A detailed analysis of the distribution, morphology, and histopathology of complex purpura in hospitalized patients: A case series of 68 patients

Jeff R. Gehlhausen, MD, PhD,[a] David A. Wetter, MD,[c] Caroline Nelson, MD,[a] Sarika Ramachandran, MD,[a] Jennifer M. McNiff, MD,[a,b] and Christine J. Ko, MD[a,b]
New Haven, Connecticut, and Rochester, Minnesota

Background: Purpura in inpatients commonly leads to dermatologic consultation. The differential diagnosis is broad and algorithms are intricate.

Objective: We evaluated inpatient consultations for complex purpura to document the most common diagnoses and to validate the true diagnostic utility of histopathology, clinical morphology, and distribution.

Methods: We reviewed a case series of 68 inpatients during a 4-year period with a dermatologic consultation for purpura and biopsy findings of vasculitis or microvascular occlusion.

Results: Key features of complex purpura are nonbranching (round) versus branching (retiform) morphology, dependent versus acral or generalized distribution, and leukocytoclastic vasculitis versus microvascular occlusion (with emphasis on depth of involvement). Dependent nonbranching purpura with only superficial vessels involved by leukocytoclastic vasculitis was most often due to IgA vasculitis or cutaneous single-organ small-vessel vasculitis. In contrast, deeper involvement by leukocytoclastic vasculitis was suggestive of systemic disease (eg, antineutrophil cytoplasmic antibody—associated vasculitis). Branching purpura was concerning, with greater than 90% sensitivity and specificity for microvascular occlusion and associated high mortality ($\approx$50%). The majority of patients who died had acral branching lesions.

Limitations: Small sample size, inpatients at a tertiary care center, and retrospective nature are some limitations.

Conclusion: Nonbranching dependent purpura corresponded to leukocytoclastic vasculitis, with the most common diagnoses being IgA vasculitis or skin-limited small-vessel vasculitis; patients with deep involvement often had systemic diseases. In this series, branching purpura was due to microvascular occlusion rather than medium-vessel vasculitis, and had associated high mortality. (J Am Acad Dermatol 2021;84:1188-96.)

Key words: ANCA-associated vasculitis; calciphylaxis; complex purpura; cryoglobulinemia; cutaneous small vessel vasculitis; distribution; histopathology; IgA vasculitis; leukocytoclastic; morphology; palpable purpura; purpura; retiform; vasculitis; vasculopathy.

From the Yale School of Medicine Department of Dermatology[a] and Department of Pathology,[b] New Haven; and Mayo Clinic Department of Dermatology, Rochester.[c]
Funding sources: None.
Conflicts of interest: None disclosed.
This study was approved by the IRB of Yale University.
Accepted for publication April 28, 2020.
Reprints not available from the authors.

Correspondence to: Christine J. Ko, MD, Yale University School of Medicine, Department of Dermatology, 333 Cedar St, PO Box 208059, New Haven, CT 06520. E-mail: christine.ko@yale.edu.
Published online May 4, 2020.
0190-9622/$36.00

https://doi.org/10.1016/j.jaad.2020.04.149

INTRODUCTION

The evaluation of complex cases of purpura, particularly those secondary to vascular damage, occlusion, or both, is critically important given the frequency of dermatology consultation and potential for mortality. Vasculitis and vasculopathy (because the latter term is relatively nonspecific, we will henceforth use the term "microvascular occlusion") often are considered simultaneously in the evaluation of complex purpura, generating a vast differential diagnosis with intricate, comprehensive algorithms.[1-5] Because these cases can be a diagnostic challenge across multiple specialties, we sought to answer the following questions: Can the cutaneous distribution and lesion morphology readily distinguish between diagnostic groups? Does histopathologic examination predict more limited cutaneous versus systemic involvement? Can a simplified clinical approach be outlined to streamline the diagnosis and evaluation of the most common causes of complex purpura in inpatients? Herein, we describe our findings, providing high-yield clues to the consultant dermatologist.

CAPSULE SUMMARY

- The initial differential and evaluation of retiform purpura often covers the spectrum of vasculitis and vasculopathy.
- For hospitalized patients, we propose a streamlined differential because just 1 branching lesion (retiform purpura) plus generalized distribution correlated with microvascular occlusion and increased mortality; retiform purpura was not caused by medium-vessel vasculitis in this series.

METHODS

Case selection

Cases were reviewed retrospectively in accordance with the institutional review board. Ninety-one total consecutive consultations for complex purpura that had a biopsy performed from January 2015 through November 2019 were identified from the Yale University Department of Dermatology consultation database. This database includes details on all consultations at Yale New Haven Hospital and Saint Raphael's Hospital in New Haven, CT, including reason for consultation, whether a biopsy was performed, clinical photographs, and (presumed) diagnosis at sign-off of consultation. Complex purpura was defined as inclusive of the terms "retiform purpura," "palpable purpura," "vasculitis," and "vasculopathy."

Through medical record review (J.R.G. and C.J.K.), abstracted data included demographic, clinical, laboratory, histopathologic, and photographic records for all cases, when available (4 cases lacked clinical photographs). The biopsy performed on consultation was reviewed for each case by J.R.G. and C.J.K., and 23 cases without clinical or histopathologic findings of vasculitis or occlusion were eliminated (6 cases of pigmented purpuric eruption, 3 cases of simple purpura, 11 inflammatory disorders [eg, stasis dermatitis, Sweet syndrome], and 1 case each of *Klebsiella* infection, scurvy, and leukemia cutis). Sixty-eight cases were included.

Lesion morphology and distribution categorization

Lesions were categorized as nonbranching or branching (Fig 1). Solid circular lesions that could appear flat (macular), raised (papular), or overlap to create larger patches or plaques ("pseudobranching"; see Fig 1) were classified as nonbranching. Some lesions classified as nonbranching included some degree of ulceration and central eschar.

Purpura that showed a branching pattern either entirely or solely at the border of a solid area was categorized as branching. Oftentimes the centers of branching lesions were solid purple to black, but the lesion border retained at least some degree of jagged linearity, creating an outline resembling part of a maple leaf. If even just 1 lesion on a patient had a branching pattern, the morphology was categorized as branching; some patients with branching additionally had nonbranching purpura including macules, papules, or patches or plaques at other body sites.

Lesion distribution was categorized as acral, dependent, generalized, or pauci-random. These distributions have been previously described as significant[6] and are defined in Fig 2. In cases that were difficult to classify, the predominant distribution was chosen. Generalized cases could have acral or dependent lesions but also had a sufficient number of lesions outside the acral and dependent distributions.

Histopathologic definitions of leukocytoclastic vasculitis and microvascular occlusion

The diagnosis of leukocytoclastic vasculitis required 3 features: evidence of vessel wall damage, ranging from swelling of vessel walls producing a "fluffy" appearance to fibrinoid necrosis of vessel walls; erythrocyte extravasation; and leukocytoclasia.[2] Microvascular occlusion was diagnosed if a

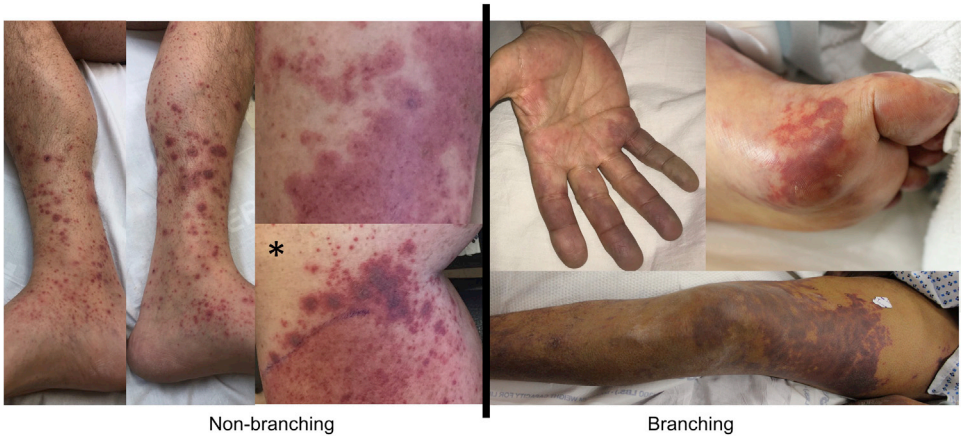

Fig 1. Nonbranching (round) and branching (retiform) purpura. Morphology of 2 major classes of purpura in hospitalized patients. Left: Nonbranching. Lesions are circular "spots" (early on, they may be macular) that can overlap and become confluent to form patches or plaques. There may be a pattern of pseudobranching either at the margins of lesions or when lesions develop central darker hemorrhage or necrosis (photograph with asterisk). Pseudobranching is most easily distinguished from true branching by the discrete 0.4- to 0.9-cm papular (nonbranching) purpura at a short distance outside of and separate from confluent foci. Right: Branching (retiform purpura). In contrast to pseudobranching, lesions just outside of the area of branching are generally absent. Branching purpura ranged in size from approximately 1 cm to greater than 30 cm in diameter or length. Patients with branching purpura may also have macules, papules, and plaques on other body sites. We classified patients as having a branching morphology if even just 1 lesion showed true branching.

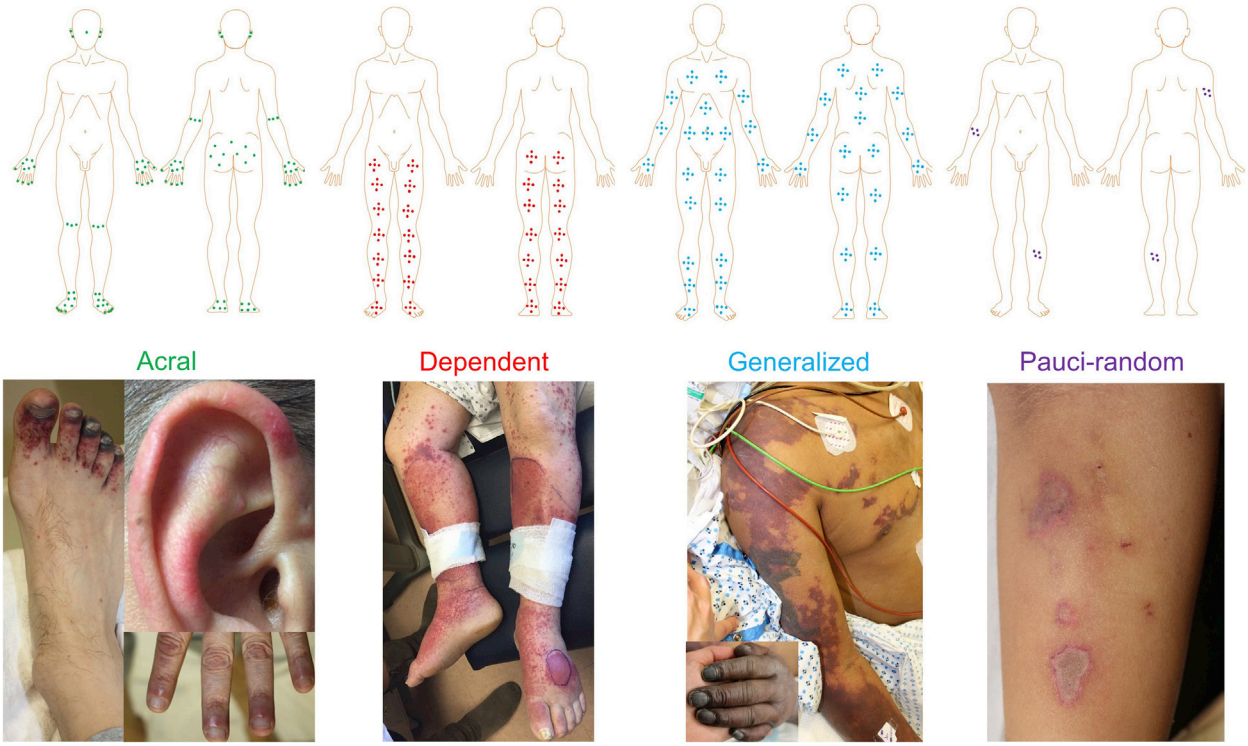

Fig 2. Distribution of purpura: definition of acral, dependent, generalized, and pauci-random. Acral lesions involve the hands, feet, ears, and nose; sometimes lesions can also be observed on the penis, elbows, knees, buttocks, breasts, and cheeks. The diagram is modified from the work of Warren W. Piette, MD, who emphasizes the importance of using lesional number/distribution patterns, morphology, and clinical context.

vessel lumen was occluded (eg, most commonly by fibrin thrombi).

Case diagnoses

Cases were classified according to the diagnosis in the medical record (Table I) but were subjected to review by J.R.G. and C.J.K. to ensure accuracy. Generally, there were not discrepancies between the original chart diagnosis and subsequent review. Special cases are noted in Supplemental Fig 1 (available via Mendeley at https://data.mendeley.com/datasets/wkf9hrj364/1).

IgA vasculitis. The diagnosis of IgA vasculitis was based on European League Against Rheumatism (EULAR) criteria for IgA vasculitis, which includes palpable purpura with lower limb predominance and at least 1 additional finding of predominant IgA deposition in any biopsy, diffuse abdominal pain, arthritis or arthralgia, or renal involvement.[7]

Sepsis associated (vasculitis/microvascular occlusion). This was generally diagnosed in the setting of septic shock and positive blood culture results, often with decreased protein C and S function and histopathologic findings of microvascular occlusion (and 1 case of leukocytoclastic vasculitis only). "Sepsis-associated microvascular occlusion (or vasculitis)" is used as opposed to purpura fulminans, acquired protein C/S deficiency, disseminated intravascular coagulation, or other terminology. Only 1 case of microvascular occlusion had detectable gram-positive cocci in the skin; this case had associated subacute bacterial endocarditis with magnetic resonance imaging of the brain compatible with septic emboli.

Vessel depth

Small vessels were defined as those present in the dermis, commonly in the superficial papillary dermis ("superficial involvement") but also throughout the reticular dermis or into the subcutis ("deep involvement"). Medium vessels were defined as those at the interface of the dermis and subcutis or within the subcutis, at least twice the diameter of a small vessel.[8]

Nomenclature

Purpura. In the text, we refer to cases of vasculitis and microvascular occlusion as complex purpura, distinct from simple (macular) purpura (eg, solar purpura, ecchymoses resulting from trauma and antiplatelet drugs).

Systemic disease. Involvement of 1 or more internal organs (renal, gastrointestinal, musculoskeletal, or liver), as defined by laboratory abnormalities or, in the case of gastrointestinal and musculoskeletal, clinical signs or symptoms, in addition to cutaneous lesions.

Table I. Diagnostic categories in this series of 68 inpatients with dermatology consultation for complex purpura

Diagnosis	No.	%
Leukocytoclastic vasculitis	42	62
IgAV	20	30
Idiopathic	6	—
Infectious	5	—
Disease	2	—
Drug	3	—
Mixed	4	—
CSVV	15	22
Idiopathic	6	—
Infectious	4	—
Mixed	3	—
Drug	2	—
Other vasculitides	6	9
AAV	2	—
Mixed cryoglobulinemia	2	—
Levamisole associated	1	—
Sepsis associated	1	—
Urticarial vasculitis	1	1
Mixed leukocytoclastic vasculitis and microvascular occlusion	3	4
Levamisole associated	2	—
Acquired protein C/S deficiency	1	—
Microvascular occlusion	23	34
Sepsis associated	8	12
Calciphylaxis	6	9
APLS	3	4
Angioinvasive fungal	1	—
Disseminated yeast	1	—
Intravascular B-cell lymphoma	1	—
Levamisole associated	1	—
Monoclonal cryoglobulinemia	1	—
Thrombocythemia	1	—
Total	68	100

Diagnostic categories are grouped by major histopathologic findings: leukocytoclastic vasculitis alone, mixed leukocytoclastic vasculitis and microvascular occlusion, and microvascular occlusion alone. See Supplemental Fig 1 for further details on subcategories under IgA vasculitis and cutaneous small-vessel vasculitis. Cases designated as mixed had at least 2 competing etiologies that were estimated to be potentially causal (eg, recent infection, course of probable antibiotic). Dashes indicate where percentages were not displayed for specific diagnoses or subcategories given the small number of cases.
AAV, Antineutrophil cytoplasmic antibodies–associated vasculitis; *APLS*, antiphospholipid syndrome; *CSVV*, cutaneous small-vessel vasculitis; *IgAV*, IgA vasculitis.

RESULTS

Histopathologic findings and diagnoses

Sixty-eight cases of vasculitis, microvascular occlusion, or both were identified in the nearly

4-year period of case review. The median age was 63 years and 54% were men. Forty-two cases of vasculitis were observed, including 20 cases of IgA vasculitis (30%) and 15 cases of isolated cutaneous small-vessel vasculitis (22%). A total of 23 cases (34%) of microvascular occlusion were observed. For more details on the case diagnoses, see Table I.

Morphology

Supplemental Fig 1 enumerates the specific morphology, distribution, and histopathologic findings in each case. Through the use of detailed morphologic analysis of clinical photographs in concert with medical record documentation, all patients were classified as having nonbranching or branching morphology (see methods).

Morphologic-based categorization revealed solely nonbranching purpura in IgA vasculitis, cutaneous small-vessel vasculitis, and urticarial vasculitis (Supplemental Fig 1), and all had leukocytoclastic vasculitis on biopsy. Pseudobranching, in which circular papules of purpura appear confluent and interconnect with a central darker pattern, was present in only 6 cases of IgA vasculitis and 0 cases of isolated cutaneous small-vessel vasculitis. In cases caused purely by microvascular occlusion, approximately 90% (21/23) had branching purpura; these patients frequently also had macules, papules, and plaques (nonbranching morphologies) at other sites in addition to branching purpura. Two cases involving neutropenic patients with microvascular occlusion caused by opportunistic mycoses were classified as having nonbranching morphology; these patients had necrotic plaques and papulonodules. The sensitivity and specificity of branching purpura on physical examination relating to evidence of microvascular occlusion on histopathology were 91% and 93%, respectively. Cases with systemic disease showed either branching or nonbranching morphology (eg, antineutrophil cytoplasmic antibody–associated vasculitis, mixed cryoglobulinemia, levamisole-associated purpura).

Distribution

The majority of IgA vasculitis (15/20, 75%) and nearly half of cutaneous small-vessel vasculitis (9/15, 60%) cases solely featured dependent purpuric lesions. The cases that had more generalized involvement overwhelmingly still had dependent purpura with additional lesions on the abdomen and upper arms (Supplemental Fig 1).

Whereas IgA vasculitis and cutaneous small-vessel vasculitis most commonly had a dependent distribution, most cases of microvascular occlusion (15/23, 65%) had either acral or generalized involvement, with acral lesions typically also present in the generalized cases. Although all 6 cases of calciphylaxis involved the thighs, the distribution was variable (dependent, generalized, or pauci-random).

Histopathology

All cases in Table I were classified by their histopathologic findings as vasculitis (42 cases, 62%), mixed vasculitis and microvascular occlusion (3 cases, 4%), or microvascular occlusion alone (23 cases, 34%) and then separated by diagnosis. Vasculitis or occlusion primarily affected small vessels. Superficial and deep involvement was observed in 11 cases (16%). Vasculitis of both small- and medium-sized vessels was observed in 5 cases (7%). A summary of lesional morphology as it relates to histopathology is shown in Fig 3.

IgA vasculitis and cutaneous small-vessel vasculitis

Using the EULAR criteria for IgA vasculitis, cases of palpable purpura with corresponding leukocytoclastic vasculitis were separated into cutaneous small-vessel vasculitis or IgA vasculitis (see methods). We identified a total of 20 cases of IgA vasculitis and 15 of cutaneous small-vessel vasculitis.

The 2 cases of isolated cutaneous small-vessel vasculitis with superficial and deep involvement did not have other organ involvement (preceding upper respiratory tract infection in one patient and idiopathic in the other). The 3 patients with superficial and deep leukocytoclastic vasculitis histopathology in the IgA vasculitis group had significant renal disease requiring renal biopsy, revealing glomerulonephritis or nephropathy and positive IgA deposition on DIF testing.

Thirteen of 20 IgA vasculitis cases (60%) had predominant IgA present on DIF testing of skin biopsy, with 3 additional cases with negative results on skin testing having predominant IgA on renal biopsy. Four cases were classified as IgA vasculitis according to EULAR criteria on the basis of systemic findings without predominant IgA on DIF testing (Supplemental Table I). The most common organ system affected in IgA vasculitis was renal (13/20, 65%), followed by gastrointestinal (8/20, 40%) and then musculoskeletal (3/20, 15%). Seventeen of 20 IgA vasculitis cases (85%) had systemic findings in total, and 13 of 16 cases (82%) with positive DIF testing results had systemic findings.

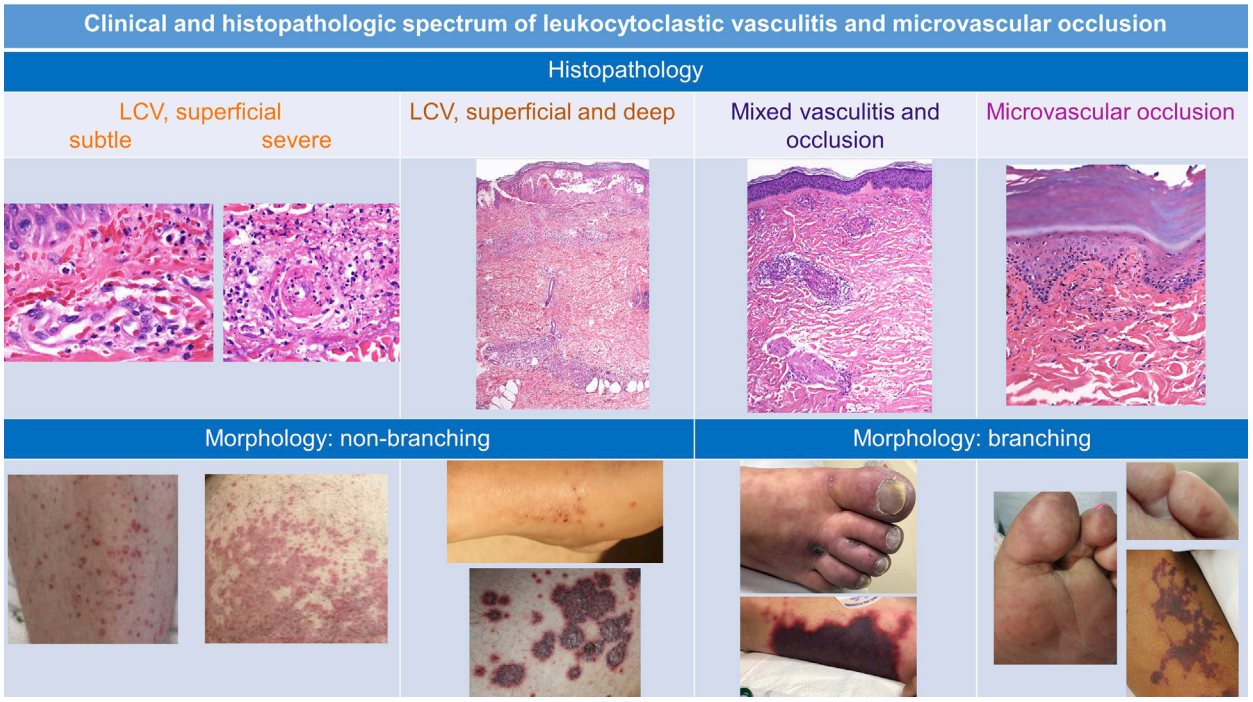

Fig 3. Clinical and histopathologic spectrum of leukocytoclastic vasculitis and microvascular occlusion. The clinical images (and histopathologic findings) are largely distinctive between nonbranching versus branching purpura. *LCV*, Leukocytoclastic vasculitis.

Summarized findings and proposed work flow

Fig 4 summarizes the key morphologic, distribution, and histopathologic findings observed in our review. On the basis of our results, we created a simplified work flow based on the distribution and morphology of complex purpura and the most common diagnoses to consider (Fig 5).

DISCUSSION

The evaluation of complex purpura in the hospitalized population is challenging. With key clinical and histopathologic findings, patient evaluation can be initially streamlined (Fig 5). Our simplified algorithm using morphology (nonbranching versus branching), distribution (dependent versus acral/generalized), and histopathology (leukocytoclastic vasculitis versus microvascular occlusion) generates a focused differential diagnosis (Fig 5) for cases with superficial leukocytoclastic vasculitis or microvascular occlusion. This streamlined algorithm is not meant to replace more comprehensive algorithms. This directed algorithm is based on the most common diagnoses observed in this series. Its use may prevent unnecessary extensive laboratory evaluation, which is costly to the health care system in terms of dollars as well as physician time because any abnormalities are followed up by further tests and specialty consultations, often despite dubious relationship to the patient's presentation. More granular details are addressed below, and there are exceptions to the algorithm. As an example, the algorithm does not address palpable purpura corresponding to leukocytoclastic vasculitis with involvement of superficial and deep vessels, which is suggestive of a systemic process; in such cases, the evaluation may include antineutrophil cytoplasmic antibodies, antinuclear antibody, rheumatoid factor, and others based on review of systems.

Morphology: nonbranching or branching

Although nonbranching (papular) lesions can become confluent to form a pseudobranching pattern (Figs 1 and 3), near adjacent, discrete, round satellite lesions can help to differentiate from true branching purpura. Branching could be subtle and represent the minority of lesions in some cases. Branching purpura on physical examination identified underlying microvascular occlusion on histopathology with a remarkable 91% sensitivity and 93% specificity. Fifteen of 68 patients died, with 13 of 15 patients having branching lesions, indicating this morphology is strongly associated with mortality ($P < .001$, Fischer exact test). Branching morphology was not associated with medium-vessel vasculitis in this series.

Subtype	Typical Distribution	Typical Morphology	Histopathology
CSVV	Dependent > Generalized	Palpable purpura (Non-branching purpura)	Superficial > superficial and deep LCV
IgAV			
Mixed cryoglobulinemia	Dependent, Acral, or Generalized*	Non-branching > branching purpura	Superficial > superficial and deep LCV*; subtle microvascular occlusion*
Calciphylaxis	Dependent, Generalized, or Pauci-Random	Branching purpura	Microvascular occlusion involving subcutaneous fat
ANCA+ vasculitis	Acral or Pauci-Random	Branching or non-branching (also macules, papules^, plaques, papulonodules^)	Superficial and deep LCV; medium-vessels may be involved^
Levamisole-associated	Acral or Generalized	Branching purpura with central purple-black necrosis and bright red border	Mixed vasculitis and/or microvascular occlusion
Sepsis-associated		Branching purpura (also macules and patches)	
APLS	Acral or Generalized		Microvascular occlusion
Opportunistic mycoses in neutropenic patients	Pauci-Random	Purpuric papules, plaques, papulonodules, bullae, and ulcers (Non-branching purpura)	Microvascular occlusion

Fig 4. Major diagnoses in 68 inpatients with purpura, categorized by distribution, morphology, and histopathology. *ANCA*, Antineutrophil cytoplasmic antibodies; *APLS*, antiphospholipid syndrome; *CSVV*, cutaneous small-vessel vasculitis; *IgAV*, IgA vasculitis; *LCV*, leukocytoclastic vasculitis. *Not observed in the 2 cases in this series. ^Papules and papulonodules caused by medium-vessel vasculitis are not necessarily purpuric.

One series of IgA vasculitis previously identified distinct morphologic features of some cases[9]; another series regarded this finding as equivocal.[10] We analyzed our cutaneous small-vessel vasculitis and IgA vasculitis cases, looking for the presence of what we term "pseudobranching" as defined by overlapping papules of purpura creating confluent plaques, sometimes with an interconnecting central pattern of darker coloration (Fig 1, asterisk), which is distinct from true branching caused by microvascular occlusion (Fig 1). The presence of pseudobranching discriminated IgA vasculitis and cutaneous small-vessel vasculitis with high specificity (100%) and low sensitivity (33%; 6 cases of pseudobranching in IgA vasculitis, 0 in cutaneous small-vessel vasculitis).

For branching purpura, the status of the patient can help to further differentiate within this group. Although 3 of the 4 patients with levamisole-associated purpura were overall well appearing and quickly improved, 1 was in the intensive care unit. The literature corroborates this; patients with levamisole-associated disease may be acutely ill, but recovery tends to be fairly rapid. Recurrences are also common.[11] This is in stark contrast with the typical profile of our patients with sepsis-associated purpura, calciphylaxis, or antiphospholipid syndrome, who remained seriously ill, and 12 patients eventually died.

Distribution: dependent versus other

Dependent versus acral or generalized distribution (see methods) discriminated well between diagnostic groups (Fig 2). For branching lesions, acral involvement was common, and generalized cases of branching typically had acral branching as well (7/10, 70%). Of the 12 dead patients with clinical photographs, 10 had acral branching lesions, typically in the setting of sepsis or antiphospholipid syndrome. There was no mortality associated with exclusively nonbranching lesions involving the feet. Thus, we suggest the phrase "acral branching is bad."

Histopathology: vasculitis versus occlusion, superficial versus superficial and deep leukocytoclastic vasculitis, and direct immunofluorescence testing

Our findings support routine biopsy for hematoxylin-eosin staining as an important initial step to confirm vasculitis versus microvascular occlusion (Fig 5). Branching lesions were the minority morphology in some patients, and histopathology was vital to direct focus toward entities caused by microvascular occlusion and away from vasculitis. Involvement of both superficial and deep small vessels by leukocytoclastic vasculitis broadened the differential diagnosis significantly, whereas leukocytoclastic vasculitis of superficial vessels

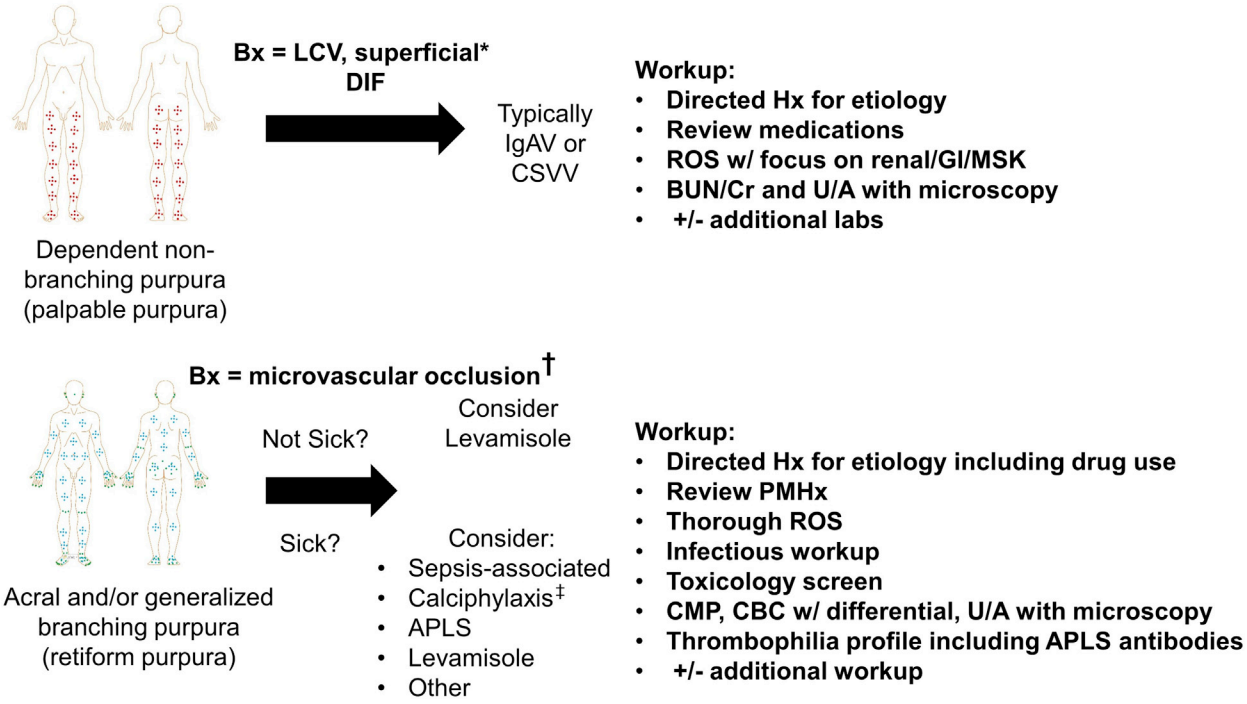

Fig 5. Two simplified algorithms for nonbranching versus branching purpura. *APLS*, Antiphospholipid syndrome; *BUN*, blood urea nitrogen; *Bx*, biopsy; *CBC*, complete blood cell count; *CMP*, comprehensive metabolic panel; *Cr*, creatinine; *CSVV*, cutaneous small-vessel vasculitis; *DIF*, direct immunofluorescence; *GI*, gastrointestinal; *Hx*, history; *IgAV*, IgA vasculitis; *LCV*, leukocytoclastic vasculitis; *MSK*, musculoskeletal; *PMHx*, medical history; *ROS*, review of systems; *U/A*, urinalysis. *On biopsy, superficial and deep involvement by leukocytoclastic vasculitis broadens the differential diagnosis (Supplemental Fig 1); 2 patients with mixed cryoglobulinemia also had findings of superficial leukocytoclastic vasculitis. †For levamisole-associated cases, biopsy findings could also be microvascular occlusion mixed with leukocytoclastic vasculitis or leukocytoclastic vasculitis alone. ‡Could also be pauci-random; the thigh was involved in all 6 cases in this series.

alone largely correlated with IgA vasculitis or cutaneous small-vessel vasculitis and 2 cases of mixed cryoglobulinemia (Fig 4). Superficial and deep leukocytoclastic vasculitis identified a systemic vasculitis with poor sensitivity (31%) but high specificity (88%), as in past studies.[12,13] Like involvement of deep small vessels, medium vessels were affected only in cases with an associated systemic process (eg, sepsis, IgA vasculitis, eosinophilic granulomatosis with polyangiitis). Therefore, dermatopathologists should report deep involvement of small- as well as medium-sized vessels.

Microvascular occlusion of small vessels in the fat was observed in all cases of calciphylaxis (6/6). This is not specific to calciphylaxis and was present in 3 other cases (levamisole associated, sepsis associated, and antiphospholipid syndrome). However, previous literature supports that deep microvascular occlusion is a clue for the diagnosis of calciphylaxis[14,15] and likely correlates to the often associated abnormalities of coagulation.[16]

LIMITATIONS

This study does not address more common causes of simple purpura (see methods). Other limitations include the small sample size, retrospective nature of the study, and the comprehensiveness of the consultation database. Because only hospitalized patients from 1 institution were included, the findings may not be generalizable to other settings.

CONCLUSIONS

In this series of 68 inpatients with dermatology consultation for complex purpura, careful assessment of lesion morphology (nonbranching versus branching), distribution (dependent versus other), and histopathology (superficial versus superficial and deep leukocytoclastic vasculitis versus microvascular occlusion) was a helpful

discriminator when correlated with the ultimate diagnosis. Although it is no surprise to confirm that nonbranching purpura corresponds well to leukocytoclastic vasculitis, in this series, branching purpura corresponded only to microvascular occlusion and not medium-vessel vasculitis. Using these features, we created an algorithm (Fig 5) to simplify the initial differential diagnosis of complex purpura. Future studies may test the utility of this algorithm.

REFERENCES

1. Carlson JA, Chen KR. Cutaneous pseudovasculitis. *Am J Dermatopathol*. 2007;29:44-55.
2. Chen KR, Carlson JA. Clinical approach to cutaneous vasculitis. *Am J Clin Dermatol*. 2008;9:71-92.
3. Johnson EF, Wetter DA, Lehman JS, Hand JL, Davis DM, Tollefson MM. Leukocytoclastic vasculitis in children: clinical characteristics, subtypes, causes and direct immunofluorescence findings of 56 biopsy-confirmed cases. *J Eur Acad Dermatol Venereol*. 2017;31:544-549.
4. Fiorentino DF. Cutaneous vasculitis. *J Am Acad Dermatol*. 2003; 48:311-340.
5. Georgesen C, Fox LP, Harp J. Part I: retiform purpura: a diagnostic approach. *J Am Acad Dermatol*. 2020;82(4):783-796.
6. Piette WW. The differential diagnosis of purpura from a morphologic perspective. *Adv Dermatol*. 1994;9:3-23. discussion 24.
7. Ozen S, Ruperto N, Dillon MJ, et al. EULAR/PReS endorsed consensus criteria for the classification of childhood vasculitides. *Ann Rheum Dis*. 2006;65:936-941.
8. Carlson JA. The histological assessment of cutaneous vasculitis. *Histopathology*. 2010;56:3-23.
9. Piette WW, Stone MS. A cutaneous sign of IgA-associated small dermal vessel leukocytoclastic vasculitis in adults (Henoch-Schonlein purpura). *Arch Dermatol*. 1989;125:53-56.
10. Helander SD, De Castro FR, Gibson LE. Henoch-Schonlein purpura: clinicopathologic correlation of cutaneous vascular IgA deposits and the relationship to leukocytoclastic vasculitis. *Acta Derm Venereol*. 1995;75:125-129.
11. Gulati S, Donato AA. Lupus anticoagulant and ANCA associated thrombotic vasculopathy due to cocaine contaminated with levamisole: a case report and review of the literature. *J Thromb Thrombolysis*. 2012;34:7-10.
12. Bouiller K, Audia S, Devilliers H, et al. Etiologies and prognostic factors of leukocytoclastic vasculitis with skin involvement: a retrospective study in 112 patients. *Medicine*. 2016;95:e4238.
13. Sanchez NP, Van Hale HM, Su WP. Clinical and histopathologic spectrum of necrotizing vasculitis. Report of findings in 101 cases. *Arch Dermatol*. 1985;121:220-224.
14. Chen TY, Lehman JS, Gibson LE, Lohse CM, El-Azhary RA. Histopathology of calciphylaxis: cohort study with clinical correlations. *Am J Dermatopathol*. 2017;39:795-802.
15. Dutta P, Chaudet KM, Nazarian RM, Kroshinsky D, Nigwekar SU. Correlation between clinical and pathological features of cutaneous calciphylaxis. *PLoS One*. 2019;14:e0218155.
16. El-Azhary RA, Patzelt MT, McBane RD, et al. Calciphylaxis: a disease of pannicular thrombosis. *Mayo Clin Proc*. 2016;91: 1395-1402.