Sorting out cutaneous vasculitis -
A rheumatologist’s perspective

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All efforts to classify vasculitis have
failed to achieve unanimity of opinion
for over a century. While superficially
this nosologic quandary may appear to
be an exercise best suited for academi-
cians to debate, there is in fact a serious
need for such a construct to help gauge
prognosis, guide therapy and provide a
diagnostic standard for the increasing
number of multi-center, randomized con-
trolled clinical trials being performed in
these relatively rare diseases.

Within these varied classification
schemes, efforts to define the cutaneous
vasculitides have been perhaps the least
satisfying. In support of this assertion is
the fact that in the 1990 classification
system proposed by the American Col-
lege of Rheumatology, the proposed cri-
teria for hypersensitivity vasculitis (HV)
yielded the poorest discriminate func-
tion and the lowest sensitivity and spe-
cificity of all the vasculitic syndromes.

Dr. Callen in his editorial comments (5)
contended that distinguishing

HSP - The rheumatologist’s perspective

Of the two syndromes, i.e. HV or CLA
and HSP, HSP clearly appears to be more
worthy of nosologic distinction. The dis-
ease has been recognized for nearly two
centuries and its clinical features in chil-
dren have been reasonably well docu-
mented (6). In addition, there is now a
significant body of data defining the cen-
tral role of IgA in its pathogenesis (7).

Unfortunately, there is no simple blood
test and few children undergo immuno-
histochemical analysis of the skin or kid-
ney allowing a definitive diagnosis as
suggested by the Chapel Hill criteria. From
a research perspective, classification
criteria such as those proposed by

Hypersensitivity vasculitis or
cutaneous leukocytoclastic angiitis -
The rheumatologist’s perspective

The definition is derived historically
from the recognition that a predomi-
EDITORIAL

nantly cutaneous leukocytoclastic vasculitis could be the result of an adverse effect from the ingestion of a drug (8). Unfortunately, the same clinical picture can be seen in the complete absence of incriminate drug exposure, and may also be found in association with a variety of other illnesses and conditions ranging from hepatitis C infection, connective tissue diseases, and neoplastic disorders to other systemic diseases (9, 10). Further complicating the nomenclature of cutaneous vasculitis is the fact that HV has also been used interchangeably with the histopathologic lesion of leukocytoclastic vasculitis (LCV) regardless of the clinical setting. Thus, over the years, the term HV has been synonymous with: 1) a form of drug-induced or allergic vasculitis; 2) a variety of primary and secondary vasculitides confined to the skin; and 3) the histopathology of any disease associated with LCV.

Despite the best efforts of the ACR and others to classify and define HV, it is this author’s opinion that the term should be discarded. Examination of the ACR methodology used to define HV in the 1980s reveals that the database of submitted cases was no doubt contaminated by several forms of secondary disease not appreciated at the time (1). For example, nearly one-fourth of the patients had detectable cryoglobulins, and thus many were likely infected with hepatitis C virus (HCV), a pathogen that had yet to be identified. Other conditions such as microscopic polyangiitis, a disorder not included in the classification scheme, likely accounted for many of the cases of cutaneous vasculitis with renal involvement. Thus, the very database from which this entity was extracted was heavily contaminated with other diseases, severely limiting its usefulness today. The Chapel Hill Consensus Conference criteria (3) suggests that cutaneous leukocytoclastic angiitis should be defined anatomically and should be limited to disease only involving the skin. This ignores the clinical significance of an identifiable precipitant and fails to accommodate those cases of cutaneous vasculitis not meeting the definition of HSP or MPA, but with some degree of visceral involvement. Clearly a more accommodating system for both diagnosis and classification is needed.

**The rheumatologist’s approach to cutaneous vasculitis**

I would like to propose a utilitarian system for disease definition that would also assist clinicians in formulating a practical clinical approach to patients with cutaneous vasculitis. Such a system could in addition be used for classification, but unfortunately would not be immune to many of the same criticisms leveled at other classification schemes due to our current lack of basic understanding of the pathogenesis and etiologies of the disorders described.

When confronting a patient with cutaneous leukocytoclastic vasculitis, the rheumatologist should start with basically the same differential diagnosis as the dermatologist (5). I would like to propose that these patients be classified descriptively based upon two variables: 1) etiology and 2) disease activity. The potential etiologies of cutaneous leukocytoclastic angiitis are shown in Table I. The similarity of this table to Dr. Callen’s is obvious, but differs by including HSP and recognizing that an etiologic agent or underlying condition may not always be identified. This proposed working system also includes an assessment of vasculitis activity in all involved organs (not limited to skin). Such a measurement would allow one to establish a record of the clinical pattern of target organ involvement, enabling the comparison of patients within etiologic categories and providing a guide for monitoring therapy when more than skin is involved. A number of currently available vasculitis activity instruments could easily be adapted for such use (11). Such a scheme should allow the identification and categorization of most, if not all, patients presenting with cutaneous vasculitis and provide a practical basis for clinical assessment, including defi-

### Table I. A working approach to cutaneous vasculitis.

<table>
<thead>
<tr>
<th>Inciting agent</th>
<th>Supporting evidence</th>
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<tbody>
<tr>
<td>1. Exogenous antigen (drug, other)</td>
<td>Exposure to a suspicious drug or environmental agent in a reasonable chronology for a hypersensitivity reaction</td>
</tr>
<tr>
<td>2. Infection</td>
<td>Multiple agents including bacteria and blood-born viruses (especially HCV, HBV, HIV, and others)</td>
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<tr>
<td>3. Henoch-Schönlein purpura</td>
<td>In children, the fulfillment of ACR () criteria or modified criteria (); in adults, pathologic evidence of IgA deposition in a target organ</td>
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<tr>
<td>3. Malignancy</td>
<td>Lymphoma most likely, occasionially encountered in association with myeloproliferative disorders and other cancers</td>
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<td>4. Paraprotein associated</td>
<td>Cryoglobulins present in significant concentrations with or without HCV infection</td>
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<tr>
<td>5. Connective tissue disease</td>
<td>Documented connective tissue disease, especially Sjögren’s syndrome, SLE, or RA</td>
</tr>
<tr>
<td>6. Systemic necrotozing vasculitis</td>
<td>In particular, ANCA-associated syndromes</td>
</tr>
<tr>
<td>7. Idiopathic</td>
<td>Unassociated with any of the above</td>
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| Activity                            | Reflects vasculitis activity in multiple organs, including the skin, determined by standardized or modified activity indices such as the BVAS or another appropriate instrument (11). |

HCV: hepatitis C virus; HBV: hepatitis B virus; HIV: human immunodeficiency virus.
ition of the prognosis and treatment. Clearly the clinician’s approach to those cases of cutaneous vasculitis associated with definable and, at times, quite treatable etiologies (i.e. drug exposure, infection) is radically different from those without. In addition this system would provide a basis to stratify patients for therapeutic trials and for the accommodation of new etiologic and pathophysiologic information as it becomes available.

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References