**ABSTRACT:**

Vasculitides are group of disorders characterized by immunoinflammatory injury to vessel wall leading to aneurysm, bleeding, stenosis, occlusion, thrombosis, embolism and ischemia. Clinical manifestations are protean depending upon size, site and type of vessel involved in different organs and upon the underlying disease. Severity of vasculitis varies from benign self limiting vasculitis to severe life threatening systemic vasculitis. Triggering factors have to be recognized and eliminated especially in secondary vasculitides. Primary vasculitides have to be treated with Corticosteroids (CS) and other immunosuppressive drugs. Pseudovasculitis should be excluded as these entities have to be treated according to their etiologies.

**INTRODUCTION:**

Vasculitides is a group of heterogeneous diseases of diverse etiologies, in which immunologically mediated inflammatory reaction of the blood vessel wall leads to vessel wall damage and weakening (aneurysm, rupture) or obstruction of lumen, leading to infarction of tissue. Ischemic and injured tissue can also induce inflammation which may lead to granuloma formation or eosinophil-rich inflammation. Triggers/antigens and clinical manifestations are diverse.

**CLASSIFICATION:**

Frequently used classification system separates the vasculitides based on whether the process is primary (i.e. of unknown cause) or secondary to some other condition.

**Primary Vasculitides:** (Table 1 and Fig 1)

**SECONDARY VASCULITIDES:**

Miscellaneous small vessel vasculitides:
- Secondary to connective tissue diseases.
- Inflammatory bowel disease.

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**Table 1** Classification of Primary Vasculitis according to the size of blood vessel involved.

| Predominantly Large vessel vasculitides | Takayasu's arteritis (TAK) (G*)  
|                                         | Giant cell arteritis (temporal arteritis) (GCA) (G*)  
|                                         | Cogan's syndrome (G*)  
|                                         | Behcet's disease (BD) (G*)  
| Predominantly Medium vessel vasculitides | Polyarteritis nodosa (PAN)  
|                                         | Cutaneous PAN  
|                                         | Buergers disease  
|                                        | Kawasaki disease  
| Predominantly Small vessel vasculitides | Immune complex mediated:  
|                                        | Goodpasture's disease (antiglomerular basement membrane disease)  
|                                        | Cutaneous leukocytoclastic angitis (hypersensitivity vasculitis) (CLA)  
|                                        | Henoch–Schonlein purpura (HSP)  
|                                        | Hypocomplementic urticarial vasculitis (HU)  
|                                        | Essential cryoglobulinemia (ECG) (‡)  
|                                        | Erythema elevatum diutinum  
|                                        | Pauci-immune ANCA–Associated disorders (AAV) (‡)  
|                                        | Wegener's granulomatosis (WG) (‡) (G*)  
|                                        | Microscopic polyangiitis (MPA) (‡) (G*)  
|                                        | Churg-Stauss syndrome (CSS) (‡) (G*)  
|                                        | Renal limited vasculitis  

(*) May involve small, medium, and large blood vessels  
(‡) Not all forms of these disorders are always associated with ANCA  
(‡) Frequent overlap of small and medium blood vessel involvement  
(G*) Granulomatous
Approach to systemic Vasculitis

**Table 2 : Typical manifestations of large, medium, and small vessel involvement by vasculitis:**

<table>
<thead>
<tr>
<th>Large</th>
<th>Medium</th>
<th>Small</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Limb claudication</td>
<td>• Red ,blue subcutaneous nodules (Panniculitis)</td>
<td>• Purpura</td>
</tr>
<tr>
<td>• Asymmetric blood pressure</td>
<td>• Vesicobullous lesions</td>
<td></td>
</tr>
<tr>
<td>• Absence of pulses</td>
<td>• Urticaria</td>
<td></td>
</tr>
<tr>
<td>• Bruits</td>
<td>• Livedo reticularis</td>
<td></td>
</tr>
<tr>
<td>• Aortic dilatation</td>
<td>• Digital gangrene</td>
<td></td>
</tr>
<tr>
<td>• Renovascular Hypertension</td>
<td>• Mononeuritis multiplex</td>
<td>• Alveolar hemorrhage</td>
</tr>
<tr>
<td></td>
<td>• Microaneurysm</td>
<td>• Cutaneous extravascular necrotizing granulomas</td>
</tr>
<tr>
<td></td>
<td>• Reno-vascular hypertension</td>
<td>• Splinter hemorrhages</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Uveitis, episcleritis, scleritis</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Mucosal ulcers in bowel</td>
</tr>
</tbody>
</table>

Constitutional symptoms like fever, weight loss, malaise, arthralgia or arthritis are common to all.

“Large” generally denotes the aorta and its major branches (e.g. subclavian and carotid arteries).

“Medium” refers to vessels that are smaller than the major aortic branches, yet large enough to contain four elements intima, continuous internal elastic lamina, muscular media and an adventitia.

“Small” vessels include capillaries, postcapillary venules, and arterioles. Such vessels are typically less than 500 μ in outer diameter. Since glomeruli have capillaries, small vessel vasculitis is associated with glomerulonephritis. Capillaries in lungs may rupture leading to alveolar haemorrhage.

**Table 3 : Triggers Vasculitis**

<table>
<thead>
<tr>
<th>Triggers</th>
<th>Vasculitis</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>PAN</td>
</tr>
<tr>
<td>Staph. Aureus</td>
<td>WG</td>
</tr>
<tr>
<td>Gr. A Streptococci &amp; Mycoplasma</td>
<td>HSP</td>
</tr>
<tr>
<td>Hepatitis C</td>
<td>Essential Cryoglobulinemia (ECG)</td>
</tr>
<tr>
<td>Drugs</td>
<td>Cutaneous leucocytoclastic vasculitis (CLA)</td>
</tr>
</tbody>
</table>

- Paraneoplastic – Lung cancer, Lympho and myeloproliferative disorders.
- Drug induced vasculitis: Allopurinol, phenytoin, NSAIDS, antibiotics, methotrexate, and diuretics. (ANCA associated and others)
- Vaccination: Pneumococcal, influenza or hepatitis B vaccine
- Post organ transplant vasculitis
- Food items, additives and smoking

**Clinical presentation:** (Table 2, 3, 4, 5)

**Table 4 : Conditions that mimic vasculitis (Pseudovasculitis)**

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sepsis</td>
<td>Sarcoïdosis</td>
</tr>
<tr>
<td>Endocarditis, Atrial myxoma</td>
<td>Amyloidosis</td>
</tr>
<tr>
<td>Granulomatous infections (TB, Fungal)</td>
<td>Lymphoma</td>
</tr>
<tr>
<td>Hepatitis B, C, HIV, CMV infections</td>
<td>Pheochromocytoma</td>
</tr>
<tr>
<td>Lyme Disease</td>
<td>Hairy cell leukemia</td>
</tr>
<tr>
<td>Cholesterol Embolic syndrome</td>
<td>Myelodysplasia</td>
</tr>
<tr>
<td>Disseminated intravascular coagulation (DIC)</td>
<td>Metastatic solid tumors</td>
</tr>
<tr>
<td>Antiphospholipid antibody syndrome (APS)</td>
<td>Vasoreactive drugs (cocaine, ergot, amphetamine)</td>
</tr>
</tbody>
</table>

**OVERVIEW OF PRIMARY VASCULITIDES:**

**Large vessel vasculitis**

**Takayasu’s Arteritis (TAK) (Pulseless disease, aortic arch syndrome):** TAK is a granulomatous, chronic panarteritis of the aorta and its major branches as well as of pulmonary and coronary arteries that predominantly occurs in young women. Exuberant collateral circulation in response to the narrowing of major arteries makes the loss of digits or limbs from ischemia extremely rare. Three clinical phases are described. First phase consists of non-specific constitutional symptoms in which patient may present as unexplained fever. In second phase, patient has painful arteries and claudicating pains and other symptoms as described in Table 2. In third phase, systemic inflammation subsides leaving behind only the symptoms associated with occlusion of aorta and its branches because of fibrotic changes. TAK appears to be commoner in Asia than Europe or North America. Ascending aortitis and abdominal aorta and branches are frequently affected in Indian patients.

**Giant cell arteritis (GCA) (Temporal arteritis):**

It is granulomatous arteritis of aorta and its major branches with a predilection for the extracranial branches of the carotid artery and often involves the temporal artery. It is believed to be rare in our country as the demographic pattern is such that only 5% of our population is above 65 years of age. Main manifestations include headache and tenderness of the scalp. Polymyalgia rheumatica i.e. myalgia with severe stiffness of neck and shoulder girdle muscles, jaw claudication, visual loss, diplopia and transient ischemic attacks may be the presenting feature. Risk to develop thoracic and abdominal aortic aneurysms was reported to be higher by 17.3 and 2.4 times respectively 1).

**Behcet’s Disease (BD):**

BD my affect small, medium and large vessels in either
Table 5: Organ Involvement in Vasculitis

<table>
<thead>
<tr>
<th>Organ / System involvement</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Kidney</strong></td>
<td>Affered in most of vasculitis except PAN &amp; TAK. Glomerulonephritis (absent in classic PAN) - Renal failure. Hypertension. Renal infarction.</td>
</tr>
<tr>
<td><strong>Lungs</strong></td>
<td>Involved in WG, CSS, MPA. Alveolar haemorrhage characterized by hemoptysis, Anemia and bilateral evanescent lung opacities. Nodules with or without cavities. Infarction. Asthma (CSS).</td>
</tr>
<tr>
<td><strong>Cardiovascular</strong></td>
<td>Myocardial infarction. Ischemic cardiomyopathy – Congestive heart failure. Pulselessness.</td>
</tr>
<tr>
<td><strong>Abdomen</strong></td>
<td>Ischemic mucosal necrosis with hemetemesis and melena. Bowel infarction. Hepatic and pancreatic infarction.</td>
</tr>
<tr>
<td><strong>CNS</strong></td>
<td>Focal neurologic deficit. Altered mental state. Seizures.</td>
</tr>
<tr>
<td><strong>Nerves</strong></td>
<td>Mononeuropathies (Acute onset). Mononeuritis multiplex.</td>
</tr>
<tr>
<td><strong>Musculoskeletal</strong></td>
<td>Arthralgia, arthritis &amp; myalgia.</td>
</tr>
<tr>
<td><strong>Muscles</strong></td>
<td>Jaw claudication (GCA). Arm claudication (TA).</td>
</tr>
<tr>
<td><strong>Genitourinary</strong></td>
<td>Testicular pain (PAN), Ependymal pain.</td>
</tr>
<tr>
<td><strong>Ocular</strong></td>
<td>Scleritis, episcleritis, uveitis, proptosis.</td>
</tr>
<tr>
<td><strong>ENT</strong></td>
<td>Otitis, nasal obstruction or epistaxis.</td>
</tr>
</tbody>
</table>

the venous or the arterial circulation. Small vessel involvement leads to mucocutaneous lesions. Aneurysms in the pulmonary and systemic arterial systems and thromboses in deep venous, vena caval, portohepatic vein and cerebral sinus may occur.

Medium vessel vasculitides:

**Classic polyarteritis nodosa (C-PAN):**

C-PAN is characterized by necrotizing inflammation of predominantly medium sized vessels leading to aneurysm formation; a component of small vessel involvement may be seen. It is usually idiopathic but in a subset of patients (7-36%) it may be secondary to hepatitis B virus (HBV) infection. Constitutional symptoms, musculoskeletal symptoms, vasculitic involvement of nerves (80%) leading to mononeuritis multiplex – wrist or foot drop and neuralgic pains, skin (palpable purpura, subcutaneous nodules, skin infarcts with vasculitic ulcers, livedo reticularis, digital gangrene), non-glomerular vessels of kidney (renovascular hypertension), gastrointestinal tract (post prandial abdominal pain, hemetemesis, melena or acute abdomen, rarely cholecystitis and appendicitis) and rarely of heart (myocardial infarction, congestive heart failure) may be seen. Inflammatory arthritis of peripheral large and small joints may occur. Orchitis is a classic symptom found more commonly in PAN secondary to HBV. Features which distinguish it from MPA are complete absence of glomerulonephritis, renal impairment and involvement of lung.

**Kawasaki Disease (KD):** Occurs exclusively in children usually before 5 years of age. Because of striking mucocutaneous findings and lymphadenopathy, it is also known as “mucocutaneous lymph node syndrome”. Features of KD are high fever, cervical adenopathy, conjunctival congestion, buccal erythema, prominence of the tongue papilla (strawberry tongue), polymorphous truncal rash, brawny induration, erythema of palms and soles, and desquamation of skin from the fingertips occurring days to weeks into the illness. Panvasculitis of coronary arteries leads to aneurysm formation and thrombosis 1-4 weeks after fever, and myocardial infarction.

**Primary angiitis of Central Nervous System (PACNS):**

True vasculitis of the CNS is different from benign angiopathy of CNS and is characterized by headache, encephalopathy, and multifocal strokes that develop in a subacute fashion. Seizures, increased intracranial pressure or myelopathy may be seen. ESR is often normal; CSF may show elevated proteins and modest monocytes.

**Small vessel vasculitides:**

**Cutaneous leukocytoclastic angiitis (hypersensitivity vasculitis) (CLA):** CLA skin lesions are all of the same age indicating exposure to the noxious agents e.g. new drugs or infections. Rash occurs over lower extremities or buttocks and may be accompanied by burning or tingling sensations. A wide array of skin lesions occur like palpable purpura, papules, urticaria, angioedema, erythema multiforme, vesicles, pustules, nerosis and rarely ulcers. Most cases resolve in 1-4 weeks. Clinical and laboratory evidence of severe systemic inflammatory disease is usually absent though renal and GI involvement may rarely occur.

**Henoch –Schonlein purpura (HSP):**

Commonest form of vasculitis in children. In adults it manifests incompletely and renal insufficiency may occur in 13% cases. Clinical manifestations are palpable purpura (100%), peripheral large joint arthritis (82%) and colicky abdominal pain (63%), GI bleed (33%) and nephritis (40%). In 50% patients upper respiratory tract infections may precede HSP. Hypersensitivity reactions to drugs, foods and insect bites have been implicated. It is benign self limiting disease, in only 2-5 % patients end stage renal disease may occur. Prognosis is generally good.

**Hypocomplementic urticarial vasculitis (HUV):**

HUV is characterized by urticarial rash which may have purpuric
component. HUV lasts more than 48 hours and associated burning or stinging sensation distinguishes it from chronic idiopathic urticaria and it resolves with postinflammatory hyperpigmentation. C3, C4, CH50 and Clq are low and should be repeated on 2 or 3 occasions over several months. HUV may be secondary to SLE, Sjogren syndrome, or represent HUV Syndrome which is a specific syndrome characterized by angioedema, moderate to severe COPD (50%), Uveitis (30%) and glomerulonephritis.

Cryoglobulinemic vasculitis (CGV):
Cryoglobulins are antibodies that precipitate from serum under conditions of cold and resolubilize on rewarming. C4, C3 levels are reduced in cryoglobulinemic vasculitis. HCV infection accounts for 80% of cases. Clinical triad consists of recurrent palpable purpura (100%), polyarthralgia (73%), and renal disease (55%).

ANCA associated Vasculitides (AAV):

Wegner’s granulomatosis:
WG is a granulomatous inflammatory disease involving the respiratory tract, and necrotizing vasculitis affecting small to medium-sized vessels. Classic WG involves the upper airways, lower airways and kidneys. Limited WG spares the kidney and accounts for 25% cases and features are nasal congestion, epistaxis, sinus pain, perforation of nasal septum, serous otitis media, oral ulcers, subglottic stenosis and saddle nose deformity. Lower airways i.e. bronchi and pulmonary parenchyma may be involved leading to dyspnoea, hemoptysis or wheezing. Asymptomatic nodules to fulminant alveolar hemorrhage may occur. Retro-orbital mass or inflammation (Pseudotumour) may be present. Inflammation of small vessels of kidney lead to glomerulonephritis which can lead to renal failure. Optic neuritis, uveitis, scleritis, conjunctivitis, ulcerative keratitis, conductive or sensorineural hearing loss, MNM and cranial neuropathies may be seen. Arthralgia or arthritis (60%), digital gangrene, palpable purpura, cutaneous nodules and ulcers may be seen. Patients are at increased risk for deep vein thrombosis and pulmonary emboli.

Microscopic Polyangiitis (MPA):
It is characterized by non-granulomatous necrotizing vasculitis with few or no immune deposits and involves small and sometimes medium-sized vessels. It has tropism for kidneys and lungs and is commonly implicated in pulmonary-renal syndrome. GN (79%), MNN (58%), fever (55%) and weight loss (73%), palpable purpura, ulcers around ankles are other manifestations. Pulmonary capillaritis may lead to hemoptysis because of diffuse alveolar hemorrhage (rare in C-PAN). Unlike WG, upper airway lesions are absent.

Churg-Strauss Syndrome (CSS):
It is a rare systemic small vessel vasculitis, characterized by hypereosinophilia, extravascular granuloma and with mean age of onset in 50s. Patients typically have a history of nasobronchial allergy and asthma. There are three overlapping phases, first phase consists of allergic rhinitis, asthma and nasal polyposis and may last for years. In second phase there is peripheral hyper eosinophilia (Eosinophils>10%, absolute eosinophil count >1500) without tissue eosinophilia. Third phase is characterized by features of vasculitis. Peripheral neuropathy and MNN is common and may occur in up to 75% of patients. Skin manifestations include palpable purpura and subcutaneous nodules. Myocarditis and heart failure is common especially in ANCA negative subgroup and leads to mortality in about 50% patients. Diarrhoea, GI bleeding, cholecystitis and bowel perforation may occur because of GI involvement. Migratory pulmonary infiltrates are seen on chest x-rays.

Clinical Approach:
Clinical presentation may be bizarre with involvement of various organs. When systemic vasculitis is suspected the first step is to exclude the mimics (Table 4). If primary vasculitis is clinically diagnosed then the disorder should be classified on the basis of size of vessels involved (Table 1 & 2). After determining the size of vessels involved, patient’s demographic characteristics (Age, sex, ethnicity, smoking status) should be look for. Systemic vasculitis usually presents in 2nd-5th decade, the exception being HSP and Kawasaki disease which are common in children. TAK occurs commonly in young females. Extent of organs involved must be assessed. Pattern of different organ system involvement may help in identifying the specific vasculitis syndrome. Establishing the diagnosis of vasculitis requires confirmation by laboratory tests viz serological tests, biopsy of an artery/organ and sometimes an angiogram may be required.

Laboratory work-up:
There may be normocytic, normochromic anemia, leucocytosis, thrombocytosis and high ESR and CRP. Eosinophilia may be seen in CSS, RA vasculitis and WG. Leucocytopenia may be seen in SLE, sepsis, aleukemic leukemia. Thrombocytopenia may be seen in SLE, DIC and APS.

Urine: Markers for renal vasculitis i.e. glomerulonephritis are haematuria associated with red cell casts and proteinuria on urinalysis. Classical PAN is not associated with active sediment.

Antineutrophilic cytoplasmic antibodies (ANCA) - C-ANCA [by immunofluorescent (IFA) method stains cytoplasm of neutrophil], with proteinase-3 specificity by ELISA is strongly suggestive of WG. While p-ANCA (perinuclear staining on IFA) with myeloperoxidase specificity are seen in MPA and in 50-70% patients of CSS. Atypical staining (A or X- ANCA) i.e. mixed pattern of fluorescence pattern and antibodies which are directed against lactoferrin and elastase of neutrophil show high association with drug induced vasculitis. ANCA should always be assessed if patient has pulmonary haemorrhage, systemic vasculitis, rapidly progressive glomerulonephritis, multiple leg nodules, chronic destructive disease of upper airways, long standing sinusitis or otitis, subglottic tracheal stenosis, MNN, other peripheral neuropathy or retro-orbital mass.

Serological tests for hepatitis B (PAN) and C (Cryoglobulinemia)
should be done if there is suspicion of these diseases.

ANA by IFA (SLE, Systemic sclerosis, Sjogren’s syndrome and mixed connective tissue disease) and anti-GBM antibody (Good-Pasture syndrome) may be done if there is clinical suspicion of these diseases.

Serum C3 and C4 are decreased in cryoglobulinemia, SLE and in immune complex vasculitis and is increased in infections.

Serum Proteins: In HSP IgA and in CSS IgE levels are increased. Complement levels are decreased in immune complex vasculitis. Cryoglobulins are present in CG vasculitis.

Renal, liver function tests should be done to know the extent of the disease.

X-ray paranasal sinuses – In WG mucosal thickening, fluid level or opacity may be seen.

X-ray chest – In WG, multiple, bilateral and chronic (> 1 month) fixed, solid nodules and cavities, while in CSS and MPA, diffuse and migratory non-cavitary infiltrates may be seen. ANCA associated vasculitides (AAV) may be complicated by intra-alveolar haemorrhage leading to extensive, evanescent bilateral lung infiltrates.

Computed tomography of lungs may show nodules, cavities/ granuloma in WG and infiltrates in CSS and MPA. Peripheral, bilateral ground-glass opacities/ alveolar hemorrhages may be seen in any of ANCA associated vasculitides.

Biopsy:

Biopsy is the gold standard for diagnosis of vasculitis provided it is obtained from involved and accessible site/organ as yield of blind biopsy is usually low. In cutaneous vasculitis, full thickness skin biopsy should be taken, if neuropathy is present then involved nerve by electroneurography should be the site of biopsy. In GCA, the changes are patchy, focal and 2-3 cm of temporal artery should be taken but false negative biopsies may still occur. In WG biopsies taken from nasal mucosa, upper air ways or lungs may demonstrate vasculitis, necrotizing inflammation and giant cell granuloma. In AAV syndromes, kidney biopsy with immunofluorescence studies shows absence or paucity of immunoglobulin (pauci-immune) deposits.

Angiography and other imaging modalities:

Angiography can demonstrate stenosis, post-stenotic dilatation, occlusion, aneurysm, dissection in large to medium sized vessels. In PAN multiple aneurysms of medium sized arteries of abdominal organs may be seen while in TAK, GCA, stenosis or complete occlusion of large arteries may be found. CT angiography of aorta and its branches may show narrowing or occlusion in TAK. In PACNS characteristic abnormality is 'string of beads' pattern produced by segmental arterial narrowing alternating with dilations.

Doppler ultrasound may demonstrate narrowing of vessel lumen non-invasively. In temporal arteritis, narrowing of lumen and associated periluminal halo may indicate oedema.

2D-Echocardiography may demonstrate aortic valve insufficiency, aortic aneurysms, coronary artery ectasia and myxoma etc.

**TREATMENT:**

**Large vessel Vasculitis:**

**Corticosteroids (CS):** Prednisolone 1mg/ kg / day for 6 weeks followed by 10-20% tapering every 2 weeks and maintenance dose (0.15mg/kg/d) for 2-4 years may be required. ESR and CRP are not reliable to monitor disease activity while IL-6 may be better marker for disease activity (9). In GCA, if there is impending visual loss, IV methyl prednisolone 500 – 1000 mg/d for 3-5 days should be given.

**Immunosuppressive drugs:**

Methotrexate (MTX) (15-25 mg/week), Azathioprine (AZA) (2mg/kg/day). Mycophenolate mofetil (1.5-2 g/day) may be added to low dose CS (0.25mg/kg/day) as steroid sparing agents.

**Medium vessel vasculitis:**

PAN: CS and Cyclophosphamide (CPm) either orally or intravenously are given. Since PAN is a monophasic illness, survival of patient is increased to 80% with CS and CPm. Patients of PAN who are positive for hepatitis B virus should be treated with interferon and Lamivudine and may be combined with plasmapheresis (to remove immune complexes) in refractory cases.

**Kawasaki Disease:** CS are contraindicated as coronary arteries may be weakened and thrombosed by the treatment with these agents. IV immunoglobulins 2g/kg as single dose may be given (70 g maximum). Low dose aspirin may be used if there is thrombocytosis as prophylactic agent.

**Small vessel vasculitis (WG,CSS,MPA):**

Induction phase: CS (1mg/kg/d) and CPm (oral 2 mg/kg/d or IV 750-1000 mg/ m2 every 4 wks) are preferred initially in patients with active severe life threatening WG for 6 months (9). Remission rates were similar for both daily and intermittent regimes (9). IV CPm pulses are associated with less adverse effects while oral CPm is associated with higher dosage and significant increase in infection risk.

**Maintenance phase:** MTX (25mg/ wk) or AZA (2 mg/kg/d) may replace CPm and is continued for 24 months and in patients who remain ANCA positive, immunosuppression should be continued up to 5 years though in one third patients ANCA levels may not correlate with activity of WG.

Patients intolerant of CPm may be given mycophenolate mofetil or leflunomide (upto 40mg/d), the latter has been used to maintain remission in an open label trial (10). In severe life threatening renal failure and pulmonary haemorrhage, plasma exchanges may be combined with CS and CPm (10).
Approach to systemic Vasculitis

Limited WG: Methotrexate (15-25 mg / wk) is preferred over CPM. Trimethoprim and sulfamethoxazol is used in limited WG of the upper airways to maintain remission and nasal mupirocin may eradicate staphylococcus aureus infection which is a trigger for relapse of WG.

CSS was associated with good outcome when CS and CPM were combined with synchronized cycles of plasmapheresis and IV immunoglobulin (12). For CSS, modulation of eosinophils with interferon–α or blockade of Il5 is being investigated.

Other small vessel vasculitis

HSP: NSAIDs for symptomatic treatment (Palpable purpura) or antihistamine for urticaria may suffice. CS and immunosuppressants for persistent renal involvement may be given.

LCA: Dapsone for mild disease while for severe systemic or recurring disease (e.g. persistent nephrotic syndrome, rapidly progressive GN, severe abdominal pain or bleeding) CS with AZA or CPM may be used to inhibit immune mediated inflammation.

CGV: For hyperviscosity plasmapheresis and for underlying malignancy chemotherapy may be required. Ribavirin (1000 -1200mg/d) and interferon –α (1 μg/kg /week) can be used in hepatitis C associated CG and may lead to viral eradication and correction of CG. For severe disease CS and CPM may be needed.

BD: Colchicine (1.5 -2 mg / d), thalidomide (100mg /d) for mild orogenital ulcers is useful. For severe disease in any organ system CS, CPM, CsA, Chlorambucil, methotrexate, interferon alfa may be given.

Table 6: Current role of biological agents in vasculitis:

<table>
<thead>
<tr>
<th>Agent</th>
<th>Indication</th>
</tr>
</thead>
<tbody>
<tr>
<td>T-cell depletion with:</td>
<td></td>
</tr>
<tr>
<td>Anti-thymocyte globulin</td>
<td>Consider in refractory AAV (little data in other vasculitides)</td>
</tr>
<tr>
<td>Anti-CD52 (CAMPATH.alemtuzumab)</td>
<td>Consider in refractory AAV (little data in other vasculitides)</td>
</tr>
<tr>
<td>B-cell depletion with:</td>
<td></td>
</tr>
<tr>
<td>Rituximab (22)</td>
<td>Consider in refractory AAV (little data in other vasculitides)</td>
</tr>
<tr>
<td>Tumour necrosis factor blockade with:</td>
<td></td>
</tr>
<tr>
<td>Etanercept</td>
<td>Consider in refractory AAV, GCA and TA</td>
</tr>
<tr>
<td>Infliximab</td>
<td>Potential alternative to infliximab</td>
</tr>
<tr>
<td>Adalimumab</td>
<td>Potential alternative to infliximab</td>
</tr>
<tr>
<td>Deoxyspergualin (23)</td>
<td>Promising results in refractory AAV</td>
</tr>
</tbody>
</table>

AAV- ANCA associated vasculitis

Limited WG: Methotrexate (15-25 mg / wk) is preferred over CPM. Trimethoprim and sulfamethoxazol is used in limited WG of the upper airways to maintain remission and nasal mupirocin may eradicate staphylococcus aureus infection which is a trigger for relapse of WG.

CSS was associated with good outcome when CS and CPM were combined with synchronized cycles of plasmapheresis and IV immunoglobulin (12). For CSS, modulation of eosinophils with interferon–α or blockade of IL5 is being investigated.

Biologicals and Newer drugs: (Table 6)

SUMMARY:

Vasculitides are group of rare heterogeneous disorders which have diverse etiologies and manifestations. Clinical manifestations are protean depending upon size, site and type of vessel involved in different organs. High index of suspicion is required so that disease is diagnosed early and appropriate therapeutic measures are taken to prevent complications, sequelae and mortality which may be very high if these entities are not treated early, adequately and appropriately.

REFERENCES: