A STUDY AND ANALYSIS OF CUTANEOUS SMALL VESSEL VASCULITIS

Dissertation Submitted in partial fulfillment
for the degree of

Doctor of Medicine

Branch - XII A

M.D., (DERMATO VENEREO LEPROLOGY)

April 2011

DEPARTMENT OF DERMATO VENEREO LEPROLOGY

MADURAI MEDICAL COLLEGE, MADURAI.

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CERTIFICATE

This is to certify that this dissertation titled “A study and analysis of cutaneous small vessel vasculitis” submitted by **DR.O.R.JAYANTHI** to the TamilNadu Dr. M.G.R Medical University, Chennai in partial fulfillment of the requirement for the award of MD degree branch – XII A, is a bonafide research work carried out by her under direct supervision and guidance.

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ACKNOWLEDGEMENT

At the outset, I thank our Dean **Dr.S.M.SIVAKUMAR** for permitting me to use the facilities of Madurai Medical College and Government Rajaji Hospital to conduct this study.

I wish to express my respect and sincere gratitude to my beloved teacher and Head of the Department of Dermatology, **Dr.S.KRISHNAN** for his valuable guidance and encouragement throughout the study and also during my post graduate course. I owe my sincere thanks to him.

I express my thanks and deep sense of gratitude to my teachers **Dr.A.S.Krishnaram** and **Dr.G.Geetharani** for their valuable guidance.

I profoundly thank the Head of the Department of Venereology i/c **Dr.D.Amalraja** for his valuable advice and support.

I sincerely thank the Head of the Department of Pathology **Dr.Usha Ravikumar** for her valuable guidance.

I also wish to thank all my Assistant Professors of the Department of Dermatology and Venereology, and all my colleagues, who have stood by me and helped me to complete my work.

Finally, I thank all the patients, who form the most integral part of the work, without whom, this study would not have been possible.

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INTRODUCTION

Vasculitis is inflammatory process affecting the vessel walls and leading to its compromise or destruction and subsequent hemorrhagic and ischemic events. Vessels of any organ can be affected that results in a wide variety of signs and symptoms[1,2] The unique feature of this group is multiorgan involvement. Because of the rich vasculature, the skin is prone to be frequently affected in vasculitis.

Cutaneous involvement in vasculitides may be primary or reflector of a fatal systemic disease or evidence of association with some other systemic disorder. Cutaneous vasculitic lesions offer a window to diagnosis and a ready source of accessible tissue for histopathologic examination.

Small vessel vasculitis is defined as one which affects mostly vessels smaller than arteries such as arterioles, capillaries and venules[3.] These heterogeneous clinical manifestations, combined with the etiologic non specificity of the histologic lesions, complicate the diagnosis of specific form of vasculitis.The gold standard for a diagnosis of vasculitis is histologic confirmation on biopsy, as few forms of vasculitis have a pathognomonic laboratory or imaging finding. As a clinicopathological process, vasculitis occurs both as a primary process or idiopathic vasculitis and as a secondary feature of other diseases such as collagen vascular diseases, infectious disorders,

malignancy and adverse drugs reaction. Many times the initial presentation of vasculitis is on the skin and it is the dermatologist who must diagnose and treat this challenging condition.

REVIEW OF LITERATURE

Classification

In 1952, Zeek- based upon vessel size and histopathology[4, 5, 6]

Gilliam and Smiley in 1976[7]- by subdividing Zeek's existing categories

In 1990, American College of Rheumatology (ACR) - based upon clinical, laboratory, and histologic criteria, and those of the Chapel Hill Consensus Conferences - based mainly upon histologic criteria[8, 9].

An attempt to present a working classification has been previously presented by

Jorizzo in 1993 and others [10, 11].

Proposed working classification of vasculitis [updated version of Gilliam's 1976 scheme] [12].

Small vessel vasculitis

Cutaneous small vessel vasculitis – not further classified

Henoch – Schonlein purpura

Essential mixed cryoglobulinemia

Waldenstroms hypergammaglobulinaemic purpura

Associated with collagen vascular disease

Urticarial vasculitis

Erythema elevatum diutinum

Eosinophilic vasculitis

Rheumatoid nodules

Reactive leprosy

Septic vasculitis

Etiology

Bacterial antigens may be noted in the wall of the small vessels, as may hepatitis B antigen[13, 14]. Still, as in all forms of vasculitis, most cases of small vessel vasculitis are idiopathic (45-54%), due to medications (10-45%), infections (10-36%), including hepatitis B (5%)[13-16]. Medications most commonly associated with small vessel vasculitis are antibiotics and NSAIDS (especially beta-lactams) and diuretics. Upper respiratory tract infections were the most common (20%) infectious cause of small vessel vasculitis in one series from Spain[14].

Autoimmune diseases associated with secondary small vessel vasculitis include rheumatoid arthritis and systemic lupus erythematosus[13-16] .Examples of implicated drugs induce vasculitis are aspirin, penicillin, thiazides, and sulphonamides. Examples of infective agents more often associated with

necrotizing venulitis are hepatitis B, streptococcal agents, and mycobacterium tuberculosis. Diseases associated with immune-complex formation include malignancies, connective tissue diseases, inflammatory bowel disease, and chronic active hepatitis[13, 17].

Pathogenesis [18, 11, 19]

Antigenic triggers of immunological responses targeted at components of blood vessel walls elicit most vasculitides. The deposition of immune complexes in blood vessel walls is the best characterized mechanism for the vascular injury associated with vasculitis [18]. Potential antigens of relevance include bacteria, viruses, drugs and other chemicals. The circulating immune complexes interact with the complement system to generate C3a, C5a, anaphylotoxins which stimulate the production of chemotactic factors and subsequent chemotaxis , the release of vasoactive amines (histamine) and the release of proinflammatory cytokines which induce expression of adhesion molecules subsequently, immune complex with a sedimentation coefficient greater than 19S are deposited in vessel walls.

Neutrophils get attracted to this site and these release lysosomal enzymes in an attempt to engulf the immune complexes. This causes degranulation and destruction of the neutrophils (leukocytoclasis) with release of collagenase and elastase, generation of reactive oxygen species, ultimately resulting in inflammation and bystander fibrinoid necrosis of vessel walls[11, 19].

It is of practical importance to appreciate that neutrophils degrade immune complexes within 24 – 48 hours they are deposited[20] usually within 24 hours. Hence direct immunofluorescence of vasculitis lesions older than 3 – 12 hours will generally yield negative results[11, 21].

Phenotypic manifestations of cutaneous lesions due to small vessel vasculitis

- The signs and symptoms of small-vessel vasculitis are extremely varied, and many are shared by all vessel vasculitis Presentation:
    - **usually:**
        - erythematous macules,
        - palpable purpura – hall mark feature, initial lesion non palpable becomes pustule or sometimes ulcerate.
    - **may also be:**
        - nodules[22]
        - hemorrhagic vesicles and bullae
        - crusted ulcers[23,24]
        - gangrene, infarct

      less commonly:

        - livedo reticularis

        - pustules[32]
        - annular lesion[26,29]
    - **lesions:**
        - 1mm to several cm diameter
        - sometimes painful[30]/ itching
        - may be:
            - single crop that subsides spontaneously after few weeks
            - crops at different stages of evolution that recur intermittently[31]
- Location:
    - predilection for dependent parts:
        - particularly lower legs[32,33]
    - rarely in previously traumatized skin:
        - Koebner phenomenon[34]
- **Extracutaneous manifestations**:
    - ≈20% of affected individuals
    - include:
        - arthralgia (synovial) (polyarthritis)
        - myositis
        - low-grade fever
        - malaise[32, 35]

- less commonly: [28,11,36,37,38]
    - renal - glomeruli (proteinuria or hematuria)
    - gastrointestinal (abdominal pain or gastrointestinal bleeding)
    - pulmonary
    - neurological[32,39] - focal or diffuse, central, or peripheral neurologic involvement.
- not predicted by severity of histopathological changes[40,35]

Laboratory findings

These are both to confirm the diagnosis and to determine the extent of systemic vasculitis, or the existence of underlying associated diseases.

Histopathology

A definitive diagnosis of vasculitis requires histological confirmation in almost all cases. The hallmark histopathologic pattern of small vessel vasculitis is leukocytoclastic vasculitis.

- Dynamic:
    - not all features necessarily present at a particular stage[30]
    - lesion of 18–24 hours' duration shows most diagnostic features[41]
- Usually in small venules (postcapillary venules) in dermis:
    - in severe cases may involve arterioles

Features

Neutrophil infiltration of vessel walls and extending into and beyond perivascular zone**,** neutrophils degenerate (leukocytoclasis) with formation of nuclear dust.

Walls thickened by:

Exudate of inflammatory cells and due to edema fluid and due to exudation of fibrin (‘fibrinoid necrosis') which often extends into adjacent perivascular connective tissue.

Endothelial cells:

Usually swollen, some degenerate.

Sometimes thrombosis can occur.

Variable:

- edema
- extravasation of red blood cells

Sometimes eosinophils and lymphocytes:

- perivascular
- longer duration lesions

Other Changes

- Macrophages scattered in interstitium:
    - even in early stages
    - time-dependent increase[42]
- Mixed inflammatory cell infiltrate of eosinophils, lymphocytes and occasional neutrophils:
    - common in vasculitis due to drugs[43]

Resolving Lesions[33]

- Usually only mild perivascular infiltrate of lymphocytes and some eosinophils
- May be rare plasma cell
- Late resolving lesions:
    - hypercellular (busy) dermis striking feature with increased number of:
        - interstitial fibroblasts
        - histiocytes
- Sometimes mild increase in acid mucopolysaccharides:
    - gives vague ‘necrobiotic’ appearance
- Uncommonly, pronounced subepidermal edema results in vesiculobullous lesions
- Cutaneous infarction:

- usually involving only epidermis and upper third of dermis
  - may follow thrombosis of affected vessels

A lymphocytic form (in which lymphocytes predominate) has also been described. There is still not enough evidence, however, to prove that the lymphocyte pattern is truly etiologically or clinically relevant. Old lesions of small vessel vasculitis may no longer demonstrate leukocytoclastic vasculitis and may contain mainly lymphocytes around blood vessels[44-48]. This latter consideration stresses the importance of timing when taking a biopsy in a dynamic process such as the vasculitic one.

Cutaneous lymphocytic vasculitis

This form of vasculitis is characterized by lymphomonocytic cell infiltration as a primary response to various antigens such as medications or antigens found in connective tissue diseases such as lupus erythematosus, primary Sjögren's syndrome. These inflammatory cells are present in the involved vessel wall, while fibrinoid necrosis and leukocytoclasis is absent. Activated lymphocytes elaborate cytokines, thereby damaging the vessel wall, either by direct action of the cytokine or promotion of apoptosis. This form of vasculitis is infrequent but poorly studied [49,50, 2,51].

Drug-induced vasculitis

Drug-Induced vasculitis should be considered in any patient with small-vessel vasculitis and will be substantiated most often in patients with vasculitis confined to the skin. Drug causes approximately 10 percent of vasculitic skin lesions. Drug-Induced vasculitis usually develops within 7 to 21 days after treatment begins [82, 32.] Most common drugs include Beta – lactams, Penicillin, Sulfadrugs , Nonsteroidal anti- inflammatory drugs[53]. Identification of tissue eosinophilia in these biopsies is a clue to a drug etiology[54].

Henoch Schonlein purpura[55-60]

It comprises about 10 % of all cases of cutaneous vasculitis and the most Common vasculitis in children (90 % of all cases)[55,56]. Upper respiratory tract infection precedes by 50% , in pediatric patients and 40% in adult patients. Other factors include drugs, malignancy, foods[57, 58]. The classic findings are palpable purpura, arthralgia and abdominal pain[58, 59]. Furthermore urticaria, vesicles, bullae and necrotic ulcers may develop.

Henoch Schonlein purpura typically involving the extensor aspect of the limbs and buttocks in a symmetrical fashion. Henoch Schonlein purpura may also affect the trunk and face[60]. Renal involvement occurring in approximately 30 – 90 % of patients and demonstrating only minimal proteinuria and

hematuria. Gastrointestinal bleeding being demonstrated in 50 – 75 % of patients.

USG Abdomen is indicated to exclude intussusceptions, bowel wall edema, thickening , or perforation. Arthritis is seen in about 75 % of patients, most frequently affecting the knees and ankles. ASO titre may be done to rule out streptococcal infection[59.] HSP is a clinical diagnosis, with conformation by direct immune fluorescence and routine histology. Histopathology shows leukocytoclastic vasculitis. Perivascular IgA deposits are characteristic of HSP.

Essential Mixed Cryoglobulinemia

Cryoglobulins are immunoglobulins that precipitate in the cold and dissolve on reworming. Type II or essential mixed cryoglobulinemia, in which the cryoglobulin contains both a polyclonal IgG (Antigen)and a monoclonal IgM Rheumatoid factor directed against the IgG. Most cases are due to chronic infection with hepatitis C virus [61-65].

Although infection with hepatitis B virus and Epstein –Barr virus have been implicated in some patients[61-67]. Type III , in which there is also mixed cryoglobulin , but both the IgG and the rheumatoid factor IgM are polyclonal.this condition is often seen in chronic inflammatory and autoimmune disorders (such as lupus and leukocytoclastic vasculitis), lymphoproliferative malignancies, and, in as many as one – half of cases, HCV infection [62,63,65,68].

The median age at diagnosis of cryoglobulinemia is early to middle sixth decade, with a female to male ratio of 2: 1 [69].

Recurrent showers of dependent palpable purpura associated with arthritis or arthralgia is the common presentation. Sometime cutaneous infarction may be the presenting feature. Histopathology shows the presence of hyaline thrombi in vessel wall with evidence of vessel wall damage. Conformation of cryoglobulins requires cryoglobulin test followed by serum protein electrophoresis[69].

Waldenstroms Hypergammaglobulinaemic Purpura

Its a polyclonal disorder most commonly linked with sarcoidosis, lupus erythematosus, sjogren syndrome and other auto immune conditions [71, 77]. The majority of patients have positive anti nuclear antibody and anti- SSA (Ro) or anti –SSB (La) antibodies[73-77.] Other features associated include arthropathy, renal tubular acidosis, chest infections, lymphopenia and immune hypersensitivity pneumonitis. Most patients are female [78].

Clinically the pattern of purpura usually consisting of crops of small erythematous macular or palpable purpuric spots on the lower leg[70-77.] Prolonged walking, standing or sitting with the legs dependent, or other increase in venous pressure, may be an obvious provocative factor[76,77.] Histology may show vasculitic change, and DIF may show immunoglobulins in blood vessel

walls[75,79, 80]. There may be an abnormal ratio of IgG subclasses, with low IgG1/IgG2 ratio[81].

Vasculitis Associated With Collagen Vascular Diseases

Around 12% of cutaneous vasculitis cases will be associated with a connective tissue disorders[55, 56.] Secondary vasculitis due to connective tissue disease should be considered in patients presenting with biopsy – proven cutaneous vasculitis who have signs and symtoms of dry eyes, drymouth, arthritis, sclerosis, photosensitivity, or serologic evidence of ANA, RF, antiphospholipid antibodies, or anti- DNA, Ro, or La antibodies. Cutaneous vasculitis occurs frequently in SLE, RA and Sjogren syndrome, less commonly in dermatomyositis, scleroderma, and polychondritis[55, 56, 82].

Increased or enhanced expression of vascular adhesion molecules attracting and activating neutrophils is suspected to play a role in the pathogenesis of connective tissue vasculitis[83.] In general, CTD vasculitis show more widespread organ involvement and the calibre of vessels affected shows more variation compared with conventional CLA. For example, lupus vasculitis patients represent a heterogenous population of which nearly 60% of cases do not fulfil the categories and definitions adopted by the CHCC[84].

Small vessel vasculitis in LV patients is predominantly cutaneous[84]. LV patients are more likely to have livedo racemosa, anemia, elevated ESR, anti-La / Sjogren syndrome (SS)-B antibodies than SLE patients without vasculitis.

Arterioles and post – capillary venules are the vessels most commonly affected by vasculitis, manifesting as purpura, vesiculobullous lesions , urticaria , and splinter haemorrhages.

Skin biopsy will reveal a mixed, mostly small and less commonly muscular vessel neutrophilic vasculitis with lesions that can resemble either typical CLA or PAN. Extravascular histologies can provide clues to the diagnosis of CTD vasculitis such as the presence of interface dermatitis with dermal mucin deposition (found in SLE and Dermatomyositis), dermal and / or subcutaneous sclerosis in scleroderma, palisaded neutrophilic and granulomarous dermatitis in RA or SLE and tissue neutrophilia in SLE and Sjogren syndrome [85].

Urticarial Vasculitis

Of patients with urticarial lesions, roughly 5-10% have urticarial vasculitius[86, 87]. It is a chronic disease, which presents as urticarial lesions that most often occur on the trunk or proximal limbs, frequently with associated angioedema[88.] Lesions differ from those of simple urticaria in that individual lesions persist for greater than 24hours, often demonstrate purpura and post inflammatory pigmentation, and cause symptoms of burning.

Two types described 1) UV associated with hypocomplementaemia 2) normocomplementaemic UV. Most UV patients are women (female to male ratio 3:2 to 4:1) in their fourth or fifth decade[55.] It is strongly associated with

connective tissue diseases (sjogren syndrome, SLE[86], physical urticarias, hepatitis B or C, IgM or IgA gammopathies, serum sickness, colon cancer and drug ingestion. UV is thought to represent a type III hypersensitivity reaction, as circulating immune complexes may be demonstrated in upto 75% of patients[89.] Lesions of UV demonstrate leukocytoclastic vasculitis.

Erythema Elevatum Diutinum

EED is a rare chronic cutaneous eruption that is most commonly seen in adults. Though the exact etiology is unknown it has been associated with autoimmune diseases such as Rheumatoid arthritis, celiac disease, inflammatory bowel disease and type I diapetes mellitu, infections (streptococcus, hepatitis, syphilis, HIV [90-100.] In addition it has been associated with hypergammaglobulinemia and IgA monoclonal gammopathies, myelodysplasia, pyoderma gangrenosum and relapsing polychondritis. The association with haematological disorders, such as multiple myeloma, is strong; however EED may precede the haematological disease by several years[101.]

Histopathology of acute lesions show leukocytoclastic vasculitis. Chronic lesions demonstrate fibrosis, capillary proliferations and infiltration of macrophages, plasma cellsand lymphocytes. Lesions of EED most commonly appear chronically in a symmetrical fashion over the dorsa of the hands, the knees, buttocks and Achilles tendons. They are red violaceous, red brown or yellowish papules, plaqus or nodules. These lesions may progress to form

atrophic scars. It may last from 5 to 35 years, with crops of new lesions developing every few weeks to months.

Eosinophilic Vasculitis

Rare vasculitis, cause is unknown. Eosinophil cytokines such as IL-5, and toxic eosinophil granule proteins such as major basic protein, have been demonstrated in serum and tissues, respectively, and presumably play a part in the tissue damage. Neutrophil elastase is predominantly around vessels, and mast cell degranulation occurs. Eosinophilic vasculitis has also been reported in a patient with the hypereosinophilic syndrome. In this patient CD40 (a glycoprotein of the TNF receptor family) was considered to be important in pathogenesis [102.]

Recurrent pruritic papules and urticarial lesions occur at any site, especially the head and neck, with angioedema of the face and extremities. Either sex and any age group may be affected. The course is long and recurrent but fever, arthralgia and visceral involvement are absent. Raynaud's phenomenon and digital gangrene were reported in a patient with cutaneous eosinophilic vasculitis associated with the hypereosinophilic syndrome [102] Histopathology shows fibrinoid deposition and necrosis of small dermal vessels with an infiltrate of eosinophils and absent or minimal leukocytoclasis.

Small vesicles containing eosinophils may be present. Immunoglobulin deposition is not a feature. This eosinophilic small vessel vasculitis is distinct

from other vasculitides such as CSS, in which medium to large vessels are affected.

Rheumatoid Nodule

Palpable subcutaneous nodules occur in approximately 20% of patients with RA. The most common site is on ulnar border of the forearm.Less commonly ,they occur on the dorsa of the hands, on the knees, on the ears, over the scapulae. They vary in size upto several centimetres in diameter, are firm in cocsistency and tend to ulcerate with trauma. Nodules are almost invariably asocited with more severe forms of the disease, and rheumatoid factor and antinuclear factor are frequently found in the serum.

Nodules were characterized by granuloma formation secondary to leukocytoclastic vasculitis[103.] Histologically, rheumatoid nodules consists of fibrous tissue in which foci of fibrinoid necrosis are scattered, surrounded by a palisade of cells, mainly fibroblasts and histiocytes. A peripheral zone of lymphocytes and plasma cells occurs. Within the necrotic area are thin reticulum fibres, amorphous material and some nuclear debris are seen.

Reactive Leprosy

Erythema nonosum leprosum (ENL) or type II reaction is an immune complex syndrome seen in multibacillary leprosy [104]. ENL usually occurs after specific treatment of lepromatous disease or borderline leprosy but may be

observed in patients who have not been treated. ENL presents with inflammatory skin nodules and involvement of multiple organs, often running a protracted course. Over one half of lepromatous patients and one quarter of borderline lepromatous patients will experience type 2 reaction[105].

The clinical manifestation is of evanescent crops of tender erythematous papules or nodules located on interlesional skin. They are all dome shaped with ill defined margins. The papules may turn into pustules or may simply ulcerate. They can also occur as subcutaneous plaques. The lesions are most common on the face and extensor surface of limbs and less commonly on the trunk, accompanied by fever, malaise, arthralgia and leukocytosis.

Lesions tend to recur at the same sites and if they do not resolve completely, a chronic painful panniculitis develops which may persist for months or years.

Histopathology: In ENL, the lesions are foci of acute inflammation superimposed on chronic multibacillary leprosy[106]. It is characterized by edema of papillary dermis and a mixed dermal infiltrate of neutrophils and lymphocytes superimposed on collection of macrophages. There may be involvement of subcutis, with the development of mixed lobular and septal panniculitis. However, in majority of case involvement of the dermis is the primary and predominant finding. Macrophage in dermis contain fragmented organism. Polymorph neutrophils may be scanty or so abundant as to form a

dermal abscess with ulceration. Whereas foamy macrophages containing fragmented bacilli are usual, in some patients no bacilli remain and macrophages have a granular pink hue on Wade-Fite staining, indicating mycobacterial debris.

Lesions exhibit necrotizing vasculitis involving capillaries, venules, and small-to-medium arteries and veins. In the superficial dermis, affected venules and capillaries showed endothelial cell enlargement and focal necrosis associated with perivascular infiltrates of lymphocytes.

In the deep dermis and subcutaneous tissue, affected venules, arterioles and arteries exhibited endothelial cell necrosis and matted fibrin in the vessel walls associated with perivascular infiltrates of neutrophils[107]. Throughout the dermis, mononuclear phagocytes with vacuoles containing numerous fragmented organisms were observed. These patients may have superficial ulceration[106].

Lucio phenomenon[108,109,110]

Lucio phenomenon is a vasculitis clinically described in 1852 and microscopically documented in 1948 in patients with diffuse lepromatous leprosy. Usually occurs in patients who have received either no treatment or inadequate treatment. In contrast to ENL, fever, tenderness and leukocytosis are absent. The lesions consists of barely palpable, hemorrhagic, sharply

marginated, irregular plaques. They develop into crusted lesions and, particularly on the legs, into ulcers.

Histopathologically, Lucio phenomenon is a distinctive type of granulomatous and necrotizing panvasculitis[108] of small vessels in the upper and mid dermis that results in ulceration of epidermis. Occasionally the process extends deep into the subcutaneous fat with small vessel vasculitis in the fat lobule[109.]

Septic Vasculitis

About 22% of all cases of cutaneous vasculitis are associated with infection, and all types of infectious agents (viruses, bacteria, fungi, protozoa and helminthes) have been associated with the development of vasculitis[55, 56]. The cutaneous pathology most often found in these cases is a small-vessel neutrophilic vasculitis affecting superficial dermal vessels.

LCV histology found in infection-related vasculitis is likely A common morphologic endpoint of several pathways: Immune complex formation, alternate pathway of complement activation, and endotoxin-mediated expression of vascular adhesion molecules[108, 109]. In the case of Immune Complex formations, infection-triggered LCV is suspected to show a greater frequency of subcorneal, intraepidermal, and subepidermal neutrophilic pustules, to have more tissue neutrophilia and predominant IgA vascular

deposits, and to have relatively fewer eosinophils and lymphocytes than idiopathic CLA and drug-related cutaneous LCV [110].

Septic vasculitis is a variant of small-vessel neutrophilic vasculitis that is typically immune-complex negative and caused by infective endocarditis or septicemia from gonococci, meningococci, pseudomonads, staphylococci, streptococci, certain rickettsial infections, and other microorganisms[55].

The clinical lesions of septic vasculitis are characterized by purpura (petechiae and ecchymoses), vesiculo-pustules (often with gray roofs signifying necrosis), hemorrhagic bullae, and, rarely ulceration. Patients with chronic gonococcemia and chronic meningococcemia have a triad of intermittent fever, arthralgia, and fewer clinical lesions, distributed over extremities, particularly acral surfaces, which are mostly petechiae surrounded by a rim of erythema vesiculo-pustules with a gray necrotic roof, and rarely hemorrhagic bullae.

Biopsy reveals mixed neutrophilic small and muscular-vessel vasculitis with deep dermal and subcutaneous vessel involvement associated with scant perivascular fibrin or fibrin thrombi, and no or little nuclear debris. These features help differentiate septic vasculitis from conventional CLA.

AIM OF THE STUDY

1) To study the epidemiological spectrum of cutaneous small vessel vasculitides.

2) To determine the clinicopathological correlation.

MATERIALS AND METHODS

A study was conducted during the period from May 2008 – May 2010 in the department of dermatology, Govt Rajaji Hospital, Madurai Medical college, Madurai, among the patients with cutaneous small vessel vasculitis attending the dermatology department as well as those referred from other departments mainly Medicine, Rheumatology and paediatrics.

Inclusion criteria:

1. All patients with clinical features suggestive of small vessel vasculitis i.e palpable purpura , infiltrated erythema , hemorrhagic vesicles and bulla, ulcers, infarct, digital gangrene, erythematous plaques and nodules, urticaria, livedoreticularis which was subsequently supported by histopathological examination.

Exclusioncriteria:

1. Patients who were unwilling for the study
2. Patients with abnormal bleeding parameters.

A proforma was filled for all patients

History:

A detailed history was taken which includes, symptoms (itching , burning sensation, pain) duration of skin lesions, occupational history, systemic symptoms, history of sore throat in the recent past, history of drug intake, history suggestive of malignancy and collagen vascular disorders.

Clinical examination:

Detailed general and systemic examinations were done. Detailed examination of skin lesion which includes morphology of skin lesions, distribution of lesions, symmetry, tenderness, diascopy were done.

Investigations:

1) Baseline laboratory investigations included are complete hemogram, serum urea, serum creatinine, liver function tests , chest X ray, urine (routine and microscopy), Mantoux test, test for stool occult blood, ASO titre, blood culture and skin smears for acid fast bacilli, USG Abdomen and pelvis .
2) Screening for HIV, Hepatitis B, C and syphilis were also done for high risk patients with history of sexual exposure or occupational exposure to blood and blood products.
3) Tests to rule out cryoglobulinemia, (cryoglobulin test , serum protein electrophoresis, complement) malignancy and collagen vascular disorders were done when indicated.

4) Incisional elliptical skin biopsies were done from the early tender skin lesions with a caution not to include the resolving lesion and they were sent to pathologist for histopahology Special stains like AFB were done when required.
5) Other tests to rule out bacterial infections include gram stain and blood culture.

Classification of patients with features of cutaneous small vessel vasculitis in our study was based on Proposed working classification of vasculitis [updated version of Gilliam's 1976 scheme [12].

Analysis :

A descriptive analysis of the clinical characteristics, laboratory parameters and histopathological features of various cutaneous small vessel vasculitis in our study was done.The data was analysed and compared with published literature.

OBSERVATION AND RESULTS

Fifty one patients with clinical features of cutaneous small vessel vasculitis were seen during the study period from May 2008 to May 2010. Of these, 11 cases were excluded from the study because of the patients denial for the study (4), not willing for biopsy (7) .40 patients were diagnosed as cutaneous small vessel vasculitis were included in our study.

Table -1

Clinical spectrum of cutaneous small vessel vasculitis

Cssv	**No.of patients**	**Percentage(%)**
Henoch schonlein purpura (HSP)	18	45
Erythema nodosum leprosum (ENL)	10	25
Collagen vascular disease vasculitis (CVDV)	7	17.5
Urticarial vasculitis (UV)	2	5
Septic vasculitis (SV)	2	5
Essential mixed cryoglobulinemic Vasculitis(EMCV)	1	2.5
Total	40	100

Key

Cssv = Cutaneous small vessel vasculitis

The common types were Henoch schonlein purpura (18) , Erythema nodosum leprosum(10), small vessel vasculitis associated with collagen vascular disease (7). The less common types were urticarial vasculitis (2), septic vasculitis (2), essential mixed cryoglobulinemia (1)

Table – 2

Sex distribution

Disease	**Male**		**Female**	
	No.of cases	%	No.of cases	%
HSP	5	28	13	72
ENL	7	70	3	30
CVDV	1	14	6	86
UV	1	50	1	50
SV	-	-	2	100
EMCV	1	100	-	-
Total	15	38	25	62

Key

HSP	=	Henoch Schonlein purpura
ENL	=	Erythema nodosum leprosum
CVDV	=	Collagen vascular disease vasculitis
UV	=	Urticaril vasculitis
SV	=	Septic vasculitis
EMCV	=	Essential mixed cryoglobulinemic vasculitis

There were 15 (38%) male and 25 (62%) female patients .

Male to female ratio is 1:1.7

Table- 3

Age distribution

Cssv	**<10 Yrs**	**10-20 Yrs**	**21-30 Yrs**	**31-40 Yrs**	**41-50 Yrs**	**51- 60 Yrs**	**>60 Yrs**	**Total**
HSP	4	8	2	4				18
ENL			2	4	3	1		10
CVDV		1	4	1	1			7
UV	1		1					2
SV	2							2
EMCV					1			1
TOTAL	7	9	9	9	5	1		40

Key – Cssv = Cutaneous small vessel vasculitis

HSP = Henoch Schonlein purpura

ENL = Erythema nodosum leprosum

UV = Urticaril vasculitis

SV = Septic vasculitis Yrs = Years.

EMCV = Essential mixed cryoglobulinemic vasculitis

Majority of patients were between the ages of 11 – 40 years.

The mean age of our study group was 31 years for males and 24 years for females.

Table -4

Etiological factors

Etiological factors	**No.of patients**	**Percentage**
Infections	22	55
Drugs	6	15
Collagen vascular disorders	7	17.5
No cause	4	10

Approximately twenty two (55%) of the patients had infections, and seven (17.5%) had positive connective tissue disease workup without any overt manifestations, six (15%) were attributed to drugs (These included NSAIDS in three, antibiotics in two, and unknown drugs in one patient). While one

(2.5%) patient had cryoglobulinemia. No cause was found in four (10%) cases.

Table -5

Symtoms

Symptoms	**No.of patients**	**Percentage (%)**
Itching	12	30
Fever	6	15
Pain at the site of lesion	5	12.5
Burning sensation	4	10

Itching was the commonest presenting symptom in twelve (30%) patients. six patients complained of fever (15%), while burning sensation and pain at the site of the lesion were encountered in four and five patients respectively.

Table – 6
Systemic symptoms

Systemic symptoms	**No.of cases**	**percentage %**
Joint pain	19	47.5
Joint swelling	5	12.5
Pain abdomen	5	12.5
Melena	4	10
Hemoptysis	1	2.5
Total	34	85

Systemic symptoms were encountered in 34 (85%) patients. Associated joint pains were the commonest systemic presentation in 19 (47.5%) patients with knee joint being the most commonly involved joint (11). Other joints involved were ankle joint and small joints of feet and wrists. Joint swelling was observed in 5 patients. There was history of abdominal pain in 5 patients, melena in 4

patients and hemoptysis in 1 patient .

Table – 7

Signs

Signs	**No.of patients**	**Percentage (%)**
Palpable purpura	21	52.5
Nodule	7	17.5
Plaque	3	7.5
Ulcers (crusted & necrotic)	3	7.5
Urticarial lesions	2	5
Bulla	1	2.5
Ecchymoses	1	2.5
Pustule	1	2.5
Gangrene of digits	1	2.5

Palpable purpura was the commonest cutaneous presentation noticed in 21 patients (16 females and 5 males). The other cutaneous lesions seen in 19 patients were in the form of nodules, plaques, ulcers, bullae, vesicles, gangrene of toes, urticarial lesions and Koebner phenomenon. The time since onset of lesions varied from 1 day to 9 months**.**

Table- 8

Distribution

Region	**HSP**	**ENL**	**CVDV**	**UV**	**SV**	**EMCV**	**TOTAL**	**%**
Face	-	3	1				4	10
Trunk	3	8	2	2	1		16	40
UL	7	3	3	1	1	1	16	40
LL	18	3	5	2	1	1	30	75

Key

HSP = Henoch Schonlein purpura

ENL = Erythema nodosum leprosum

CVDV = Collagen vascular disease vasculitis

UV = Urticaril vasculitis

SV = Septic vasculitis

EMCV = Essential mixed cryoglobulinemic vasculitis

LL = Lower limb UL = Upper limb

The commonest sites were lower limb (75 %) mainly the legs and anklle followed by upper limb, trunk and face.

Table – 9
Laboratory findings

Laboratory parameters	No.of patients	Percentage (%)
Anaemia	16	40
Leukocytosis	12	30
Raised ESR	27	67.5
Elevated urea	6	15
Elevated serum creatinine	6	15
Albuminuria	7	17.5
Urine examination		
RBC	7	17.5
Pus cells	-	-
Bacilli	-	-
Stool for occult blood	8	20
Abnormal chest x ray	1	2.5
Anti nuclear antibody	5	12.5
Rheumatoid factor	2	5
ASO titre	10	25
Mantoux test	1	2.5
Hepatitis B Virus	-	-
Hepatitis C Virus	-	-
HIV	-	-
Cryoglobulin Test	1	2.5
USG abdomen – abnormality	1	2.5

KEY

ESR	=	Erythrocyte sedimentation rate
ASO titre	=	Anti streptolysin O titre
RBC	=	Red blood cells
USG abdomen	=	Ultrasonography abdomen
HIV	=	Human immunodeficiency virus.

The hematological and biochemistry workup revealed anemia in sixteen (40%)patients, leukocytosis in twelve(30%), elevated ESR in twenty seven(67.5%), raised serum-urea in six and raised creatinine levels in six patients. Routine urine examination showed albuminuria in seven patients, while urine microscopy demonstrated blood cells in seven patients. The stool for occult blood was positive in eight patients. Chest x ray showing cavity in one patient with history of hemoptysis. Smear from pustular lesion in one patient revealed gonococci. Blood culture from one patient with ecchymoses showed growth of Pseudomonas aeruginosa. Anti-nuclear antibody and rheumatoid factor were positive in five and two patients, serum cryoglobulins were positive in one patient . ASO titer was also raised in ten patients, while Mantoux was positive in one patient. USG abdomen showed bowel wall edema in one patient with henoch schonlein pupura.

Table - 10

Histopathology

Clinical diagnosis		**No .of cases**	**%**	**Histopathological diagnosis**	**No. Of cases**	**%**	**NEV**	**%**
HSP		18	45	LCV	15	37.5	3	7.5
ENL		10	25	LCV , mixed panniculitis	8	20	2	5
CVDV	LE	6	15	LCV	5	12.5	1	2.5
	RA	1	2.5	LCV	1	2.5		
Urticarial Vasculitis		2	5	LCV	2	5		
Septic vasculitis		2	5	LCV	2	5		
Essential mixed cryoglobulinemic vasculitis		1	2.5	LCV with hyaline thrombi	1	2.5		
Total		40	100		34	85	6	15

Key – LCV = Leukocytoclastic vasculitis LE =Lupus erythematosus

NEV = No evidence of vasculitis RA = Rheumatoid arthritis

HSP = Henoch Schonlein purpura

ENL = Erythema nodosum leprosum

CVDV = Collagen vascular disease vasculitis

Based on histopathological findings, 34 (85%) patients were given a diagnosis of leukocytoclastic vasculitis, while 6 (15%) patients showed perivascular lymphocytic infiltrates with no evidence of vasculitis. The skin biopsy showed typical features of endothelial swelling, fibrinoid necrosis, RBC extravasation and leukocytoclasis. Additional findings include subepidermal bulla , Hyaline thrombi and mixed panniculitis were seen.

DISCUSSION

Cutaneous small vessel vasculitis is a poorly understood entity due to its protean clinical manifestation and its overlap with various infections, collagen vascular disorders and malignancies. In our study, we analyzed cases of cutaneous small vessel vasculitis diagnosed on the basis of history, clinical features, and various laboratory tests. The clinical diagnosis was supported by skin biopsy. Our study confirmed various established facts regarding cutaneous small vessel vasculitis and throws light on some new aspects.

One of the published study on cutaneous vasculitis was by Gupta et al[112] between 2004 -2006 Postgraduate Institute of Medical Education and Research, Chandigarh, India. They included 50 patients. The results of the study by Gupta et al [112] indicated that there were 20 male and 30 female patients. The mean age of the study group was 41.1 years for males and 35.9 years for females. In our study, 15(32%) were male and 25(62%) females. Females were more commonly affected than males in our study consistent with the study by Gupta et al.[112] . The mean age of our study group was 31 years for males and 24 years for females in comparision with study by Gupta et al[112].

Etiology

A possible etiological association was suspected in 90% of our patients which was comparable to 67.2% seen by Sais et al [111]. Most common cause found in our study was infections 55%, mainly upper respiratory tract infections and this is consistent with study by Martinez-Taboada et al[14] collagen vascular disorders (17.5%) and drugs (15%) were other causes of cutaneous small vessel vasculitis in our study. Lupus erythematosus was the common collagen vascular disease found in our study. NSAIDS were the common drugs followed by antibiotics. This was comparable with the results of the study by Sams et al [13], Callen et al[15], Hautmann et al[16].

Symptoms

The common symtoms observed in cutaneous lesions of our study were itching (30%), pain (12.5%) and burning sensation (10%). This was comparable with earlier studies by Sais et al[111] where 41.3% patients complained of itching and 30% had painful lesions. Fever was seen in 15% of our patients while it was 31.6% in the study by Sais et al [111].

Signs

The most common clinical presentation in our study was crops of nonthrombogenic palpable purpura, primarily involving dependent areas such as legs, ankles, feet and buttocks seen in 52.5% of patients. This was comparable

with earlier studies by Sais et al[111] , Ekenstam et al[113], Gupta et al[112] and Lopez Maturana et al[116] in 89.2%, 62%, 86% and 62% of cases, respectively. Koebner phenomenon was observed in two (5%) patients as reported in standard literature[34] . The second most common type of lesion in our study was cutaneous nodules which comprised 17.5% of patients as against 2% observed by Sais et al[111].This may be due to high percentage of reactive leprosy in our study and high prevalence of multibacillary leprosy patients in India.

Systemic involvement

Systemic involvement was observed in 87.5% of patients with the joint pain being the commonest presenting manifestation (52.5%). This was again in consonance with the systemic involvement observed by Ekenstam et al[113] in 51% of patients where the musculoskeletal system was most commonly involved (43%). However Sais et al [111] observed systemic involvement only in 20% of the cases with joint involvement in 36.7% of all cases.

Gastrointestinal involvement mainly in the form of abdominal pain, melena, occult blood in stools and bowel edema in Ultrasonography abdomen, was observed in 13(32.5%) patients which was consistent with 9.5% cases reported by Sais et al[111].

Winkelmann and Ditto[114] found renal involvement in 61% of their patients, while in our study, renal involvement was seen in only 11(27.5%) of patients. In our study renal involvement was seen in and collagen vascular

disorders in the form of elevated serum urea and creatinine, proteinuria and microscopic hematuria. In patients of Henoch Schonlein purpura with renal involvement, three had extensive cutaneous lesions all over the body while seven patients had musculoskeletal symptoms. This is consistent with study by Gupta et al[112] where 16 % of cases had renal involvement, in that 3 had extensive cutaneous lesions, while 3 had musculoskeletal symptoms.

Pulmonary involvement was seen in only one case in the form of positive mantoux test and cavities (tuberculosis) in a patient of Henoch Schonlein purpura vasculitis. Tuberculosis was seen in (2.5 %) of our patients in contrast to no case detection in study by Sais et al [111] and Ekenstam et al[113]. This was probably due to the high prevalence of tuberculosis in India.

Laboratory findings

The laboratory parameters reflecting systemic inflammatory responses were elevated ESR in 27 (67.5%) patients, anemia in 16 (40%) and leukocytosis in 12(30%) patients. It was consistent with study by Sais et al[111] where elevated ESR (52.4%), anemia (37%) and leukocytosis (18%) was observed.

The renal functions were altered in 6 (15%) patients in the form of elevated urea and creatinine and abnormal urine examination in 14 (35%) patients. Sais et al [111] found these parameters to be 26 and 21.1%, respectively. Liver function tests were within normal limits in all patients while Sais et al[111] observed elevated transaminase levels in 18% of patients.

The collagen vascular disease workup revealed positive Anti nuclear antibodies in 12.5% and rheumatoid factor in 5% patients, which was in consistent with study results reported by Gupta et al [112] . In addition serum cryoglobulins were found positive in 1 (2.5%) patient consistent with study by Gupta et al in which 1(2%) patient had serum cryoglobulin. ASO titer was raised in 10 (25%) patients, while Mantoux test was positive in one (2.5%) of our patients. Gupta et al [112] reported ASO titre was found raised only one (2%) patient.

Histopathology

Histopathology showed features of leukocytoclastic vasculitis in 34 patients. In the remaining 6, perivascular lymphocytic infiltrate with no evidence of vasculitis was observed which was consistent with study by Gupta et al[111] where out of 42 patients, 5 patients did not show evidence of vasculitis. Hence the diagnosis of cutaneous small vessel vasculitis was considered on the basis of high index of clinical suspicion. Moreover, histopathology was noncontributory in these cases, probably due to the biopsy of the lesion at a late stage in the disease evolution as mentioned in the literatue[44-48]. We found 25 % of patients with Erythema nodosum leprosum showing features of leukocytoclastic vasculitis in addition to mixed panniculitis as reported by Giam YC et al[115].

SUMMARY

40 patients, diagnosed with cutaneous small vessel vasculitides, based on history, clinical features, laboratory findings, histopathology were included in the study. This study was done for a period of 24 months (May2008 to May 2010) .

Sex

15 were male (38%) and 25 were female (62%). The male : female ratio was 1:1.7.

Age

Majority of patients were between the ages of 11 – 40 years. The mean age of our study group was 31 years for males and 24 years for females.

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Clinical spectrum

The common types of cutaneous small vessel vasculitis included Henoch Schonlein purpura (45%), Erythema nodosum leprosum (25%), connective tissue disorders with vasculitis (17.5%). The less common types were urticarial vasculitis (5%), septic vasculitis (5%) and Essential mixed cryoglobulinemic vasculitis(2.5%).

Aetiology

Infections(55%) mainly the upper respiratory tract infections were the commonest underlying cause encountered in our study followed by collagen vascular disorder (17.5%) and drugs (15%).

Symptoms associated with skin lesions

Itching was the predominant symptom noted in 30 % of patients followed by fever and burning sensation.

Systemic symptoms

Joint pain was the most common systemic symptom observed in 47.5% of patients followed by joint swelling. In patients of HSP with renal involvement, three had extensive cutaneous lesions all over the body while seven patients had musculoskeletal symptoms.

Morphology & distribution

The morphology of lesions and their distribution were concordant with those described in the literature . Clinically most of the patients presented with palpable purpura in the dependent parts especially the legs. Legs involvement and palpable purpura were noted in 100% of cases of Henoch Schonlein purpura. Koebner phenomenon was observed in two patients.

Laboratory findings

Common laboratory findings observed were elevated ESR(67.5%), and anemia (40%) .

Histopathology

Leukoocytoclastic vasculitis was the most common histopathological pattern observed in 34 cases.We found a significant proportion(25%) of patients with ENL presenting as leukocytoclastic vasculitis in addition to mixed panniculitis.

CONCLUSION

1. Henoch Schonlein purpura was the most common cutaneous small vessel vasculitis followed by Erythema nodosum leprosum.
2. Cutaneous small vessel vasculitis was more common in females.
3. Majority of the patients were between 11 – 40 years of age.
4. Upper respiratory tract infection was the commonest etiologic factor in cutaneous small vessel vasculitis.
5. Joint pain was the common systemic symptom found in majority of patients.
6. Nonthrombogenic palpable purpura represents clinical hallmark in cutaneous small vessel vasculitis.
7. Widespread cutaneous manifestations may be the cutaneous marker of serious systemic involvement.
8. Elevated ESR and anemia were the common laboratory abnormalities.
9. Leukocytoclastic vasculitis was the common histopathological pattern in cutaneous small vessel vasculitis.
10. Significant proportion of patients with Erythema nodosum Leprosum presenting as leukocytoclastic vasculitis .
11. Early biopsy and Clinicopathological correlation is necessary for the diagnosis of cutaneous small vessel vasculitis.

KEY TO MASTER CHART

Morphology

1 = Palpable purpura

2 = Nodules

3 = Plaques

4 = Nodules and plaques

5 = Ulcer

6 = Urticaria

7 = Gangrene

8 = Pustules

9 = Bulla with / without ulcer

10 = Ecchymoses

DSL = Duration of skin lesions

Symptoms

1 = Burning sensation

2 = Itching

3 = pain

4 = Fever

Systemic symptoms

1 = Joint pain

2 = Joint swelling

3 = Melena

4 = Abdominal pain

5 = Diarrhoea

6 = Hemoptysis

Drugs

1 = NSAIDS (Non steroidal anti inflammatory drugs)

2 = Antibiotics

3 = Unknown

Region

1 = Lower limb

2 = Lower limb and trunk

3 = lower limb, trunk and upper limb

4 = Lower limb and upper limb

ASO titre = Anti Streptolysin O titre

Urine routine

1 = Hematuria

2 = Proteinuria

3 = Hematuria and Proteinuria

RFT = Renal function test

1 = Elevated urea and creatinine

LFT = Liver function test

RF = Rheumatoid factor

ANA = Anti nuclear antibody

CRGT = Cryoglobulin test

CXR = Chest X ray

Cavt = Cavity

MX = Mantoux test

USG Abdomen = Ultrasonography of Abdomen

B.E = Bowel wall edema

SSS = Slit skin smear

CD = Clinical diagnosis

HSP = Henoch Schonlein purpura

LEV = Lupus erythematosus with vasculitis

RAV = Rheumatoid arthritis with vasculitis

ENL = Erythema nodosum leprosum

UV = Urticarial vasculitis

SV = Septic vasculitis

EMCV = Essential mixed cryoglobulinemic vasculitis

HP = Histopathology

LCV = Leukocytoclastic vasculitis

MP = Mixed panniculitis

NEV = No evidence of vasculitis

P = Positive

N = Negative

NRL = Normal

F = Female

M = Male

Y = Years

M = Months

D = Days

MASTER CHART

	Name	Age / Sex	Morplology	DSL	Symtoms	Systemic symtoms	Sore Throat	Drugs	Regions	ASO titre	Stool Occult Blood	Urine Routine	RFT	LFT	RF	ANA	CRGT	CXR	MX	Virual Markers	USG Abdomen	Leuko Cytosis	Anemia	Elevated ESR	SSS	CD	HP
1	Deepika	12y/F	1	2w	2	1	P	_	3	P	P	3	1	NRL	N	N	N	NRL	N	N	NRL	P	P	P	_	HSP	LCV
2	Arul pondi	19y/M	1	3M	2	4	_	_	3	P	P	3	1	NRL	N	N	N	NRL	N	N	B.E	P	_	P	_	HSP	LCV
3	Sumathy	28y/F	2	2M	_	1	_	_	1	_	_	_	NRL	NRL	N	N	N	NRL	N	N	NRL	_	P	P	P	ENL	LCV, MP
4	Arumugam	50y/M	7	15D	_	_	_	_	4	_	_	_	NRL	NRL	P	N	P	NRL	N	N	NRL	_	_	P	_	EMCV	LCV
5	Baby of Gayathiri	15D /F	8	5D	4	2	_	_	4	_	_	_	NRL	NRL	N	N	N	NRL	N	N	NRL	P	_	P	_	SV	LCV
6	Abdul Majeet	45y/M	2	6M	_	_	_	_	3	_	_	_	NRL	NRL	N	N	N	NRL	N	N	NRL	_	_	P	P	ENL	LCV, MP
7	Dinesh Kumar	9y/M	1	1D	4	1	P	_	1	P	P	_	NRL	NRL	N	N	N	NRL	N	N	NRL	P	P	_	_	HSP	NEV
8	Deepa	18y/F	1	1M	4	1	_	_	1	_	_	2	1	NRL	N	P	N	NRL	N	N	NRL	_	P	P	_	LEV	LCV
9	Bhuvana	7 y/F	1	1D	_	1	P	_	1	P	_	1	NRL	NRL	N	N	N	NRL	N	N	NRL	P	_	P	_	HSP	LCV
10	Perumal	50y/M	2	6M	_	0	_	_	3	_	_	_	NRL	NRL	N	N	N	NRL	N	N	NRL	P	_	_	P	ENL	LCV, MP
11	Alagu	48y/M	5	1M	3	1	_	_	3	_	_	2	1	NRL	N	P	N	NRL	N	N	NRL	_	_	P	_	LEV	LCV
12	Priya	3y/F	10	2D	_	_	_	_	1	_	_	_	NRL	NRL	N	N	N	NRL	N	N	NRL	P	_	P	_	SV	LCV
13	Praveen	7 y/M	6	15D	1	4	_	_	4	_	_	_	NRL	NRL	N	N	N	NRL	N	N	NRL	_	_	P	_	UV	LCV
14	Kavitha	6 y/F	1	7D	2	2	P	_	2	P	P	_	NRL	NRL	N	N	N	NRL	N	N	NRL	P	_	_	_	HSP	NEV
15	Angayarkanni	28y/M	5	6M	3	1	_	_	1	_	_	_	NRL	NRL	N	N	N	NRL	N	N	NRL	_	P	P	_	LEV	LCV
16	Eswar	40y/M	4	9M	3	_	_	_	1	_	_	_	NRL	NRL	N	N	N	NRL	N	N	NRL	P	P	_	P	ENL	NEV
17	Pondiammal	40y/F	9	9M	_	2	_	_	1	_	_	_	NRL	NRL	P	P	N	NRL	N	N	NRL	P	P	_	_	RAV	LCV
18	Angammal	35 y/F	1	6M	2	6	_	3	2	_	_	1	NRL	NRL	N	N	N	Cavt	P	N	NRL	_	_	_	_	HSP	LCV
19	Karthick	40y/M	1	3D	2	3	_	2	1	_	P	_	NRL	NRL	N	N	N	NRL	N	N	NRL	_	_	P	P	HSP	NEV
20	Panchavarnam	23y/F	2	3M	_	1	_	_	3	_	_	_	NRL	NRL	N	N	N	NRL	N	N	NRL	_	_	_	P	ENL	LCV, MP

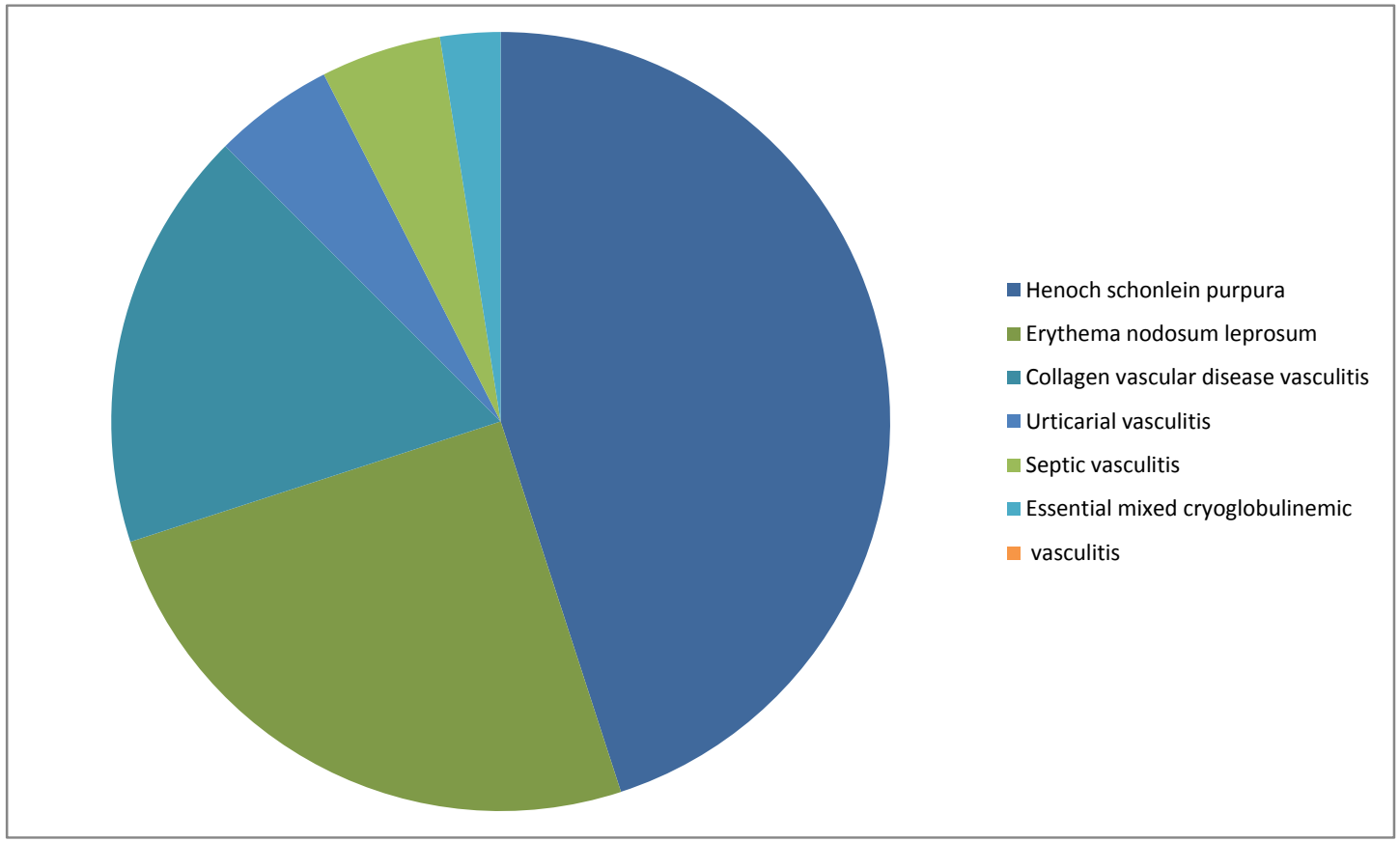

Figure 1: Clinical Spectrum

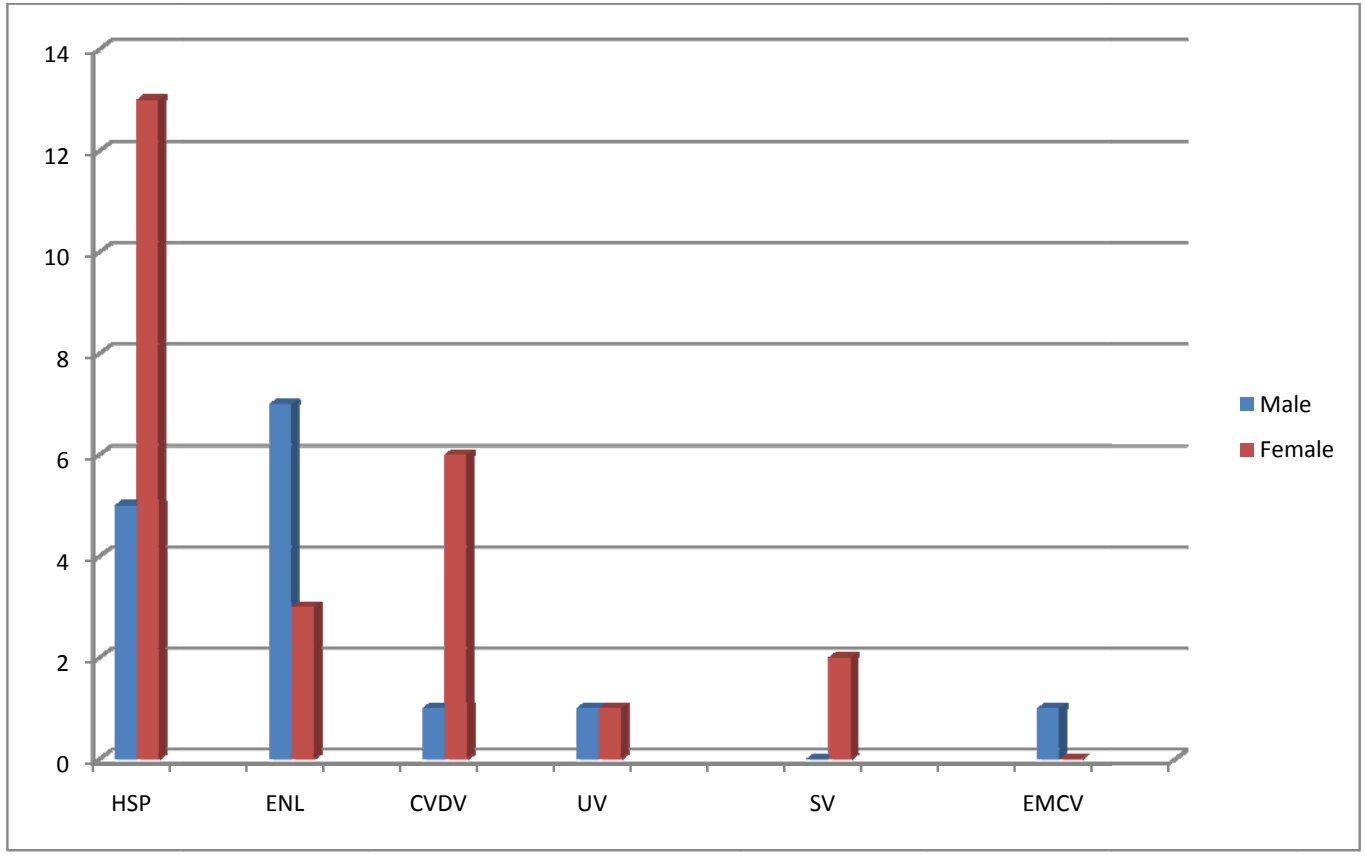

Figure 2: Sex Distribution

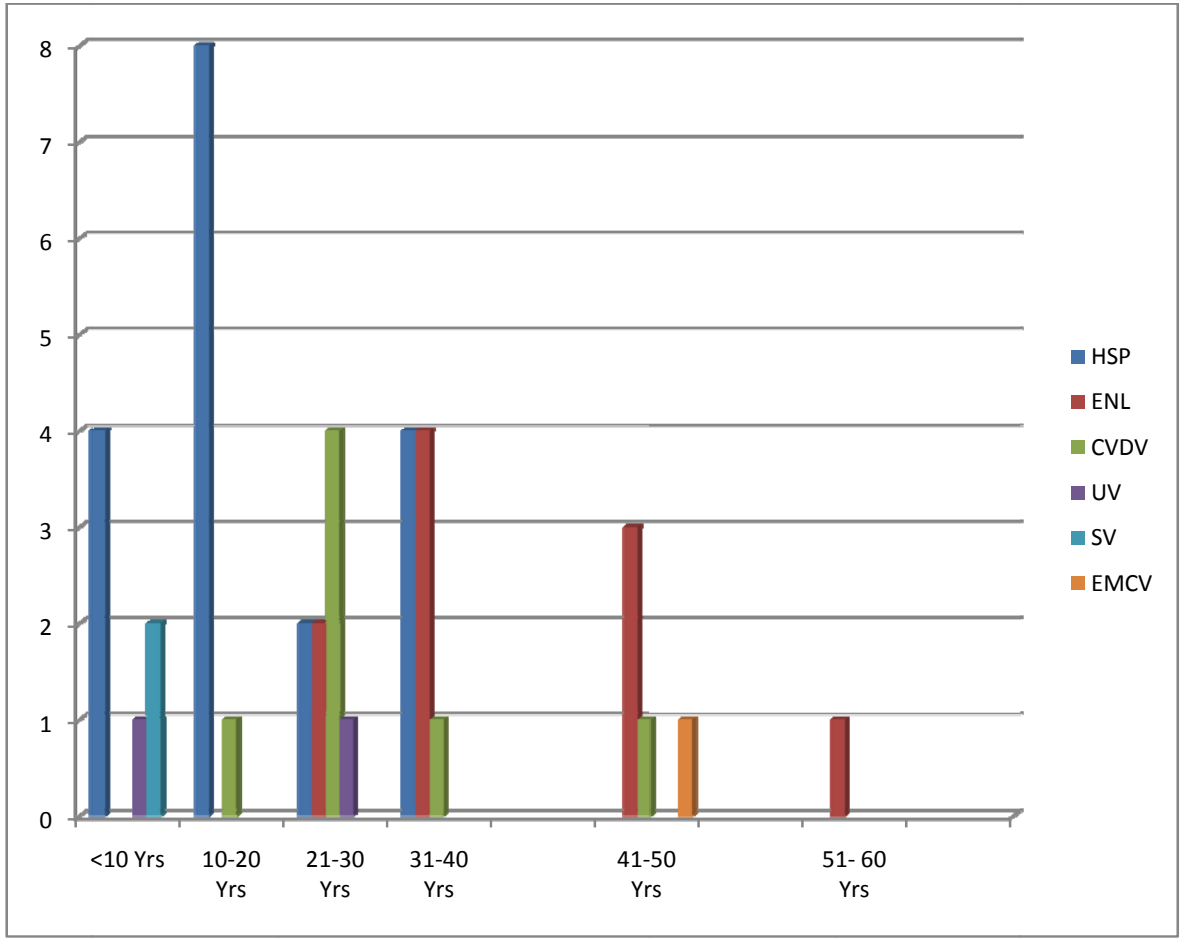

Figure 3: Age Distribution

PROFORMA

- Name
- Age
- Sex
- Hosp.No
- Occupation
- Presenting complaint
- Duration of skin lesions
- **Precipitating factors**
    - Drugs
    - Infection(sore throat)
    - Trauma
- **Symptoms**
    - Fever
    - Pain
    - Burning sensation
    - Itching
    - Symmetrical
    - Site, Description
- **Systemic symptoms**
    - Joint pain
    - Joint swelling
    - Melena
    - Abdominal pain
    - Diarrhoea
    - Hemoptysis
- **General Examination**
    - Weight
    - Temperature
    - Pallor
    - Lymphadenopathy
- **Type of skin lesion**
    - Purpura
    - Nodule
    - Plaque
    - Ulcer

Urticaria
Gangrene
Pustule
Bulla
Ecchymoses

- **Systemic examination**
  - CVS
  - RS
  - CNS
  - GIT
- **Investigations**
  - ASO titre
  - Stool occult blood
  - Urine examination
  - Complete hemogram
    - Hb (gm%)
    - TC
    - DC
    - ESR
    - Platelet count
  - Diascopy
  - LFT
  - RFT
  - ANA
  - RF
  - Cryoglobulin test
  - Chest x ray
  - Mantoux test
  - Viral markers (Hep B , C and HIV)
  - USG Abdomen
  - Slit skin smear for AFB
  - Skin Biopsy
  - Special stain
- Histopathological findings
- Final diagnosis

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