Cutaneous vasculitis: An etiological and clinicopathological study

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***Abstract*- Background:** Cutaneous vasculitis has varied clinical manifestations. Skin is involved in both small vessel vasculitis and medium vessel vasculitis. Skin biopsy is the gold standard for the diagnosis of cutaneous vasculitis. Based on histology, vasculitis can be classified on the size of vessels affected and the dominant immune cell mediating the inflammation. Along with histopathology, other investigations like complete hemogram and serology are needed to make an etiological diagnosis.

Objectives: 1. To study the different patterns of cutaneous vasculitis along with their underlying etiologic factors
2. To assess the clinicopathological correlation.

Materials and methods: A retrospective study over a period of 3 years from July 2011 to July 2014 was conducted. Histopathologically diagnosed cases of cutaneous vasculitis were included in the study and analyzed with the clinical details and investigations.

Results: Out of 56 patients, 35 patients had idiopathic cutaneous small vessel vasculitis (CSVV) and 10 patients had urticarial vasculitis. Purpura was the most common cutaneous manifestation, seen in 41 patients. Histologically the most common pattern observed was leukocytoclastic vasculitis, seen in 32 of cases.

Conclusion: The workup of patients with cutaneous vasculitis includes detailed history, clinical examination, skin biopsy and other investigations to rule out multisystem involvement. Follow up is essential as cutaneous manifestation may be the early indication of serious systemic involvement.

***Index Terms*-** Leukocytoclastic vasculitis, cutaneous vasculitis

I. INTRODUCTION

Vasculitis is the inflammation of blood vessel wall. It has a wide range of clinical manifestations. It can range in severity from a self-limited single-organ disorder to a life-threatening disease with the prospect of multiple-organ failure.[1] It may be a primary disorder or a presenting sign of primary systemic vasculitis such as Polyarteritis nodosa (PAN), Wegener's granulomatosis (WG), Churg Strauss syndrome (CSS) or secondary to drugs, infections or systemic diseases such as connective tissue disease (CTD) and malignancy. [1, 2]

Based on the size of the vessel wall affected, cutaneous vasculitis is classified as small vessel vasculitis (SVV), medium vessel vasculitis (MVV) and large vessel vasculitis. Skin is affected in both SVV and MVV. Cutaneous vasculitides are usually characterized histologically by leukocytoclastic changes. Their histology shows infiltration of neutrophils within and around blood vessel walls, leukocytoclasia (degranulation and fragmentation of neutrophils leading to the production of nuclear "dust"), fibrinoid necrosis of the damaged vessel walls, and necrosis, swelling and proliferation of the endothelial cells.[3]

Clinical manifestations of cutaneous vasculitis occur when small and/or medium vessels are involved. Small vessel vasculitis can present as palpable purpura, urticaria, pustules, vesicles, petechiae, or erythema multiforme-like lesions. Signs of medium vessel vasculitis include livedo reticularis, ulcers, and subcutaneous nodules. [4]

The classification of vasculitis is controversial with no generally accepted classification system. The classification system of the American College of Rheumatology (ACR) and of the Chapel Hill Consensus Conference (CHCC) have gained wide acceptance. Classification system of ACR of 1990 is based on clinical, histological and disease history while that of CHCC is based solely on histopathology.[5, 6]

Although there is a multitude of causes of cutaneous vasculitis, most of the cases are idiopathic.[4] The frequency of each of the cause is variable depending upon the epidemiological difference and prevalence of infections. Histopathology can be significantly variable and several overlapping features are seen between SVV and MVV.

There are only few studies from India on cutaneous vasculitis. This study was undertaken to evaluate the etiological factors and clinicopathological association with clinical lesions in patients with cutaneous vasculitis.

II. MATERIALS AND METHODS

The medical records of histopathologically proven cases of cutaneous vasculitis over a period of 3 years from July 2011 to July 2014 were analyzed at the Department of Dermatology, Father Muller Medical College, Mangalore, Karnataka, India. Age, sex, clinical history, possible etiologic factors, associated conditions and examination details of all the patients were recorded. A detailed perusal of the recorded history was done regarding the duration of vasculitis, constitutional and systemic symptoms, infections, drug intake, food allergy, malignancy, collagen vascular disease and any other coexisting systemic disorder. The investigative profile of each patient was noted. Histopathological re-evaluation of the skin biopsies stained with haematoxylin and eosin stain was done and findings were recorded. The diagnosis of cutaneous leukocytoclastic vasculitis was confirmed in the patients by the presence of an inflammatory infiltrate predominantly constituted by neutrophils, nuclear fragmentation, extravasation of RBCs and necrosis of dermal vessel walls.

RESULTS

Table 1 shows age distribution of the patients where minimum age was 11 years and maximum age was 63 years with mean age of 34±12.12 years. There were 32(57.14%) females and 24 (42.85%) males.

Minimum duration of disease was 2 days and maximum 90 days with more than 75% of the patients giving history of sudden onset of the symptoms. About 78.57% cases had a rapid progression of disease.

Aggravating factors included, drugs in 17.8% cases, exercise in 16%, and trauma and water exposure in 1.7% each. History of drug intake was present in 9 (30%) patients. The drugs associated with vasculitis were NSAIDs in 4 (40%) cases, antibiotics, antidiabetics and homeopathic drugs in 2 cases each.

Table 2 shows the symptoms of the patients where 30 (53.5%) patients had developed pain, 22 (39.3%) itching, 16 (28.5%) burning sensation. Constitutional symptoms such as fever was present in 13 (23.2%), arthralgia in 10 (17.8%) and myalgia in 8 (14,2%) of the patients. Systemic symptoms such as abdominal pain was present in 7 (12.5%), cough in 6 (10.7%), hematuria in 4 (7.1%), paresthesia in 3 and oral ulcers in 1of the patients. The involvement of body parts of the patients showed 56 (100%) of lower extremity, 8(14.2%) of upper extremity, 6 (10.7%) of trunk and generalized 4 (7.1%) involvement.

The morphology of lesion of the patients were 73% of palpable purpura(figure 1), more than 58% of petechiae, 35% of plaques, 28.5% papules, more than 16% ulcers, 28.5% vesicles and less than 10% pustules and necrosis. The most common combination of lesions was purpura and petechiae which was 18(32%)(figure 2)

Table 3 shows laboratory tests done in the patients. ESR was raised in 12(21%) of the patients, anemia was found in 4(7.14%) of the patients. Leukocytosis was found in 3 of the patients. Albuminuria and hematuria in urine examination was found in 2 patients each. ANA was positive in 1 patient. Renal function tests and liver function tests were normal in all patients.

Histopathological and direct immunofluorescence findings are shown in Table 4. Leukocytoclastic vasculitis (figure 3) was the most common pattern seen in 32 (57.1%) patients whereas lymphocytic vasculitis (figure 4) was noted in 22 (39.2%), granulomatous and eosinophilic vasculitis in 1 patient each.

Out of 56, DIF was done on 10 patients. Among them 6 (10.7%) had IgA and C3 deposits and 3 (5.3%) had fibrin and C3 deposit. No deposition was found in 1 case.

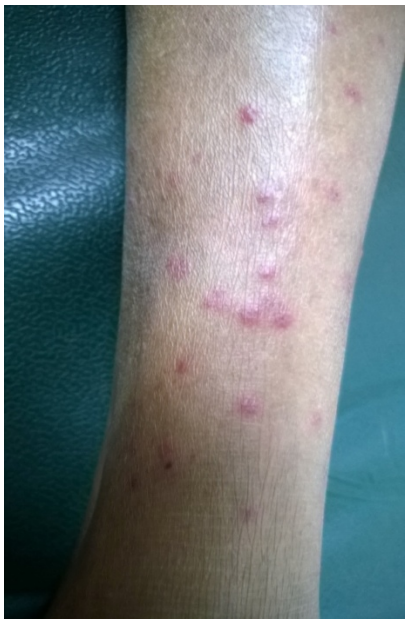

Figure 1: Palpable purpura

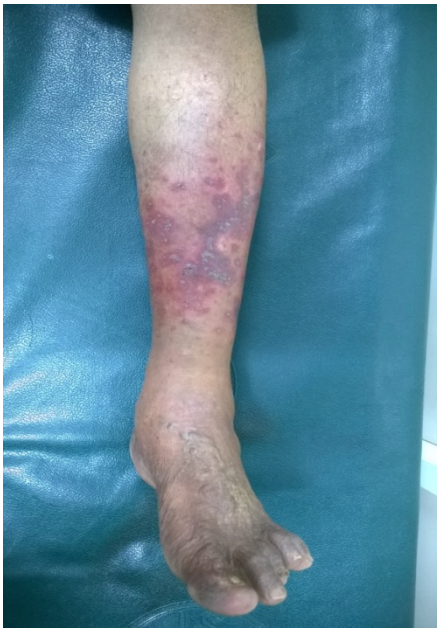

Fig 2: purpura and petechiae

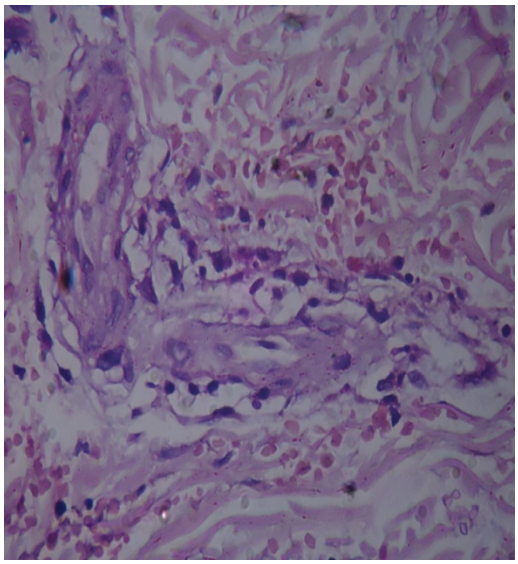

Figure 3: leukocytoclastic vasculitis showing fibrinoid necrosis

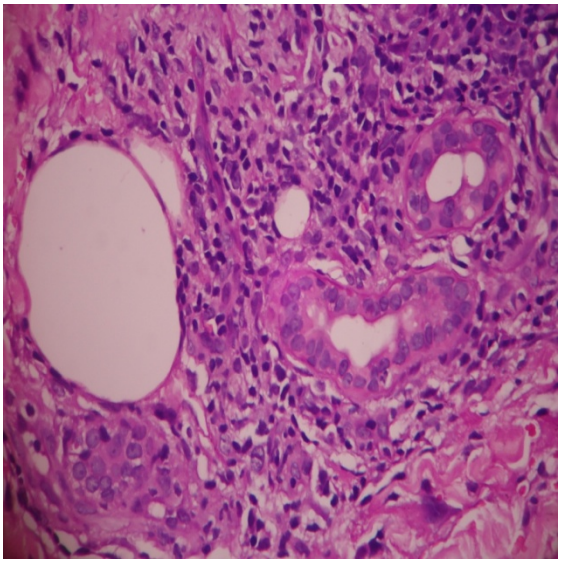

Figure 4: lymphocytic vasculitis showing lymphocytic infiltration.

Table 1: Demographic and clinical characteristics of study population (n=56)	
Age(years)	
Minimum	11
Maximum	63
Mean age	34±12.12
Sex, n (%).	
Male	24(57.14%)
Female	32(42.85%)
Mode of onset, n (%)	
Sudden	42(75%)
Insidious	14(25%)
Duration of disease(days)	
Minimum	2
Maximum	90
Mean	32±10.14
Progression of disease, n (%)	
Rapid	44(78.57%)
Slow	12(21.42%)
Aggravating factors, n (%)	
Drugs	10(17.86%)
Exercise	9(16.07%)
Trauma	1(1.78%)
Exposure to water	1(1.78%)
Drug history, n (%)	
Present	10(17.86%)
Absent	46(82.14%)
Drugs used, n=10(%)	
NSAIDs	4(40%)
Antibiotics	2(20%)
Antidiabetics	2(20%)
Homeopathic medications	2(20%)

Table 2:Symptoms, morphology and distribution(n=56)	
Presenting symptoms	
Pain	30(53.58%)
Itching	22(39.3%)
Burning	16(28.57%)
Constitutional symptoms	
Fever	13(23.21%)
Arthralgia	10(17.85%)
Myalgia	8(14.28%)
Systemic symptoms	

Abdominal pain	7(12.5%)
Cough	6(10.71%)
Hematuria	4(7.14%)
Paresthesia	3(5.35%)
Oral ulcer	1(1.7%)
Morphology of lesions	
Palpable purpura	41(73.21%)
Petechiae	33(58.92%)
Plaques	20(35.71%)
Papules	16(28.57%)
Vesicles and bullae	16(28.57%)
Ulcers	9(16.07%)
Urticarial lesions	9(16.97%)
Pustules	1(1.7%)
Necrosis	1(1.7%)
Combination of lesions	
Purpura and petechiae	18(32.14%)
Purpura, papules and petechiae	12(21.42%)
Purpura and ulceration	10(17.85%)
Others	16(28.57%)
Sites affected	
Lower extremities	56(100%)
Upper extremities	8(14.28%)
Trunk	6(10.71%)
Generalised	4(7.14%)

Table 3: Laboratory parameters	**n(%)**
ESR	12(21%)
Anemia	4(7.14%)
Leukocytosis	3(5.35%)
Albuminuria	2(3.57%)
Hematuria	2(3.57%)
ANA	1(1.7%)

Table 4: Histopathological and DIF findings	
Leukocytoclastic vasculitis	32(57.14%)
Lymphocytic vasculitis	22(39.28%)
Granulomatous vasculitis	1(1.7%)
Eosinophilic vasculitis	1(1.7%)
Immunoreactants (n=10)	
IgA and c3	6(10.71%)
Fibrinogen and c3	3(5.35%)
No deposit	1(1.7%)

Table 5: Histopathological feature	
Inflammatory infiltrate	56(100%)
Leukocytoclasia	30(53.5%)
Endothelial cell swelling	28(50%)
Dermal edema	26(46.4%)
RBC extravasation	20(35.7%)
Fibrinoid necrosis	15(26.7%)
Fibrin deposition	9(16%)

Table 5 shows the histopathological features in the slides examined. Inflammatory infiltrate was seen in all cases (100%). The second most common finding was leukocytoclasia, seen in 30(53.5%) of the slides, followed by endothelial cell swelling in 28(50%), dermal edema in 26(46.4%). Fibrin deposition was seen only in 9(16%) of the slides

Table 6:Clinical diagnosis	**no**	**Histopathological diagnosis**	**No**
HSP	6	Leukocytoclastic vasculitis	6
Urticarial vasculitis	10	Leukocytoclastic vasculitis	10
CTD	1	Leukocytoclastic vasculitis	1
PAN	2	Lymphocytic vasculitis	1
Eosinophilic vasculitis	1	Eosinophilic vasculitis	1
Idiopathic CSVV	35	Leukocytoclastic vasculitis	25
		Lymphocytic vasculitis	9
		Granulomatous vasculitis	1

Table 6 shows the clinicopathological correlation between clinical and histopathological diagnosis. Among the cases of HSP, leukocytoclastic vasculitis was seen histologically in all 6 patients. All 10 cases of urticarial vasculitis showed leukocytoclastic vasculitis on histopathology. Among the 35 cases of idiopathic CSSV, 25 cases show leukocytoclastic vasculitis, 9 cases showed lymphocytic vasculitis and 1 case showed granulomatous vasculitis

III. DISCUSSION

Cutaneous vasculitis is a poorly understood entity due to its varied clinical manifestation and its overlap with various infections, connective tissue disorders and malignancies. In this study, history, clinical features, and various laboratory tests were recorded and analysed to reach a clinical diagnosis of cutaneous vasculitis. An attempt was also made to categorize the disease entities seen. Our study confirms various established facts regarding cutaneous vasculitis.

The medical records of a total of 56 patients were analyzed, their age ranged from 11 years to 63 years with mean age of 34±12.12 years. Males and females were almost equally affected in our study. A study by Leelavathi et al[7] showed age range of

13-93 years and mean age was 36.5 years, with equal occurrence among males and females, which was similar to our study.

In our study history of aggravating factors were identified in 21 (37.5%) patients; among them drugs, 10 (47.8%), exercise, 9 (42.8%), trauma and water exposure were the listed factors. In a study by Chowdhury et al,[8] drugs(30%), exercise(26%) were the aggravating factors. In another study by Sais et al, [9] exercise (30.5%) was the main aggravating factor of cutaneous vasculitis. These results are similar to our findings.

The duration of lesions ranged from 2 to 90 days. We found that in most of the cases, the onset of disease was sudden (75%) and the progression of disease was rapid (78%). This is similar to the study by Chowdhury et al.[8]

Pain was the most common presenting symptom in our study, present in 53% of the patients. This was followed by itching in 39.3%, burning sensation in 28.57% of the patients. Constitutional symptoms such as fever were present in 23.21%, arthalgia in 17.8% and myalgia in 14.2 % of the patients. Systemic symptoms such as abdominal pain was present in 12.5%, cough in 10.7% of the patients. This is similar to study by Chowdhury et al[8] where pain was present in 86% of the patients.

Several types of cutaneous lesions were seen in our patients. Palpable purpura was the most common type of lesion found in 73% of the patients. Petechiae were the second most common type of lesions found in 58% of the patients. All the patients had involvement of lower limbs. These findings are similar to the reports by Chowdhury et al[8] who found palpable purpura in 43.3% of their patients, petechiae in 58% of the patients. Also, in another study by Gupta et al, [10] 86% of skin lesions were palpable purpura. In studies by Chowdhury et al[8] and Alexander et al, [11] 100% patients and 38% patients respectively had involvement of lower limbs, similar to our study.

Histopathological slides were re-examined in all cases which showed leukocytoclastic vasculitis in 57% of the cases, where predominant finding was leukocytoclasia. Lymphocytic vasculitis was seen in 39% of the cases. These findings are similar to studies by Gupta et al[10] where 72% cases of leukocytoclastic small vessel vasculitis were found in their patients and study by Chowdhury et al[8] where leukocytoclastic vasculitis was seen in 70% and lymphocytic vasculitis in 27% of their patients.

ESR was raised in 12(21%) of the patients, anemia was found in 4(7.14%) of the patients. Leukocytosis was found in 3 patients. Albuminuria and hematuria in urine examination was found in 2 patients each. ANA was positive in 1 patient. These findings are similar to study by Gupta et al[10] where 20% of the patients had elevated ESR, anemia was seen in 8% and leukocytosis 12% of their patients.

In our study, idiopathic Cutaneous small vessel vasculitis (CSVV) was found in 35(62.5%) cases, urticarial vasculitis in 10(17.8%) of the patients and HSP in 6(10.7%) of the patients. We found 10 (17.85%) of our cases were drug induced. Causes of vasculitis were undefined in 35 (62.5%) of our patients. In a study by Alexander et al[11] 78% cases were idiopathic, this was similar to our study. However, our findings differ from a study by Chowdhury et al[8] where in etiology was not defined in 46.7% of their patients.

IV. CONCLUSION

Although the relatively benign condition of primary cutaneous small vessel vasculitis is the commonest type encountered in adults, a wide spectrum of clinical associations and laboratory anomalies have been observed. Based on our data, work-up for patients with cutaneous vasculitis including clinical history and examination, skin biopsy, haemogram, ANA, routine biochemical profile, and urine examination is recommended. Lastly, careful follow-up of these patients is necessary as cutaneous manifestations might be just the forme fruste of serious systemic disease.

REFERENCES

[1] Chen KR, Carlson JA. Clinical approach to cutaneous vasculitis: Treatment. Am J Clin Dermatol. 2008; 9:71-92

[2] Carlson JA, Ng BT, Chen KR. Cutaneous vasculitis update: diagnostic criteria, classification, epidemiology, etiology, pathogenesis, evaluation and prognosis. Am. J. Dermatopathol. 2005; 27; 504–28

[3] Carlson JA, Chen KR. Cutaneous vasculitis update: neutrophilic muscular vessel and eosinophilic, granulomatous, and lymphocytic vasculitis syndromes. Am. J. Dermatopathol. 2007; 29; 32– 434.

[4] Khetan, P., Sethuraman, G., Khaitan, B. K., Sharma, V. K., Gupta, R., Dinda, A. K ET AL. An aetiological & clinicopathological study on cutaneous vasculitis. Indian J Med Res2012; 135: 107–13.

[5] Jennette JC, Falk RJ, Andrassy K et al. Nomenclature of systemic vasculitides. Proposal of an international consensus conference. Arthritis Rheum. 1994; 37; 187–92

[6] Hunder GG, Arend WP, Bloch DA, Arend WP, Bloch DA, Calabrese LH, et al. The American College of Rheumatology 1990 criteria for the classification of vasculitis: introduction. Arthritis Rheum.1990;33:1065–7

[7] Leelavathi M, Aziz SA, Gangaram H B et al. Cutaneous vasculitis: A review of aetiology and clinical manifestations in 85 patients in Malaysia. Med J Malaysia. 2009;64:210-2

[8] Chowdhury MMH, Jaigirdar MQH, Asaduzzaman ATM, Mahmud MM, Choudhury AM, Paul HK. Clinicopathological study cutaneous vasculitides. JPAD.2014;24:8-14

[9] Sais G, Vidaller A, Jucgla A et al. Prognostic factors in leukocytoclastic vasculitis: a clinicopathologic study of 160 patients. Arch Dermatol. 1998;134:309-15

[10] Gupta S, Handa S, Kanwar AJ, Radotra BD, Minz RW .Cutaneous vasculitides: Clinico-pathological correlation. Indian J Dermatol Venereol Leprol 2009; 75: 356-62.

[11] Alexander B, Rameshkumar K, Layaseelan E. Cutaneous Vasculitis - A dynamic process posing diagnostic challenge. JAPI. 2003; 51:574-7.

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