Cutaneous Vasculitis — A Dynamic Process Posing Diagnostic Challenge

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Abstract
Aim: To characterize the clinicopathologic features and to assess the therapeutic outcome in cutaneous vasculitis.

Material and Methods: Fifty biopsy proven cases of cutaneous vasculitis seen between January 1998 and July 1999 were studied.

Results: The commonest presentation was palpable purpura. The site most commonly affected was the extremity, irrespective of the age (adults - 40 and children - 10) and sex. The histopathologic picture ranged from an acute to chronic process, which besides the classic picture included bullous presentation, granulomatous histology and nonspecific features. Clinical correlation and investigations including direct immunofluorescence (DIF) were required to differentiate primary from secondary vasculitis (SLE - 4, dermatomyositis -2, rheumatoid arthritis -1, HIV -1, septicaemia -1 and drug reaction 2). DIF was diagnostic in 13 out of 21 cases providing evidence of an immune-mediated pathogenesis. Drugs used in the treatment included dapsone, colchicine, pentoxyphiline and steroids.

Conclusions: The clinical picture and outcome of primary cutaneous vasculitis were benign while the prognosis of secondary vasculitis depended on the primary disease, irrespective of the histopathological picture.

INTRODUCTION
Cutaneous vasculitis has protean manifestations. It may occur as an isolated process or as a manifestation of a systemic disorder. The cutaneous presentations of vasculitis are diverse ranging from maculopapular rashes to gangrene. The acute histopathological picture may progress rapidly, within as short as 48 hours, to a chronic picture. The clinical and pathological manifestations of vasculitis are not specific for a particular category of vasculitis, and overlapping features occur between different categories. Conversely, a single aetiological agent can give rise to varied expressions. Therefore to reach an aetiological diagnosis of vasculitis, clinical and pathological features need to be correlated and supplemented by other laboratory investigations. The present study was done to elucidate the clinicopathological features of patients with cutaneous vasculitis and to assess the therapeutic outcome.

MATERIAL AND METHODS
Fifty cases of biopsy proven cutaneous vasculitis that presented at St John’s Medical College Hospital from January 1998 to July 1999 were retrospectively analyzed.

The cases were accessed based on histopathology reports. The pathological diagnosis in each case was confirmed by review of haematoxylin and eosin stained sections. Additional special stains such as periodic acid schiff and Ziehl Nielsen stains were used in selected cases to confirm the diagnosis. Direct immunofluorescence was performed using fluorescein-labeled antibodies to IgG, IgM, IgA and C3. The identification of immune complex deposits in the vessel wall was considered diagnostic of immune-mediated vasculitis. Clinical details were obtained from the case records and from the treating clinician.

Other laboratory investigations carried out depended on the individual cases. These included total blood count, erythrocyte sedimentation rate, complete urine analysis, blood culture and x-ray-chest. Special tests like VDRL, Elisa for HIV, antibodies to CMV, antistreptolysin O titer, ANA, anti-ds DNA, ANCA (by immunofluorescence method), rheumatoid factor and cryoglobulins were done in appropriate cases. Levels of creatine kinase, lactic dehydrogenase, serum...
glutamic oxaloacetate transaminase and serum glutamic pyruvate transaminase were estimated in suspected cases of dermatomyositis.

**RESULTS**

**Clinical profile**

There were 40 adults (18 males; 22 females) and 10 children (age ≤ 14). The age range was from 9 months to 75 years with the maximum incidence between 30 and 40 years.

A wide spectrum of lesions was encountered ranging from a single type to a combination of two or more types of lesions like palpable purpura with erythematous rash (Fig. 1). The most common presentation was palpable purpura (25/50). The types of cutaneous presentations with aetiologic details are shown in Table 1. The most common site of affection was the lower limbs (n=19). The other sites affected were the upper limbs, trunk and face in that order of frequency, either alone or in combination. The duration of the lesions at the time of presentation ranged from less than a week to six months or recurrent lesions over a period of one to two years. Acute disease was defined in terms of short presentation (less than three months) and chronic disease when duration was longer than 3 months.5

In this series 78% (n=39) were of primary vasculitis while 22% (11 cases) were secondary vasculitis. The lesions in five cases of secondary vasculitis (SLE-2, dermatomyositis -2, HIV-1) were chronic, exceeding three months of occurring as recurrent crops. Three cases of Henoch Schonlein purpura presented with recurrent palpable purpura, over a period of six months, with joint pain, abdominal pain and renal involvement. The types of cutaneous presentations with aetiologic details are shown in Table 1. A 9-month-old child was found to be HIV positive by ELISA, in addition to IgA positivity for CMV infection. Blood culture in one case revealed Gram-negative septicemia. The details of systemic manifestations are shown in Table 2.

**Histopathology** : The different histological features in these cases included leucocytoclastic vasculitis, lymphocytic vasculitis, and granulomatous and bullous morphology besides nonspecific features (in 11 cases) that could only suggest the diagnosis of vasculitis. The microscopic features of each category are summarized in Table 3.

**Direct immunofluorescence** was done using fluorescein labelled antibodies to IgG, IgA, IgM and C3 in 21 cases. Immune complex deposits in the vessel walls were detected in 13 cases. Six cases with classical leucocytoclastic features

<table>
<thead>
<tr>
<th>Types of Lesions</th>
<th>No of cases</th>
<th>Primary</th>
<th>Secondary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Palpable purpura</td>
<td>26</td>
<td>22</td>
<td>4</td>
</tr>
<tr>
<td>Erythematous rash</td>
<td>15</td>
<td>7</td>
<td>8</td>
</tr>
<tr>
<td>Urticarial rash</td>
<td>9</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>Vesicles/bullae</td>
<td>5</td>
<td>4</td>
<td>1</td>
</tr>
<tr>
<td>Papules/plaques</td>
<td>4</td>
<td>-</td>
<td>4</td>
</tr>
<tr>
<td>Ulcers</td>
<td>3</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Gangrene</td>
<td>1</td>
<td>-</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 2 : Systemic manifestations associated with cutaneous vasculitis

<table>
<thead>
<tr>
<th>Involved organ or system/manifestations</th>
<th>No of cases and aetiology</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastrointestinal (abdominal pain, diarrhea)</td>
<td>8 (Henoch Schonlein purpura-3)</td>
</tr>
<tr>
<td>Musculoskeletal (arthralgia, myositis)</td>
<td>8 (Dermatomyositis -2, Henoch Schonlein purpura -3)</td>
</tr>
<tr>
<td>Renal</td>
<td>8 (SLE - 4, Henoch Schonlein purpura -3)</td>
</tr>
<tr>
<td>Lymphadenopathy</td>
<td>3 (Drug reaction -2, HIV - 1)</td>
</tr>
</tbody>
</table>

Fig. 1 :
The pathologic features of cutaneous vasculitis have been variously termed as allergic angiitis, allergic vasculitis, necrotising vasculitis or cutaneous systemic vasculitis. Cutaneous vasculitis may present as a primary disease or be a part of a systemic disorder such as SLE, dermatomyositis, septicemia and HIV infection.

The duration of vasculitis was acute in 78% , chronic in 16% and relapsing in 6% of cases. Chronic lesions were those associated with connective tissue disorders and HIV infection. In our series 78% (n=39) were of primary vasculitis while 11 cases were secondary vasculitis. Handel, Mackel et al., and Ekenstam have reported primary vasculitis in 54% to 61% than primary vasculitis. As the outcome of the primary vasculitis was favourable and the secondary vasculitis depended on the cause, it is essential to rule out a systemic cause, before labeling the lesion as primary vasculitis. Recurrent crops of cutaneous lesions occurred in cases of Henoch Schonlein purpura. In some of the cases the lesions initially presented as macules and later progressed to papules and plaques. The larger lesions presented as ecchymotic patches. The colour of the lesions ranged from red to purple as the extravasated red blood cells degenerated. Similar to the studies by Winklemann and Sais et al., in the present series, palpable purpura was the most common presentation.

Histopathology, although usually characteristic and confirmatory may be nonspecific. This depends on the severity of the lesion and the duration of the lesion at the time of biopsy. The severity may not always be indicative of extracutaneous involvement. An acute leucocytoclastic picture was seen even in lesions of long-standing duration, a lymphocytic infiltration in lesions of short duration and non-specific features such as just a perivascular inflammatory infiltrate in cases that were clinically diagnosed as vasculitis. The lesion must be biopsied ideally within 24 hours of onset of the lesion to demonstrate the characteristic features in this dynamic process. An acute histopathological picture can progress within as short a time as 48 hours to a chronic picture. It is also imperative, that the biopsy is deep enough so as not to miss medium sized vessels, as cutaneous vasculitis can be a feature of systemic vasculitis.

The results of the immunofluorescence study also indicates that best results are obtained on early lesions. Positivity was demonstrated only in 62% of the cases in which direct immunofluorescence was done. C3 positivity was demonstrated in majority of the cases (8/13). Other studies have reported similar findings. There is considerable data based on morphology, experimental work and immunological studies which suggest that cutaneous vasculitis as an immunocomplex disease.

**REFERENCES**

Announcement

AWARD SESSIONS
1. Dr. DP Basu Young Award in Cardiology
2. E Merck Award
3. Dr. JN Berry Memorial Award and
4. Dr. MJ Shah Memorial Award in Tropical Medicine

There will be four award sessions at the 2004 Annual Conference of API at Hyderabad. The rule and regulations of these awards are as under:

1. Papers that are accepted for presentation in the Award Session at the Annual Conference will be divided subject-wise into four groups:

   GROUP I  CARDIOLOGY  DP BASU YOUNG AWARD
   GROUP II CHEST DISEASES E MERCK AWARD
   GROUP III OTHER SPECIALITIES JN BERRY MEMORIAL AWARD
   GROUP IV TROPICAL MEDICINE MJ SHAH MEMORIAL AWARD

   The Award of Dr. JN Berry Memorial Award and E. Merck Award are given in alternate years in Group II and III papers. At the 2004 Annual Conference at Hyderabad, Dr. JN Berry Memorial Award will be for ‘Other Specialities’ and E Merck Award for ‘Chest Diseases’. Dr. DP Basu Young Ward will be for ‘Cardiology’ and Dr. M. J. Shah Memorial Award for ‘Tropical Medicine’.

2. The competitor must be the first author of the paper submitted for presentation at the API sessions of the Annual Conference. A testimonial must be submitted from the Head of the institution that the major work has been done by the competitor. Papers which are previously presented or published will not be considered. The competitor should also give a written pledge stating that the work has not been presented or published before. He should be a member of API.

3. Dr. JN Berry Memorial and DP Basu Young Awards are worth Rs. 1000/- each. E Merck Award Rs. 2000/- and Dr. MJ Shah Memorial Award is worth Rs. 2500/-.

4. The upper age list of the competitor is 40 years.

5. The decision will be taken by a panel of judges appointed by the Governing Body of API.

6. The candidate must apply for the award and full manuscript of the paper will have to be submitted. The paper will be presented in separate award session.

7. Eight copies of full manuscript will have to be submitted to Dr. (Maj. Gen.) S. Venkataraman, President - Elect and Chairman Scientific Committee, APICON 2004, Flat No.137, Air Force & Naval Officers Enclave, Plot No.11, Sector - 7, Papan Kalan, Dwarka, New Delhi - 110 045 of API by 31st July, 2003. One copy of the paper should be sent to Dr. Sandhya Kamath, Hon. General Secretary of API at Mumbai.

8. The decision of the panel judges will be final and binding to all concerned.

PRESTIGIOUS AWARDS OF API
1. GIFTED TEACHER (2003)
2. DISTINGUISHED MEMBER (2003)

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Dr. Sandhya Kamath,
Hon. General Secretary, API