Review Article

Cutaneous vasculitis

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Abstract

Vasculitides constitute a heterogeneous group of inflammatory disorders involving walls of blood vessels of integument and viscera. Depending on the size of blood vessels affected and organs involved, different subsets can vary in clinical presentation, histopathology, laboratory markers, treatment and prognosis. The present review focuses on recapitulating the vasculitides involving skin in a tabulated form.

Key words

Cutaneous vasculitis, classification, clinical presentations, treatment, diagnosis.

Introduction

Vasculitis is inflammation of blood vessels with a wide range of clinical and histological presentations. Its severity may range from self-limited to life threatening. The subject has been discussed in varying details as regards its classification, etiology, clinical presentations, histopathology, treatment and prognosis. Size of the vessels affected which is considered the most important parameter as regards various classifications of vasculitis, forms the basis of this tabulated version of vasculitis. Some of the vasculitides which at different periods of time have been included and excluded from true vasculitis because of one reason or the other have also been discussed here.
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<th>Treatment options</th>
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<tr>
<td>Predominantly small vessel</td>
<td>Usually a single crop of asymptomatic purpura, papules, vesicles, and urticarial lesions on dependent areas. 10% are chronic.</td>
<td>Endothelial swelling</td>
<td>IgM and C3 perivascular deposits in superficial dermal papillary vessels.</td>
<td>For diagnosis: Detailed history, thorough examination, skin biopsy. For association: Blood and urine examination and culture. HBV, HCV, HIV serology, connective tissue profile, lymph node, liver, and bone marrow biopsies.</td>
<td>Mild cases: NSAIDs, antihistamines, colchicine. In recurrent or resistant cases: Dapsone, azathioprine, methotrexate, cyclosporin, cyclophosphamide.</td>
<td>90% have single episode, 10% chronic (arthralgia, absence of fever, cryoglobulinemia). 90% have single episode, 10% chronic (arthralgia, absence of fever, cryoglobulinemia).</td>
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<tr>
<td>Cutaneous small vessel vasculitis (CSVV)</td>
<td></td>
<td>Fibrinoid necrosis of vessel walls</td>
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<tr>
<td>Cutaneous small vessel vasculitis (CSVV)</td>
<td></td>
<td>Extravasation of RBCs</td>
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<tr>
<td>Cutaneous small vessel vasculitis (CSVV)</td>
<td></td>
<td>Leucocytoclasia</td>
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Table 1 [1-44]
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<tr>
<th>Classification (Based on vessel size)</th>
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<th>Histopathology immunofluorescence</th>
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<th>Prognosis and follow up</th>
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<tbody>
<tr>
<td>Cryoglobulinemic vasculitis (CV)</td>
<td><strong>Cutaneous (15%)</strong>&lt;br&gt;Common&lt;br&gt;Purpura&lt;br&gt;Ecchymosis&lt;br&gt;erythematous papules&lt;br&gt;dermal nodules&lt;br&gt;Raynaud’s phenomenon</td>
<td><strong>Histopathology</strong>&lt;br&gt;Leukocytoclastic vasculitis</td>
<td><strong>For diagnosis</strong>&lt;br&gt;Same as for CSVV circulating cryoglobulin levels, &amp; serum Complement profile.</td>
<td><strong>For</strong>&lt;br&gt;HCV-associated disease&lt;br&gt;Ribavirin with or without alpha interferon</td>
<td>Treatment of underlying disorder is the key to recovery. However, with most treatment higher cryoglobulin levels may persist even after resolution of symptoms.</td>
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<td><strong>Uncommon</strong>&lt;br&gt;Urticaria, Livedo reticularis&lt;br&gt;Bullous lesions&lt;br&gt;ulcerations</td>
<td><strong>Immunofluorescence</strong>&lt;br&gt;Deposition of IgM and IgG complexes in the vessel wall.</td>
<td><strong>For extent of disease</strong>&lt;br&gt;Renal function tests.</td>
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<td><strong>Systemic</strong>&lt;br&gt;Arthralgias, arthritis and weakness&lt;br&gt;Peripheral neuropathy&lt;br&gt;Nephritis or nephritic syndrome</td>
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<tr>
<td><strong>Urticarial vasculitis.</strong>&lt;br&gt;Normocomplementemic (NUV) and hypocomplementemic (HUV)</td>
<td><strong>Cutaneous</strong>&lt;br&gt;Urticarial lesions lasting more than 24 hours with purpura, Post inflammatory pigmentation and burning.</td>
<td><strong>Histopathology</strong>&lt;br&gt;Leucocytoclastic vasculitis. HUV has more interstitial neutrophils than eosinophils as in NUV.</td>
<td><strong>For diagnosis</strong>&lt;br&gt;Lesions lasting more than 24 hours, pain rather than itch and presence of purpura. Complement levels(C3, C4), ANA. Urinalysis for hematuria.</td>
<td>Antihistamines&lt;br&gt;NSAIDS&lt;br&gt;Corticosteroids&lt;br&gt;Colchicines&lt;br&gt;Hydroxychloroquine&lt;br&gt;Dapsone alone or with pentoxiphylline, Mycophenolate mofetil.</td>
<td>Unpredictable course. Average duration 3 years.</td>
</tr>
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<td><strong>Systemic</strong>&lt;br&gt;Eye symptoms (iritis, uveitis, episcleritis)&lt;br&gt;Angioedema&lt;br&gt;Obstructive airway disease</td>
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<td><strong>Henoch-Schonlein Purpura (HSP)</strong></td>
<td><strong>Cutaneous</strong>&lt;br&gt;Symmetrical purpura</td>
<td><strong>Histopathology</strong>&lt;br&gt;Leucocytoclastic vasculitis</td>
<td><strong>For diagnosis</strong>&lt;br&gt;Same as CSVV Evidence of streptococcal infection Circulating IgA complexes</td>
<td>Corticosteroids&lt;br&gt;Dapsone&lt;br&gt;IVIG&lt;br&gt;Factor VIII Replacement&lt;br&gt;Ranitidine.</td>
<td>Self-limited. Mild relapses in 40%</td>
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Table 2 [45-54]

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<thead>
<tr>
<th>Classification (Based on vessel size)</th>
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<th>Histopathology/Immunofluorescence</th>
<th>Work up</th>
<th>Treatment options</th>
<th>Prognosis and follow-up</th>
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<tbody>
<tr>
<td>Predominantly medium-sized vessel vasculitis</td>
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<tr>
<td>Polyarteritis nodosa (PAN)</td>
<td>Cutaneous (20-50%)</td>
<td>Necrotizing obliterative arteritis</td>
<td>For diagnosis</td>
<td>NSAIDS, aspirin,</td>
<td>Outcome favourable,有时候 regressing spontaneously but high recurrence rate with prolonged course.</td>
</tr>
<tr>
<td></td>
<td>Systemic</td>
<td>For extent of disease</td>
<td>Thorough examination</td>
<td>Renal biopsy and angiography p-ANCA in 20%</td>
<td>Ribavirin with PEX in HBV associated disease.</td>
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<td>Weight loss, Arthralgias, Malaise, Abdominal pain, Mononeuritis multiplex, hypertension, Orchitis and Congestive cardiac failure</td>
<td>Muscle and sural nerve biopsies</td>
<td>Skin biopsy</td>
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</table>
### Table 3 [55-60]

<table>
<thead>
<tr>
<th>Classification (Based on vessel size)</th>
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<th>Histopathology</th>
<th>Work up</th>
<th>Treatment options</th>
<th>Prognosis and follow-up</th>
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</thead>
<tbody>
<tr>
<td><strong>Predominantly small and medium sized vessel vasculitis</strong></td>
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<tr>
<td>Microscopic polyangiitis (MPA)</td>
<td><strong>Cutaneous</strong> Palpable purpura</td>
<td><strong>Histopathology</strong> Segmental vascular necrosis, Leucocytoclasia.</td>
<td>Blood picture for leukocytosis, anemia, and ESR C reactive protein Urinalysis for RBCs, cast, and protein. p-ANCA more than c-ANCA, RF. Chest radiography for pulmonary infiltrates. Renal biopsy</td>
<td><strong>Limited disease,</strong> Corticosteroids. <strong>Renal or pulmonary disease</strong> Pulse steroids PEX Cyclophosphamide</td>
<td>Frequent relapses. Poor prognostic markers are: Increasing age Raised cretonne levels, Pulmonary hemorrhage c-ANCA associated disease <strong>Follow-up</strong> ESR Creatinine levels Chest x-rays.</td>
</tr>
<tr>
<td><strong>Systemic</strong> Constitutional symptoms, Necrotizing GN (79-90%), Pulmonary hemorrhage (12-29%)</td>
<td><strong>Immunofluorescence</strong> Few or no immune deposits</td>
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### Classification (Based on vessel size)

<table>
<thead>
<tr>
<th>Classification (WG)</th>
<th>Clinical features</th>
<th>Histopathology</th>
<th>Work up</th>
<th>Treatment options</th>
<th>Prognosis and follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Cutaneous</strong> (46-66%). Palpable purpura Oral ulcers Papulonecrotic lesions Subcutaneous nodules Ulcers.</td>
<td><strong>Histopathology</strong> Perivascular leucocytoclastic and/or granulomatous infiltrate</td>
<td>Same as for MPA. e-ANCA more than p-ANCA.</td>
<td><strong>Limited disease</strong> Corticosteroids. Remission induction, Corticosteroids, Cyclophosphamide Methotrexate alone or in combination</td>
<td><strong>Remission maintenance</strong> Cyclophosphamide PEX Methotrexate Azathioprine Sulfamethoxazole-trimethprim.</td>
<td>Same as for MPA.</td>
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**Systemic**
Upper and lower respiratory tract sympotms (60-80%) Renal disease(18%) Conjunctivitis Scleritis Uveitis

**Refractory disease**
Antithymocyte globulin Anti-CD4 and antiCD52 monoclonal antibodies
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<tr>
<td>Churg-Strauss syndrome (CSS)</td>
<td><strong>Cutaneous</strong> (40-70%) Palpable purpura Subcutaneous nodules Urticaria Livedo reticularis Papulonecrotic lesions. <strong>Systemic</strong> Allergic rhinitis, Nasal polyps, Asthma, Pneumonitis, Gastroenteritis, Necrotizing GN, Mononeuritis multiplex, Granulomatous myocarditis</td>
<td>Eosinophilic infiltrate of tissue, Formation of extra vascular granulomas of visceral and cutaneous tissue, Necrotizing vasculitis of arteries and veins.</td>
<td>Same as for MPA Eosinophilia, Raised IgE levels. P-ANCA more than C-ANCA.</td>
<td>Same as for MPA.</td>
<td>Same as for MPA.</td>
</tr>
<tr>
<td>Drug-induced</td>
<td><strong>Cutaneous</strong> Acral purpuric plaques and nodules, Digital gangrene. <strong>Systemic</strong> Glomerulonephritis Pulmonary hemorrhage.</td>
<td>Lymphocytic vasculitis, Little leucocytoclasia, tissue eosinophilia.</td>
<td>Drug history Eosinophilia Normal complement levels ANCA may be positive.</td>
<td>Withdrawal of offending drug. Corticosteroids, Immunosuppressive agents.</td>
<td>Skin lesions heal by stopping the offending drug. <strong>Follow-up</strong> Renal function Urinalysis</td>
</tr>
<tr>
<td>Classification (Based on vessel size)</td>
<td>Clinical features</td>
<td>Histopathology immunofluorescence</td>
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| **Vasculitis associated with connective tissue diseases** (SLE, RA, Sjogren’s syndrome) | **Cutaneous** Palpable purpura, petechiae, Digital infarcts, Ulcers, Nodules, Livedo reticularis, Urticaria or papulonecrotic lesions. Punched out ulcers represent systemic vasculitis.  
  
**Systemic** GI tract, heart, lungs, or kidneys in RA.  
Central and peripheral nervous system, GIT, lungs, heart, and genitourinary system in SLE.  
CNS, GIT, muscle, kidney, and parotid glands in Sjogren’s syndrome. | **Histopathology** Vascular changes are infrequent in SLE but hyaline changes and fibrinoid degeneration can occur in vascular walls.  
**Immunofluorescence** IgG and C3 deposits at basement membrane zone | Connective tissue profile Similar histopathological and IF studies. | **For mild cases** Corticosteroids Penicillamine.  
**For severe cases** Cyclophosphamide Azathioprine Chlorambucil MTX PEX. | Recurrences common Response to treatment good  
**Follow-up** Renal function test, Echocardiography, Pulmonary function test |
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<tr>
<th>Other disorders showing LCV</th>
<th>Clinical features</th>
<th>Histopathology immunofluorescence</th>
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<th>Treatment options</th>
<th>Prognosis and follow up</th>
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<tbody>
<tr>
<td>Erythema elevatum diutinum</td>
<td>Cutaneous</td>
<td>Grenz zone Leucocytoclastic vasculitis Eosinophils in upper and mid-dermis Older lesions show fibrosis and mixed infiltrate Cholesterol deposits in the intra and extracellular tissue</td>
<td>For diagnosis Detailed history Clinical examination Skin Biopsy</td>
<td>Dapsone Nicotinamide, High potency topical or intralesional steroids Other therapies used in CSVV</td>
<td>New crops may appear for 5-35 years</td>
</tr>
<tr>
<td></td>
<td>Systemic</td>
<td>None</td>
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<tr>
<td>Granuloma faciale</td>
<td>Cutaneous</td>
<td>Grenz zone, Leucocytoclastic vasculitis, Neutrophilic and eosinophilic infiltrate</td>
<td>Clinically typical lesion. Typical histopathology</td>
<td>Intralesional steroids, with or without cryosurgery Clofazamine Dapsone Surgery Laser</td>
<td>Recurrences are common Resistant to treatment</td>
</tr>
<tr>
<td></td>
<td>Systemic</td>
<td>None</td>
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### Table 5 Neutrophilic vascular reactions [62, 66-69]

<table>
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<tr>
<th>Clinical features</th>
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<tr>
<td>Pyoderma gangrenosum (PG)</td>
<td>Papular or pustular lesion with violaceous undermined edges, later ulcerating and healing with cribriform scar.</td>
<td>Central necrosis and ulceration of epidermis and dermis surrounded by an intense neutrophilic infiltrate No leucocytoclasia</td>
<td>Detailed history Physical examination, Skin biopsy for histopathology and culture for bacteria, mycobacteria, fungi and occasionally viruses</td>
<td>Mild cases Topical or intralesional steroids Hydrophilic occlusive dressings Tacrolimus etc.</td>
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<tr>
<td>Sweet’s syndrome</td>
<td>Constitutional symptoms Painful erythematous papules, plaques, nodules, Psuedovesicular, uustular lesions</td>
<td>Dense neutrophilic infiltrate in upper dermis, Neutrophil karyorrhexis, Leucocytoclasia.</td>
<td>For diagnosis Fever, typical skin lesions &amp; typical histopathology Neutrophilia</td>
<td>Excellent response to: Systemic steroids, Potassium iodide and Colchicine. Somewhat lesser response to: Dapsone Clofazamine Cyclosporin Indomethacin Etretinate Alpha interferon.</td>
</tr>
</tbody>
</table>

**For diagnosis**
- Fever, typical skin lesions & typical histopathology Neutrophilia

**Negative IF**
- Evidence of malignancy, respiratory or GI infections, connective tissue profile

**For associations**
- Evidence of malignancy, respiratory or GI infections, connective tissue profile
Cont...

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<tr>
<th>Neutrophilic vascular reactions</th>
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</thead>
</table>
| Nodular vasculitis              | Tender, dusky, often suppurative nodules or plaques on posterolateral legs of obese women with venous stasis | Leucocytoclastic vasculitis of subcutaneous tissue leading to necrotic reaction in subcutaneous tissue and deep dermis | **For diagnosis**
   Same as for CSVV
   Deep skin biopsy. | **Tuberculous patients**
   Antituberculosis treatment for a minimum of 9 months.
   Tuberculosis not present
   Supportive measures
   Systemic steroids
   Potassium iodide or any treatment mentioned for CSVV | Same as PG |
| Bowel associated dermatitis arthritis syndrome | Constitutional symptoms followed by crops of macular, papular or pustular lesions, and oral ulcers | Same as Sweet’s syndrome | Same as for CSVV
   Barium studies and endoscopy | **For bowel pathology**
   Surgical correction | Same as PG |
| **For others**                  |                   |                                   |        |                   |                        |
|                                 |                   |                                   |        |                   |                        |

ANCA, antineutrophilic cytoplasmic antibodies; CSVV, cutaneous small vessel vasculitis; CV, cryoglobulinemic vasculitis; HSP, Henoch-Schönlein purpura; HUV, hypocomplementemic urticarial vasculitis; IF, immunofluorescence. IVIG, intravenous immunoglobulin; MPA, microscopic polyangiitis; MTX, methotrexate; NUV, normocomplementemic vasculitis; PEX, plasma exchange; PG, pyoderma gangrenosum; WG, Wegener’s granulomatosis
References

cutaneous vasculitis


52. Bajema IM, Hagen EC. Evolving concepts about the role of antineutrophil cytoplasm autoantibodies in systemic


**Erratum**

In the article “Histopathological spectrum of cutaneous leishmaniasis in North West Frontier Province” published in the October-December, 2004 issue of JPAD (*J Pak Assoc Dermatol* 2004; **14**: 209-14), the name of one of authors was misprinted as Shagufta Nazir. Her correct name is Shagufta Nasir.