheumatologist with expertise in SLE. Our database recorded 'vasculitis' as part of the SLEDAI.

CONCLUSION

This is the largest prospective multiethnic study with long-term follow-up examining the clinical and serological associations of cutaneous vasculitis in patients with SLE. Our study determined the increased risk of cutaneous vasculitis in African-American race and the considerable risk of recurrence of this manifestation. It highlights the temporal association between the development of cutaneous vasculitis and clinical manifestations such as discoid rash, Raynaud's phenomenon, myositis, anaemia, Coombs' positivity, leucopenia and immunological manifestations such as anti-Smith and anti-RNP positivity. Our study did not find any association between cutaneous vasculitis and either antiphospholipid antibodies or Sjögren's syndrome. Our study stresses on the importance of cutaneous vasculitis as a disease manifestation, considering its association with increased organ damage.

Contributors RK contributed to the conception, design, interpretation of the data and writing of the manuscript. DG contributed to the design, analysis and interpretation of the data. MAP contributed to the collection of cohort data, conception, design, interpretation of the data and writing of the manuscript.

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Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not required.

Ethics approval The cohort was established in 1987 and has been approved by the Johns Hopkins University School of Medicine Institutional Review Board on a yearly basis.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available on reasonable request.

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