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Original Research Article

An insight into the etiopathogenesis, clinical patterns, treatment outcome and repercussions of cutaneous small-vessel vasculitis

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ABSTRACT

Background: Cutaneous small-vessel vasculitis (CSVV) is a group of disorder which is characterised by involvement of capillaries, arterioles and venules. CSVV can be idiopathic or primary, or secondary to infection, drugs or as a part and parcel of underlying systemic disease. The aim of our study is to find out the etiological factors, treatment options and their outcome in CSVV.
Methods: We analysed 75 cases of CSVV out of patients who attended Dermatology OPD, in a tertiary care-centre from April 2017 to March 2018.The study design was descriptive study. A detailed history taking, thorough clinical examination and appropriate relevant investigations including biopsy were done for all the patients fulfilling the inclusion criteria and exclusion criteria.
Results: A sample size of 75 patients (53 women and 22 men) were included in the study. Their mean age was found to be 25 years (range 18-40). The following etiological factors were made out in our study: Benign isolated (40) patients, (53%), infective etiology (14) patients, (19%), vasculitis in background of ANA/dsDNA/ANCA positivity (12) patients, (16%), drug induced (9), patients (12%). The main clinical manifestations of CSVV in our study were found to be the following viz, palpable purpura in all 75 patients (100%), fever & malaise in 30 patients, (40%), ulcers in 30 patients (40%) arthritis/arthralgia in 15 patients, (20%). After a median follow up of 6 months, complete recovery was observed in all patients, although relapses occurred in 8 patients (11%).
Conclusions: CSVV is usually associated with other vasculitis and connective tissue disorders and patients turning ANCA positive somewhere in the course of the disease is of ominous sign and hence, it becomes mandatory to keep these patients on a long term vigil.

Keywords: Cutaneous small vessel vasculitis, Anti-nuclear antibody, Leucocytoclastic vasculitis, Fibrinoid necrosis, Vasculitic ulcers, Anti-neutrophil cytoplasmic antibody positive vasculitis

INTRODUCTION

Cutaneous small vessel vasculitis also called Immune-complex small vessel vasculitis, can be an isolated phenomenon or presenting feature of a connective tissue disorder like SLE, or can present as a severe, life-threatening syndrome, including ANCA-associated vasculitis.

Cutaneous vasculitis (CV) encompasses a wide and heterogeneous group of disorders characterized by the presence of necrotizing inflammatory lesions in the cutaneous blood vessels.[1-3] They may range from an

isolated CV to a severe, life-threatening syndrome, including ANCA-associated vasculitis.[4]

Cutaneous small-vessel vasculitis (CSVV) is a single organ vasculitis producing leucocytoclastic angiitis of cutaneous vasculature.[2] The presence of three of the following five criteria given by The American College of Rheumatology (ACR) is essential for the diagnosis of CSVV. (i) age greater than 16 years at disease onset, (ii) history of taking medication prior to onset, (iii) presence of palpable purpura, (iv) presence of maculopapular rash, (v) biopsy demonstrating granulocytes around an arteriole or venule.[5,6]

The basic challenge thrown to a dermatologist is as such, to find out, with the help of appropriate investigations, whether the patient they deal with, is prima facie a case of cutaneous small vessel vasculitis or is it the first symptom complex of a moribund illness like SLE or a concern of infectious origin like pulmonary Koch.

METHODS

A Descriptive study of CSVV of a series of 75 patients who attended Dermatology OPD in a tertiary care centre from April 2017 to March 2018 was conducted. Etiological factors, its associations, treatment outcome and prognosis were studied using an appropriate univariate analysis.

Inclusion criteria

Inclusion criteria were patients willing to give a written consent; patients of either sex of age >18 years; patients who satisfy at least three out of five American College of Rheumatology (ACR) Criteria.

Exclusion criteria

Exclusion criteria were patients with purpuric lesions and leg ulcers due to causes other than vasculitis; patients not willing to give a written consent; patients who are on immuno-suppressants already, for any coexisting steroid responsive dermatoses; pregnant women.

Complete blood count, coagulation profile, liver and renal function tests, urine analysis, electrocardiogram were performed at the time of diagnosis in all patients, as part of routine work-up. An immunological work-up profile was carried out for ANA, dsDNA and ANCA. Serological markers of acute inflammation namely ESR and CRP were monitored. A complete Tuberculosis work-up, consisting of Mantoux, Chest radiograph, Gene-Xpert was done. The diagnosis of CSVV was based on (i) skin biopsy showing characteristic histological findings of vasculitis (neutrophilic infiltration, leucocytoclasia, fibrinoid necrosis or erythrocyte extravasation into the vessel wall) and/or (ii) the presence of typical non-thrombocytopenic palpable purpura.

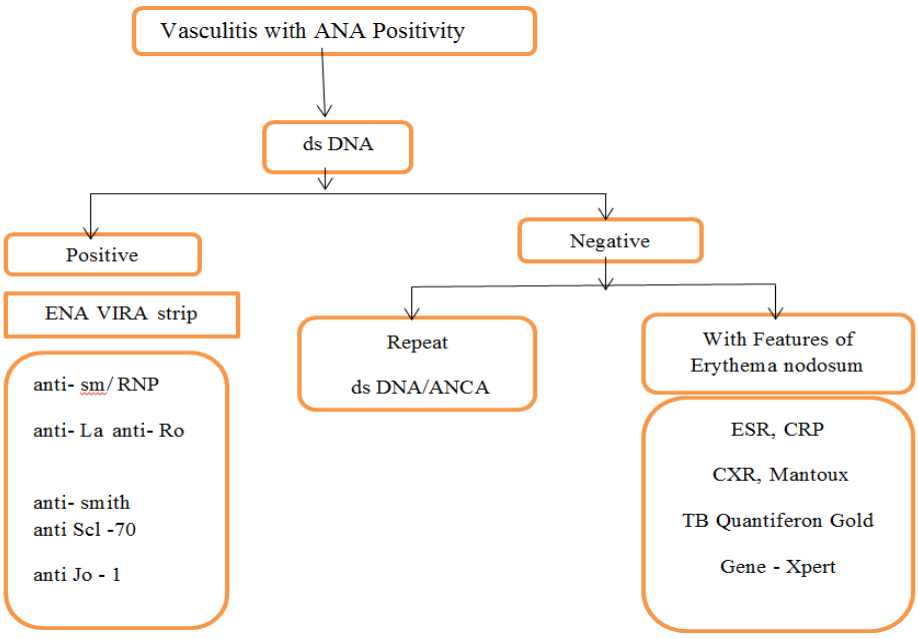

Figure 1: Algorithm for work up of a patient of CSVV in the background of ANA positivity.

Patients were treated with any one of the following drugs Viz., systemic steroids, colchicine, dapsone, azathioprine and methotrexate as per the clinical condition and disease severity. They were regularly followed up once in two weeks till complete recovery. ANA and ANCA, screening and titre were done once in 3 months to assess the disease severity in recalcitrant patients.

RESULTS

In our study of 75 patients, 53 were women and 22 were men, with the mean age of 25 years and the range being 18-40. The main etiological factors for CSVV in our study were the following: benign isolated (40) patients, (53%), infectious etiology (14) patients, (19%), Vasculitis in background of ANA/dsDNA/ANCA positivity (12) patients, (16%), drug induced (9) patients, (12%).

The main clinical manifestations of CSVV in our study were found to be the following viz, palpable purpura in all 75 patients (100%), fever & malaise in 30 patients, (40%), ulcers in 30 patients (40%) arthritis/arthralgia in 15 patients, (20%).

60 Patients (80%) responded to systemic corticosteroids, 11patients (15%) to colchicine/dapsone and 4 patients (5%) were treated with azathioprine/methotrexate.

They were regularly followed up once in two weeks till complete recovery, although relapses occurred in 8 patients (11%).

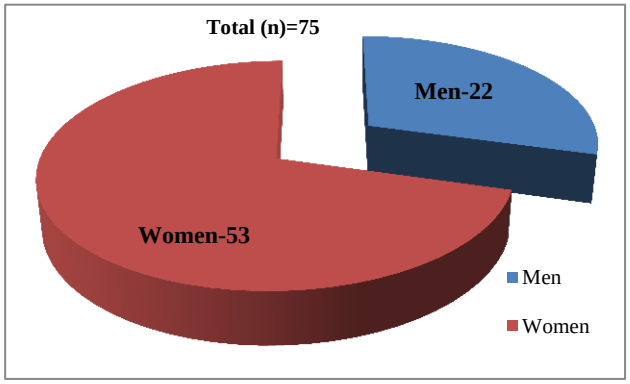

Figure 2: Sex distribution of cases with cutaneous small vessel vasculitis.

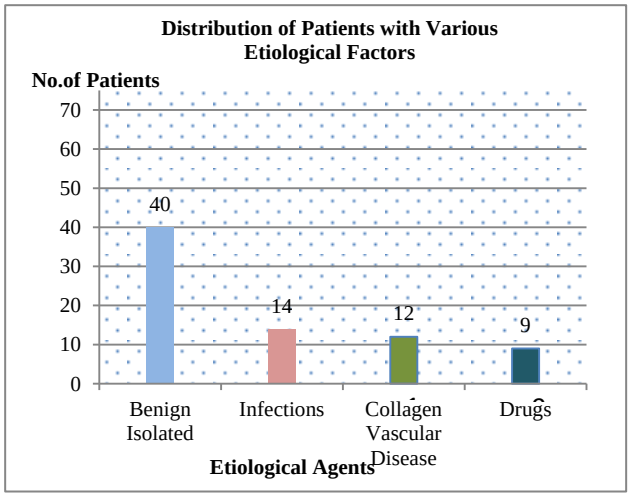

Figure 3: Etiological factors of CSVV.

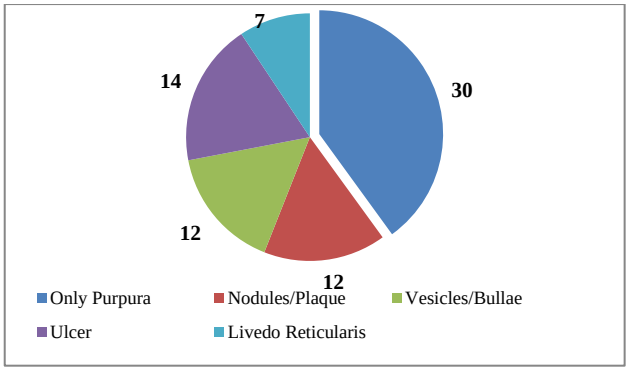

Figure 4: Cutaneous manifestation of CSVV.

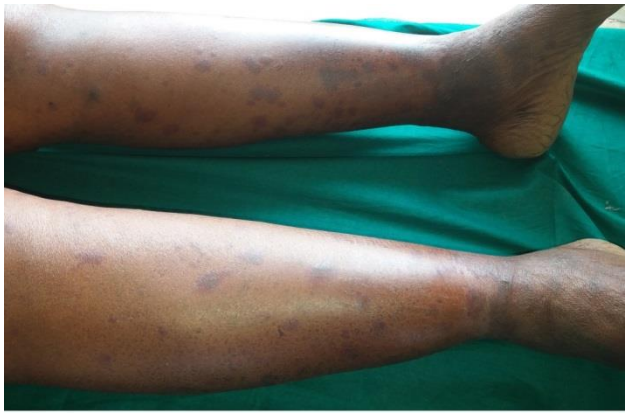

Figure 5: Non-thrombocytopenic palpable purpura.

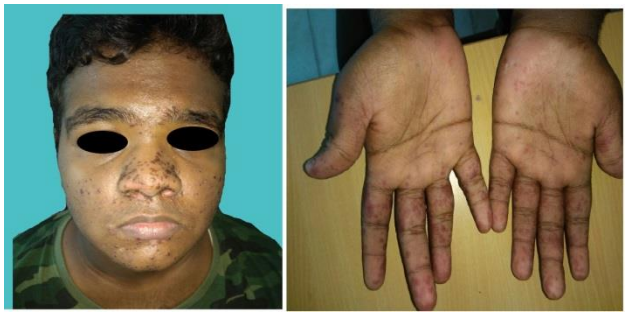

Figure 6: HFMD associated cutaneous small vessel vasculitis.

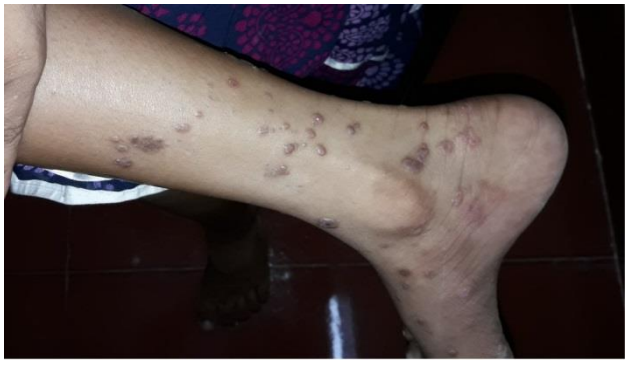

Figure 7: Papular and nodular vasculitic lesion.

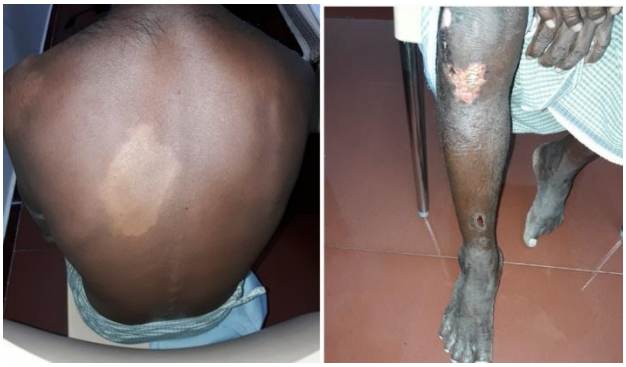

Figure 8: *M. leprae* causing vasculitic ulcer.

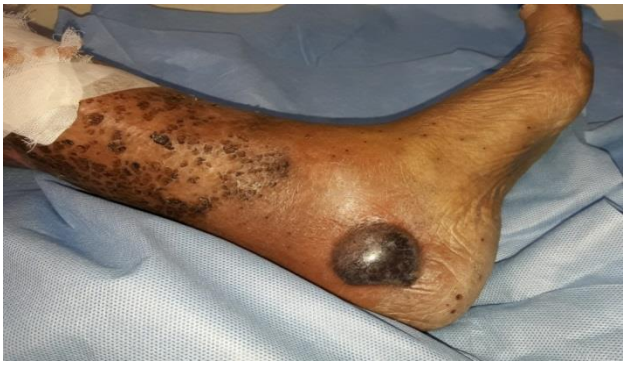

Figure 9: A large Hemorrhagic blister in vasculitis.

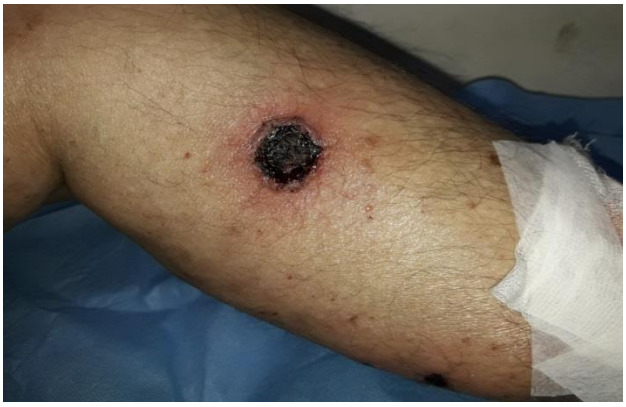

Figure 10: Vasculitic ulcer with central eschar and perilesional erythema

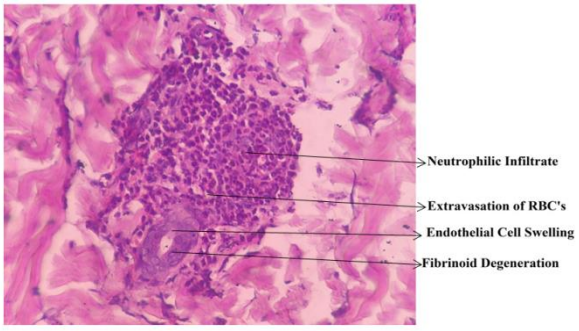

Figure 11: HPE showing leucocytoclastic vasculitis, with angiocentric segmental inflammation.

DISCUSSION

In our study out of the sample size of 75 patients, 40 patients (53%) were found to be of the benign isolated type, which correlates very well with the previous studies wherein, benign idiopathic type accounts for 50%.

Vasculitis resulting out of infections in our study were found to be due to viral and bacterial origin Viz., *Coxackie virus, M. leprae* constituting 19% which correlates with the previously documented studies wherein, infections can lead on to vasculitis to an extent of 20%.[19]

Vasculitis occurring as part and parcel of connective tissue disorders in our study amounts to 16% which is on par with the previously established study findings of 15-20% of inflammatory etiology.[19]

9% of our study population were found to have vasculitis of drug induced origin which correlates with the previous established studies of 10-15%.[19]

After starting the patient on treatment, monitoring of disease activity and response to treatment can be assessed by the following clinical and lab parameters.

Clinical

1. Existing lesions of vasculitis starts healing which is made out clinically by fading out of maculo-papular dusky red erythematous lesion leaving a hemosiderin induced post-inflammatory hyperpigmentation.
2. No new lesions of vasculitis should be encountered.

Lab parameters

1. Fall in the titre of markers of acute inflammation like ESR & CRP.
2. Fall in the titre of ANA, dsDNA and ANCA.
3. Reduction in the Brimingham Vasculitis Activity Score (BVAS)

Patients have to be monitored with repeated blood tests, once in 3 months to watch for markers of further progression of disease in the form of appearance of neoantigens and antibody like dsDNA becoming positive later in the course of the disease.[20,21]

In our study, in majority of patients (53%), the etiology was idiopathic. Vasculitis in the background of SLE contributed to 12 patients (16%). ANA titre and other antibodies were monitored more diligently in those patients.

In our study, one patient who was recalcitrant to treatment, progressed to ANCA positivity during the course of illness and developed endophthalmitis and interstitial lung disease.

CONCLUSION

On long term, CSVV either settles down and disappears completely or either evolves into one of the well documented vasculitis of the medium sized and large vessels supplying vital organs and thereby leads to conditions like panophthalmitis, endophthalmitis and interstitial lung disease and thus turns fatal. This happens wherein a patient of idiopathic CSVV while on treatment, at one point of time suddenly turns into ANCA positive. CSVV in the background of ANA positivity has to be investigated over a period of time for ruling out evolution of SLE, and these patients should be offered a kind of guarded prognosis for the fear of developing full blown SLE, wherein CSVV has presented, as the fore-runner of SLE.

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Conflict of interest: None declared
Ethical approval: The study was approved by the institutional ethics committee

REFERENCES

1. Griffiths C, Barker J, Bleiker, Chalmers R. Rook's Textbook of Dermatology: 9th ed. London, UK: Wiley Blackwell; 2016: 102(1-8).
2. Jennette JC, Falk RJ, Bacon PA, Basu N, Cid MC, Ferrario F, et al. 2012 revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. A rthritis Rheum. 2013;65(1):1–11.
3. Calabrese LH, Michel BA, Bloch DA, Arend WP, Edworthy SM, Fauci AS, et al. The American College of Rheumatology 1990 criteria for the classification of hypersensitivity vasculitis. Arthritis Rheum. 1990;33(8):1108 –13.
4. Garcia-Porrua C, Gonzalez-Gay MA. Comparative clinical and epidemiological study of hypersensitivity vasculitis versus Henoch-Schonlein purpura in adults. Semin Arthritis Rheum. 1999;28(6):404-12.
5. Watts RA, Jolliffe VA, Grattan CE, Elliott J, Lockwood M, Scott DG. Cutaneous vasculitis in a defi ned population – clinical and epidemiological associations. J Rheumatol. 1998;25(5):920-4.
6. Martinez-Taboada VM, Blanco R, Garcia-Fuentes M, Rodriguez-Valverde V. Clinical features and outcome of 95 patients with hypersensitivity vasculitis. Am J Med. 1997;102(2):186-91.
7. Boom BW, Mommaas AM, Vermeer BJ. Presence and interpretation of vascular immune deposits in human skin: the value of direct immune-fluorescence. J Dermatol Sci. 1992;3(1):26-34.
8. Garcia-Porrua C, Gonzalez-Gay MA. Bacterial infection presenting as cutaneous vasculitis in adults. Clin Exp Rheumatol. 1999;17(4):471-3.
9. Cribier B, Couilliet D, Meyer P, Grosshans E. The severity of histopathological changes of leukocytoclastic vasculitis is not predictive of extracutaneous involvement. Am J Dermatopathol. 1999;21(6):532-6.
10. Mukhtyar C, Lee R, Brown D, Carruthers D, Dasgupta B, Dubey S, et al. Modification and validation of the Birmingham Vasculitis Activity Score (version 3). A nn Rheum Dis. 2009;68(12):1827-32.
11. Podjasek JO, Wetter DA, Pittelkow MR, Wada DA. Cutaneous small vessel vasculitis associated with solid organ malignancies: the Mayo Clinic experience, 1996 to 2009. J Am Acad Dermatol. 2012;62(2):55-65.
12. Blanco R, Martı´nez-Taboada VM, Rodrıguez-Valverde V, Garcı´a-Fuentes M. Cutaneous vasculitis in children and adults: associated diseases and etiologic factors in 303 patients. Medicine. 1998;77:403-18.
13. Jennette JC, Falk RJ, Andrassy K, Bacon PA, Churg J, Gross WL, et al. Nomenclature of systemic vasculitides. Proposal of an international consensus conference. Arthritis Rheum. 1994;37:187-92.
14. Loricera J, Calvo-Rı´o V, Ortiz-Sanjua´n F, González-López MA, Fernández-Llaca H, Rueda-Gotor J, et al. The spectrum of paraneoplastic cutaneous vasculitis in a defined population: incidence and clinical features. Medicine. 2013;92:331-43.
15. Loricera J, Calvo-Rı´o V, Mata C, Ortiz-Sanjuán F, González-López MA, et al. Urticarial vasculitis in northern Spain: clinical study of 21 cases. Medicine. 2014;93:53-60.
16. Soter NA, Austen KF. Cutaneous necrotizing angiitis. In: Samter M, editor. Immunological diseases. Boston:Little, Brown; 1978: 993.
17. Ekenstam E, Callen JP. Cutaneous leukocytoclastic vasculitis: clinical and laboratory features of 82 patientsseen in private practice. Arch Dermatol 1984;120:484-90.
18. Lotti T, Comacchi C, Ghersetich I. Cutaneous necrotizing vasculitis. Int J Dermatol. 1996;35:457-74.
19. Griffiths C, Barker J, Bleiker, Chalmers R. Rook's Textbook of Dermatology. 8th ed. London, UK: Wiley Blackwell; 2010:50:13.
20. Comacchi C, Ghersetich I, Lotti T. Vasculite necrotizzante cutanea. G Ital Dermatol Venereol 1998;133:23-49.
21. Ryan TJ. Cutaneous vasculitis. In: Rook A, Wilkinson DS, Ebling FJG, editors. Textbook of dermatology. Oxford: Blackwell Scientific Publications; 1992: 1893-1861.

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