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A Study And Analysis Of Cutaneous Small Vessel Vasculitis In Tertiary Care Hospital.

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ABSTRACT

Cutaneous small vessel vasculitis (CSVV) is an immune-complex-mediated disease targeting the postcapillary venules of the skin. Several classifications and synonyms have been proposed; however, simplified diagnostic criteria include palpable purpura with histopathology demonstrating leukocytoclastic vasculitis, in the absence of systemic small or medium-vessel vasculitis. CSVV is considered to be a reactive process, with underlying triggers (infection, drug, autoimmune disease, or neoplasm, though ≥40% of cases remain idiopathic). The triggers can be conceptualized as antigens to which antibodies are generated, with subsequent immune complex deposition, complement activation, neutrophil influx, and damage to the vessel wall. The inflammatory infiltrate contributes to the raised nature and erythema of the lesions, while vessel damage and hemorrhage result in non-blancheable purpura. The differential diagnosis includes macular purpura due to coagulation defects, other inflammatory skin diseases, and infections. While CSVV is generally limited to the skin, any site where immune complex could be filtered and deposited is potentially involved. Therefore, patients must be evaluated for both end-organ involvement/ systemic vasculitis syndromes and underlying triggers. Evaluation should also include punch biopsy for histopathology and direct immunofluorescence. Treatment includes removal of triggers and empiric anti-inflammatory agents for more severe disease.
Keywords: palpable purpura, leukocytoclastic vasculitis, small-vessel vasculitis, skin

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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 [1]. Vessels of any organ can be affected that results in a wide variety of signs and symptoms The unique feature of this group is multiorgan involvement. Because of the rich vasculature, the skin is prone to be frequently affected in vasculitis [2]. Cutaneous involvement in vasculitis's may be primary or reflector of a fatal systemic disease or evidence of association with some other systemic disorder. Cutaneous vasculitis 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 [4]. 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 [5]. 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 drug's reaction [6]. Many times, the initial presentation of vasculitis is on the skin and it is the dermatologist who must diagnose and treat this challenging condition [7].

MATERIALS AND METHODS

A study was conducted during the period from May 2021 – May 2022 in the Department of Rheumatology, Government Kilpauk Medical College, Chennai, Tamil Nadu, India among the patients with cutaneous small vessel vasculitis attending the dermatology department as well as those referred to Rheumatology department.

Inclusion criteria

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.

Exclusion criteria

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

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. 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. 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. 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. Tests to rule out cryoglobulinemia, (cryoglobulin test, serum protein electrophoresis, complement) malignancy and collagen vascular disorders were done when indicated. 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. 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.

RESULTS

Fifty-one patients with clinical features of cutaneous small vessel vasculitis were seen during the

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study period from May 2021 – May 2022. Of these, 11 cases were excluded from the study because of the patient's denial for the study (4), not willing for biopsy (7) .40 patients were diagnosed as cutaneous small vessel vasculitis were included in our study. There were 15 (38%) male and 25 (62%) female patients. Male to female ratio is 1:1.7.

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

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: 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 3: Symptoms

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 4: 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 5: 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 6: 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

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.

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Table 7: 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

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 [9]. Our study confirmed various established facts regarding cutaneous small vessel vasculitis and throws light on some new aspects. Palpable purpura was the most common cutaneous lesion seen in our patients as already been reported. Systemic involvement was seen in 50% of our patients as already been reported in other studies.[10] Musculoskeletal involvement was most common feature like other series. In this study, renal involvement was seen in only one case, renal involvement as most common feature. In a recent series from India, 22% of patients had GI involvement [11]. In this study, gastrointestinal involvement was seen in 12.8% of patients. Most common laboratory abnormality seen in 34.28% of our patients, but in earlier studies, elevated ESR was the most common laboratory abnormality. A causal agent or an underlying condition has been reported in 20-85% of the cases with vasculitis [12]. The aetiological association was seen in 62.2% of our cases. Infections and CTD are the two most common associated conditions in Europe. In our study, drugs were found to be the commonest factor associated with vasculitis, Histologically, in skin biopsy of all cases, the inflammatory infiltrate was localised to upper and mid dermis in most cases, though lower dermal and panniculus involvement was also seen. Panniculus involvement was seen in palpable purpura, wheals, nodules, crusted plaques and ulcers [13]. Most of the patients with LCV and HSP showed SVV with both neutrophilic and oeosinophilic infiltrate. Seven patients showed predominantly lymphocytic vasculitis, which could be explained by advanced age of lesion biopsied [14]. In patients with CTD, predominantly neutrophilic infiltrate was seen admixed with oeosinophils, which is similar to the observations reported earlier. Tissue oeosinophilia was found to be a reliable indicator of drug induced vasculitis, but here in this study, we did not find any significant difference for tissue oeosinophilia in those patients with and without drug history [15]. Only 2 cases of oeosinophilic vasculitis were observed. Although almost half of the cases with CSVV are idiopathic, a detailed investigation for any underlying causes or associations is essential (1). CSVV may be caused by infections (15%–20%), autoimmune connective tissue diseases or inflammatory conditions (15%–20%), drugs (10%–15%), and hematologic or solid malignancies (5%) (1, 12) [16]. In our study group, the main cause was the presence of simultaneous drug usage and infection (12 patients, 21%). The second and third most common causes were drug usage alone (10 patients, 17.5%) and having an infection alone (8 patients, 14%) respectively [17]. Drug- and infection-induced vasculitis was observed more frequently in our study group than in previous studies. This may be due to the fact that patients applying to a tertiary institution were more likely to be complicated by an infection and consequently had increased use of medication [19]. Leukocytoclastic vasculitis primarily involves the small caliber blood vessels of the skin, but in approximately 50% of the patients, the small vessels of the joints, gastrointestinal tract, kidneys, muscles,

lungs, and peripheral nerves could be involved, leading to multisystem organ involvement [20]. We observed systemic involvement in approximately one-third of our patients. Arthralgia and arthritis, namely joint involvement, were the most frequent extra cutaneous findings of our study. The other frequent extra cutaneous findings were renal and gastrointestinal involvements, respectively. In line with the findings of our study, several studies evaluating the sites of involvement in LCV reported that the most frequent non-cutaneous finding was joint involvement In the present study, the most frequent laboratory abnormality was an elevated CRP level, followed by elevated ESR and anemia. However, there is no relationship between high ESR, presence of leukocytosis, high CRP, and presence of systemic involvement. Most of the studies revealed that ESR was the most frequent pathological laboratory finding whereas some of them also indicated a relationship between elevated ESR and systemic involvement

CONCLUSION

Cutaneous small vessel vasculitis of no known aetiology is the most common form of vasculitis presenting clinically. The heterogeneity of this group of disorders is well represented in this study. Histologically, the majority had leukocytoclastic vasculitis though other types were also present. To reach an aetiological diagnosis of vasculitis, clinical and pathological features need to be correlated and supplemented by laboratory investigations.

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