

## **Clinicopathological study of cutaneous vasculitis**

**Dr. Sudharani Chintagunta\***, Dr. Katukuri Pavani, Dr. Geeta Kiran Arakkal

*Department of Dermatology, Venereology and Leprosy, Gandhi Medical College, Hyderabad, Telangana, India*

### **\*Correspondence Info:**

Dr. Sudharani Chintagunta

Assistant Professor of Dermatology,

Venereology and Leprosy,

Gandhi Medical College, Hyderabad, Telangana, India

E-mail: [schintagunta@gmail.com](mailto:schintagunta@gmail.com)

### **Abstract**

**Introduction:** Cutaneous vasculitis has varied clinical manifestations. It may be idiopathic or associated with a spectrum of underlying conditions. Skin is involved in both small vessel vasculitis and medium vessel vasculitis. Majority of vasculitic cases are relatively benign and self limiting in nature associated with wide spectrum of clinical associations. The histopathological features may help in the confirmation of clinical diagnosis.

**Materials and Methods:** The study was conducted at department of dermatology for a period of two years. Patients clinically diagnosed as cutaneous vasculitis were included in the study. 38 patients with features suggestive of cutaneous vasculitis were included. Detailed history and clinical examination were done and two skin biopsies were taken from each patient for routine histopathology and direct immunofluorescence

**Results:** A Total of 38 patients studied, clinically 27(71.05%) were Leucocytoclastic vasculitis (LCV) and 10(26.1%) cases were Henoch Schonlein purpura (HSP) and one (2.63%) was Urticarial vasculitis. Based on histopathological examination majority 92.1% were diagnosed as leukocytoclastic vasculitis. DIF showed immune reactants in 76.47% of which IgA deposits were commonest in 69.23% followed by C3 in 61.53% and IgG, IgM in 7.69% each. Systemic involvement was seen in 52.63% patients. About 57.89% cases were found to be idiopathic Drugs were implicated in 21.05% cases, infections in 18.42% and connective tissue disorders in 2.63%.

**Conclusions:** Skin biopsy and DIF were in concordance with clinical diagnosis in majority of the cases

**Keywords:** Leucocytoclastic vasculitis, Henoch Scholein purpura, DIF, Skin Biopsy.

### **1. Introduction**

The vasculitides are a heterogenous group of uncommon diseases characterized by inflammatory cell infiltration and necrosis of blood vessels compromising their function leading to haemorrhagic or ischaemic events [1] Blood vessels of any caliber in any organ system may be involved with wide variety of clinical manifestations.

Systemic and localized vasculitides frequently manifest in the skin because of the abundant vascular supply in the dermis and subcutaneous tissue, hydrostatic pressure within these vascular beds and proximity to environmental influences. [2]

Clinically, cutaneous vasculitis can present with varied morphologies that include urticaria, purpura, haemorrhagic vesicles, ulcers, papules, nodules, livedo-reticularis, infarcts and digital gangrene [3] The type of cutaneous lesions closely correlate with the size of the vessel affected. Cutaneous vasculitis presents in wide variety of conditions with different degrees of systemic involvement. [4]

Etiologically vasculitis can be primary vasculitis, occurring in the absence of a recognized precipitating cause

or secondary vasculitis which is a manifestation of connective tissue disease, infection, adverse drug eruption, or a paraneoplastic phenomenon. Skin biopsy along with clinical history, physical and laboratory findings helps to arrive at specific diagnosis.

Skin biopsy provides diagnostic confirmation of cutaneous vasculitis and should be performed in all suspected cases of vasculitis. The biopsy provides information regarding size of involved vessel and the type of inflammatory infiltrate. The diagnostic yield of a biopsy depends on the timing, type, and site and the location chosen to biopsy. [3] Direct immunofluorescence should be considered in addition to HPE, depending on the clinical presentation.

### **2. Materials and Methods**

The study was conducted at department of dermatology over a period of two years. All patients clinically diagnosed as cutaneous vasculitis irrespective of age and sex were included in the study. Patients with thrombocytopenia

(platelet count <50,000/c mm) and disorders of coagulation were excluded.

A detailed history including age, sex, occupation, duration, present history, past history and drug history were carefully recorded as per the proforma and thorough clinical examination was done. Baseline investigations like complete blood picture, erythrocyte sedimentation rate, complete urine examination for albumin, sugar, casts, 24 hr urinary protein, stool for occult blood, markers for hepatitis B, C and HIV, random blood sugar, RFT, LFT, chest X ray, ultrasound abdomen, ASO titres, Mantoux test, rheumatoid factor, antinuclear antibody and skin biopsy were done in all cases. Antineutrophilic cytoplasmic antibody titres were done wherever feasible.

Histopathological examination of lesional skin was performed in all patients. Skin biopsy (two biopsies) was taken from a lesion less than 24- 48 hours and sent for light microscopy and DIF. Direct immunofluorescence was done in 17 patients and studied with fluorescein isothiocyanate labeled IgG, IgA, IgM and C3.

### 3. Results

Out of 38 patients 60.52% were male and 39.47% were females. Male to female ratio was 1.5:1. Age of the patients ranged from 7 to 66 years. The commonest age group affected was 11 to 20 years. Mean age of study group was 26.24 years. Time since onset of lesions varied from 1 day to 2 months. 20 (52.63%) patients had onset of lesions for a duration of less than 1 week, followed by more than 1 week in 7(18.42%), more than 2 weeks in 5 (13.15%) and more than 3 weeks in 2.63%. Skin lesions were asymptomatic in 55.26% while symptomatic in 44.7% patients.

Palpable purpura was the commonest cutaneous sign noticed in 86.84% patients. The other cutaneous lesions were plaques in 7.89%, vesicles in 7.89%, bullae 10.52%, ulcers 5.26% and wheals in 2.63% patients. Commonest sites were lower limbs in 94.73%, thighs 36.84%, buttocks 13.15%, trunk 13.15%, upper limbs 34.21%, face 5.26% patients respectively. There was history of recurrence in 26.31%.

Systemic involvement was encountered in 52.63% patients. Fever was the commonest symptom seen in 39.47% patients. Arthralgia was the commonest systemic presentation seen in 47.36% patients. Gastrointestinal involvement is 39.47% in the form of pain abdomen in 34.21%, diarrhoea in 13.15% and melena in 5.26% patients.

About 57.89% cases were found to be idiopathic. History of drug intake was present in 21.05% and upper respiratory tract infection in 18.42% of cases. Collagen work up was positive in one (2.63%) case in the form of ANA positivity. Malignancy was not detected in any of our cases. 2.63% patient gave a past history of tuberculosis.

Laboratory work up revealed anemia in 52.63%, leucocytosis in 10.52%, elevated ESR in 7.89%, proteinuria in

7.89%, hematuria in 5.26%, elevated bilirubin levels in 2.63% patient each. Serum amylase and stool for occult blood were positive in 5.26% cases. Rheumatoid factor was positive in 5.26%, ANA in 1 2.63%, and ASO titres in 7.89%

Direct immunofluorescence results were available for 17 patients only. Out of which 13 (76.47%) showed evidence of immune deposits and negative in 23.52%. IgA deposits were commonest and seen in 9(69.23%) patients followed by C3 in 8 (61.53%) and IgG, IgM in one (7.69%).

Clinically 23 out of 38 (60%) cases were diagnosed as leucocytoclastic vasculitis, 14 (26.31%) Henoch Schonlein purpura and one (2.63%) cases as urticarial vasculitis. Based on histopathological examination, 35 out of 38 (92.1%) were diagnosed as leucocytoclastic vasculitis and 3 (7.89%) showed no evidence of vasculitis. Out of 23 clinically diagnosed LCV, 20 were consistent with the histopathology and there was no evidence in the rest. Out of 14 cases of Henoch Schonlein Purpura all the 14 showed features of leucocytoclastic vasculitis on histopathology.

**Table 1: Cutaneous signs**

Signs	No. of cases	Percentage (%)
Palpable purpura	33	86.84%
Plaques	3	7.89%
Vesicles	3	7.89%
Bullae	4	10.52%
Ulcers	2	5.26%
Urticarial lesions	1	2.63%

**Table 2: Systemic Features**

Clinical features	No. of cases	Percentage (%)
Arthralgia	15	47.36%
Fever	18	39.47%
Pain abdomen	4	34.21%
Diarrhoea	13	13.15%
Joint swelling	5	10.52%
Melena	2	5.26%

**Table 3: Laboratory Findings**

Lab Findings	No. of Cases	Percentage
Anemia (Hb < 10 gm %)	20	52.63
Leucocytosis (>11, 000 cells/dl)	4	10.52
Raised ESR (> 20mm)	3	7.89
Raised Bilirubin	1	2.63
Proteinuria(>150mg/24hrs)	3	7.89
Hematuria(>5 RBC/hpf)	2	5.26
Pus Cells (>5)	1	2.63
Stool for occult blood	2	5.26
Raised ASO Titre(200 IU)	3	7.89
Positive Rheumatoid factor	2	5.26
ANA positivity	1	2.63
Positive Mantoux test (>15 mm in duration)	1	2.63

**Table 4: Clinical Diagnosis Vs Histopathological Diagnosis in cutaneous vasculitis**

Clinical diagnosis (No. of cases)	Histopathological diagnosis (No. of cases)
LCV (23)	LCV(20), NEV(3)
HSP(14)	LCV (14)
UV (1)	LCV (1)

LCV – Leucocytoclastic vasculitis; HSP – Henoch Schonlein purpura; UV - Urticarial Vasculitis

**Table 5: Direct immune fluorescence**

	No. of Patients	Percentage
DIF Positive	13	76.47%
DIF Negative	4	23.52%

**Table: 6 Type of immune deposits on Direct Immunofluorescence**

Type of immune deposits	No. of patients	Percentage
IgA	9	69.23%
C3	8	61.53%
IgG, IgM	1	7.69%

#### 4. Discussion

In our study we analysed the clinical features, histopathological features, relevant history and various investigations to arrive at a diagnosis of cutaneous vasculitis.

Clinically 23 (60%) patients were diagnosed as leucocytoclastic vasculitis, 14 (37%) as Henoch Schonlein purpura and one (2.63%) case as urticarial vasculitis. Whereas Gupta *et al* [5] diagnosed 82% as leucocytoclastic vasculitis, 4% as Henoch Schonlein Purpura and 4% as urticarial vasculitis.

Histopathology was consistent with diagnosis of vasculitis in 35( 92.1%) in our study, while it was positive in 59.6% and 72% in studies by Gupta *et al* and Sais *et al*. Direct immunofluorescence results were positive in 13( 76.47% ) which was similar to 73.9% by Gupta *et al*. It was reported as 84.3% by Sais *et al*. [5,6]

IgA deposits were commonest in 9(69.23%) patients in our study which was similar to 64.7% as observed by Sais *et al*. [6] Out of 14 patients of Henoch Schonlein purpura, DIF results were available for 7 patients, out of which 4 (57%) showed IgA deposits and only one (25%) had renal involvement in the form of proteinuria.

The next common immune deposit was C3 seen in 61.53% in our study which was similar to 52.2% reported by Gupta *et al*. [5] IgG and IgM were seen in one ( 7.69%) each in our study which was in contrast to 42.2% IgG and 49% IgM as reported by Sais *et al* and 52.2% as reported by Gupta *et al*. [6,5]

The most common and the initial clinical presentation in our study was palpable purpura seen in 86.84%. This was comparable with studies by Sais *et al*, Gupta *et al*, and Martinez *et al* in 89.2%, 86% and 80% respectively. [5-7]

Lower limbs were the most commonly involved sites in our study in 94.3%. This was similar to 94% as reported by Martinez *et al*. [7] This could be due to sluggish blood flow in dependant areas which facilitate deposition of immune complexes.

Skin lesions were asymptomatic in 55.26%, symptomatic in 44.7%. This was in contrast to Gupta *et al* who reported asymptomatic skin lesions in 90%. [8]

A possible precipitating agents were suspected in 42.1% of our patients which was similar to 44.7% as reported by Ekenstam *et al*. [8]

History of drug intake was seen in 21.05% of our patients which was comparable to 28.2% by Leelavati *et al* and infection prior to the onset of skin lesions was present in 18.42% of our study which was comparable to 20.2% in study by Leelavati *et al*. [9] In majority of cases upper respiratory tract infection precipitated the illness.

Collagen work up was positive in 2.63% cases in the form of ANA positivity while it was seen in 6% in the study by Sais *et al*. [6]

Systemic involvement was observed in 52.63%. This was similar to 51% and 50% as reported by Ekenstam *et al* and Gupta *et al* respectively. [8,5]

Fever was seen in 39.47% of our patients which was similar to that seen in 31.6% by Sais *et al*. [6] Arthralgia was the commonest extra cutaneous manifestation seen in 47.36% in our study which was similar to Ekenstam *et al* who reported 43% cases with joint involvement. [8]

Gastrointestinal tract involvement was seen in 39.47% of our patients in the form of pain abdomen, diarrhoea and melena while it was seen in 9.5% cases by Sais *et al*. [6] Presentation with pain abdomen was common in HSP in 60% and gastrointestinal hemorrhage in 20% patients as seen in our study. Renal involvement was seen in 10.52% patients in our study whereas Gupta *et al*, Sais *et al* found renal involvement in 16% and 13% respectively. [5,6] Pulmonary involvement was not seen in our study, whereas Winkelman *et al* reported 40% and Ekenstam *et al* reported in 8% of their patients. [10,8]

Past history of similar cutaneous lesions were obtained in 10 (26.31%) of our patients while Gupta *et al* reported it as 18%. [1]

Past history of tuberculosis was seen in 2.63% of our patients. It was seen in 6% of cases by Gupta *et al*. [5] HCV positivity was not seen in our study, while it was observed in 2% of patients by Gupta *et al* and 21% by Sais *et al*. [5,6]

Laboratory work up revealed anemia in 52.63%, leucocytosis in 10.52%, elevated ESR 7.89% in our study. Sais *et al* reported anemia in 37%, leucocytosis in 18% and raised ESR in 52.4%. Elevated bilirubin levels in 2.63% patient. LFT was normal in all cases reported by Gupta *et al* while Sais *et al* observed elevated transaminases in 18%. [5,6] ASO titres were positive in (3) 7.89% of our patients while Gupta *et al* reported raised ASO titres in 2% of their cases. [5] Mantoux was positive in 2.63% of our patients while Gupta *et al* reported as 4%. [5] Rheumatoid factor was positive in (2) 5.26% which was similar to 6% by Gupta *et al*. It was seen in 26.4% by Sais *et al*. [5,6] ANA was positive in (1) 2.63% of our patients whereas it was reported as 6% by Gupta *et al* and 28.5% by Sais *et al*. [5,6]

Palpable purpura was the commonest cutaneous sign noted in 86.84%) patients; commonest site was the lower limbs. Systemic involvement was encountered in 20 (52.63%) patients. Gastrointestinal tract involvement observed in 39.47% and renal involvement in 10.52% patients.

Pulmonary, Cardiac and Central Nervous System were not involved in our study.

57.89% cases were found to be idiopathic .History of drug intake in 21.05% and upper respiratory tract infection in 18.42% of cases. Collagen work up was positive in 2.63%. Malignancy was not detected in any of our cases. History of recurrence was noted in 26.31%.

Out of 38 cases 27 (71.05%) were diagnosed as leucocytoclastic vasculitis, 10 (26.31%) Henoch Schonlein purpura and one (2.63%) as are with urticarial vasculitis. Based on histopathological examination majority 92.1% were diagnosed as leukocytoclastic vasculitis, one (2.63%) with lymphocytic vasculitis and three (7.89%) showed no evidence of vasculitis. DIF showed immune reactants in 76.47% of which IgA deposits were commonest in 69.23% followed by C3 in 61.53% and IgG, IgM in 7.69% each.

## 5. Conclusions

This study showed that the commonest presentation of cutaneous vasculitis was palpable pupura which mainly affected the lower limbs. The disease was self limiting in majority of cases. Though systemic involvement was present in (52.63%) cases in our study it was mild and transient and resolved without any sequelae.

The most common precipitating cause of cutaneous vasculitis was drugs and infections. This highlights the importance of a detailed history in patients presenting with cutaneous vasculitis .A number of screening investigations were performed to evaluate the possible underlying etiology of cutaneous vasculitis. Skin biopsy and DIF were in concordance with clinical diagnosis in majority of the cases, hence may be utilized for confirmation of leucocytoclastic vasculitis.

Patients with recurrent vasculitis should be evaluated regularly as cutaneous vasculitis may signal an underlying serious systemic disease which may present later in the course.

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