Original Article

# Vasculitic Neuropathy: A Retrospective Analysis of Nerve Biopsies and Clinical Features from a Single Tertiary Care Center

**Monalisa Hui, A. K. Meena[1], Liza Rajasekhar[2], Yareeda Sireesha[1], Jabeen Afshan[1], Rukmini Mridula[1], Rupam Borgohain[1], Megha S. Uppin**

Departments of Pathology, [1]Neurology and [2]Rheumatology, Nizam's Institute of Medical Sciences, Hyderabad, Telangana, India

## Abstract

**Objective:** Vasculitic neuropathy can be either restricted to the peripheral nerves or associated with systemic involvement of other organs. The objective of this study was to analyze the nerve biopsies reported as "vasculitic neuropathy" with clinical features. **Materials and Methods:** All cases diagnosed with vasculitic neuropathy were retrospectively analyzed and categorized as systemic vasculitis and nonsystemic vasculitic neuropathy based on the clinical features. The histological features were further evaluated and classified according to the Peripheral Nerve Society Guidelines. **Results:** Of the 126 cases, there were 65 nonsystemic vasculitis, 45 secondary systemic vasculitis, and 16 primary systemic vasculitis. Definite vasculitis was more common in the systemic vasculitis group. The epineurial vessels were predominantly involved with chronic axonal changes. **Conclusion:** The sensitivity of definite vasculitis on nerve biopsy was 54.76%. The sensitivity increases when the diagnostic criteria of definite and probable vasculitis were applied taking into account perivascular inflammation accompanied by vascular changes and axonopathy.

**Keywords:** Axonopathy, definite vasculitis, nonsystemic vasculitic neuropathy

## Introduction

Vasculitis is an important differential diagnosis of neuropathy presenting with asymmetric and progressive clinical course.[1] Tissue evidence of vasculitis helps in ruling out the other mimics as well as facilitates the clinician in proper management. Nerve biopsy is an essential tool for the diagnosis of suspected vasculitis which is a treatable cause of neuropathy.[2] Neuropathy in vasculitis can be either isolated or associated with systemic involvement of other organs. Systemic vasculitis is classified as primary without any underlying etiology or secondary to a connective tissue disorder, infection, or drugs.[1] Diagnosis of peripheral neuropathy presenting as a part of the systemic disease is relatively easier to diagnose than when it presents as an isolated and initial manifestation of the disease.[2] Histologic evidence of vasculitis is revealed by the presence of inflammation predominantly affecting the epineural vessels leading to thrombosis and subsequent ischemic damage. However, as the disease is patchy, these classic features may not be seen in all nerve biopsies. To increase the diagnostic yield, vasculitis is thereby classified into definite, probable, or possible on the basis of morphological features.[3] In this article, we have analyzed the nerve biopsies diagnosed with "vasculitic neuropathy" with respect to the clinical features, evidence of systemic disease versuss nonsystemic vasculitic neuropathy (NSVN), and pathologic features on nerve biopsies.

## Materials and Methods

The study is a retrospective evaluation of all nerve biopsies diagnosed with "vasculitic neuropathy" from January 2012 to June 2017. All the biopsies included in the study were taken from sural nerve which was involved in electrophysiology. The biopsies were performed after obtaining written informed consent. The clinical data including the type of neuropathy and details about the nerve conduction studies (NCS) were retrieved from medical records. The evidence of the presence of systemic disease versus isolated NSVN was based on through the clinical evaluation, history of drug intake, infection or any other associated medical condition, or systemic organ involvement. In addition, the analysis of laboratory parameters including routine hemogram with erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), rheumatoid factor, antinuclear antibody (ANA), anti-dsDNA, anti-smith antibody, anticardiolipin antibody, lupus anticoagulant, and antineutrophil cytoplasmic antibody (c-ANCA and p-ANCA) were done in all patients.

The transverse and longitudinal sections of nerve biopsies were analyzed with the help of hematoxylin and eosin, Masson's

**Address for correspondence:** Dr. Megha S. Uppin, Department of Pathology, Nizam's Institute of Medical Sciences, Punjagutta, Hyderabad - 500 082, Telangana, India.
E-mail: drmegha_harke@yahoo.co.in



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trichrome (for fibrosis), Perl's stain for hemosiderin, and myelin (Kulchitsky Pal) stains. The type of vessel involved, type of inflammatory infiltrate, and evidence of axonal damage were analyzed in all biopsies. The biopsies were classified as definite, probable, or possible, on the basis of Peripheral Nerve Society Guidelines.[3] Multiple serial sections were examined in each case. A minimum of 15–20 serial sections were analyzed. Further serial sections were examined to look for vascular wall destruction in cases where only perivascular inflammatory infiltrates were seen in the initial sections.

## Results

Of the total 126 nerve biopsies analyzed, there were 76 male and 50 female patients with an M: F ratio of 1.52:1.Both NSVN and patients with systemic vasculitic neuropathy (SVN) showed a distinct male predominance. The female preponderance was observed only in vasculitic neuropathy associated with systemic lupus erythematosus (SLE).The age of the patients ranged from 18 to 75 years with a peak in the age group of 4$^{th}$ to 6$^{th}$ decade. The mean age at the presentation for patients of NSVN (44.1 years) was lower than SVN patients (58.4 years). The most frequent clinical presentations included pain, paresthesia, burning sensation in 82 patients (65.07%), and weakness in 39 patients (30.95%). The lower limbs were more commonly involved than the upper limbs with a predominant distal involvement. The duration of symptoms ranged from 1 to 60 months, and the mean duration was shorter in SVN than in NSVN group (5.5 vs18 months, respectively). The constitutional features were more common in the SVN patients ($n$ = 47) and included fever, myalgia, weight loss, and fatigue. The biopsies were classified as primary systemic vasculitis (16 cases, 12.69%), secondary systemic vasculitis (45 cases, 35.71%), and NSVN (65 cases, 51.58%).

### Electrophysiology

On NCS, the majority of the patients presented with mononeuritis multiplex (MNM) (70 cases, 55.56%) followed by asymmetrical polyneuropathy (30 cases, 23.80%) and myeloradiculopathy (7 cases, 5.55%). There were six patients with mononeuropathy, five distal symmetric polyneuropathy, and three with sensory ganglionopathy. NCS details were not available in five patients.

### Primary systemic vasculitis ($n$ = 16)

These included five patients of polyarteritis nodosa (PAN) and 11 of ANCA-associated vasculitis. The additional associated features in primary SVN included the presence of polyarthralgia ($n$ = 12), digital gangrene ($n$ = 9), skin rashes ($n$ = 8), oral ulcer ($n$ = 2), cranial nerve involvement ($n$ = 2), and pulmonary hemorrhage ($n$ = 1). Two of these patients showed evidence of vasculitis on skin biopsies as well.

### Secondary systemic vasculitis ($n$ = 45)

In secondary SVN group, the most common underlying etiology were rheumatoid arthritis (RA) ($n$ = 15) followed by SLE ($n$ = 12), undifferentiated connective tissue disorder ($n$ = 6), and Sjogrens ($n$ = 5). The comorbidities in 12 patients of SLE included overlap RA ($n$ = 2), secondary antiphospholipid syndrome positive for lupus anticoagulant and anticardiolipin antibodies ($n$ = 2), dermatomyositis ($n$ = 1), and endocarditis ($n$ = 1). All the SLE patients had skin rash and arthritis, and none had lupus nephritis.

The paraneoplastic vasculitis was seen secondary to lung adenocarcinoma ($n$ = 2) and adenocarcinoma colon ($n$ = 1). SVN was also seen in two patients of erythema nodosum leprosum who were on multidrug treatment for lepromatous leprosy. Both of them had painful erythematous tender rashes, fever, arthralgia, loss of sensation, and muscle weakness. There was one patient with systemic sclerosis presenting with diffuse skin thickening and one associated with hepatitis B infection.

### Nonsystemic vasculitic neuropathy ($n$ = 65)

There were 65 patients with 37 males and 28 females with a mean age of 44.1 years including four patients with diabetic radiculoplexus neuropathy. NCS predominantly revealed MNM and asymmetric polyneuropathy. There was no clinical, radiological, or pathological evidence of systemic organ involvement. The constitutional symptoms such as weight loss and fever were seen in eight patients. The other markers of systemic inflammation were absent.

### Investigations

The routine hemogram revealed anemia ($n$ = 6) and leukocytosis ($n$ = 16) and peripheral eosinophilia ($n$ = 4). The serologic workup in SVN showed ANA positivity in twenty patients and high titers of rheumatoid factor in 22 patients. All the patients of SLE were positive for ANA and anti-ds DNA. Anti-smith antibodies were positive in five patients. Among the ANCA-associated vasculitis, pANCA was elevated in eight patients and c ANCA in three patients ESR was elevated in 34 patients and increased CRP in seven patients. The serologic investigations in NSVN were normal except for the positive ANA in four patients. The clinical and laboratory features of primary SVN, secondary SVN, and NSVN group are summarized in Table 1.

### Histopathology

On histopathology, the biopsies were classified into definite (69 cases 54.76%), probable (52 cases, 41.26%), and possible (5 cases, 3.96%) based on the Peripheral Nerve Society Guidelines [Figures 1-4]. Definite evidence of vasculitis was more common in SVN as compared to NSVN patients (32.53%vs 22.22%). The features of probable and possible vasculitis were seen in 52 and 5 biopsies, respectively. However, probable vasculitis was seen more commonly in NSVN (29.36%) as compared to SVN (11.9%).The histopathological classification of vasculitic neuropathy is elaborated in Table 2.

### Blood vessel changes

There was predominant involvement of the epineurial vessels. The endoneurial vessels were involved in only three

**Table 1: Clinical and laboratory features of systemic vasculitic neuropathy and nonsystemic vasculitic neuropathy**

| Clinical and laboratory features | Primary SVN (*n*=16) | Secondary SVN (*n*=45) | NSVN (*n*=65) | VN (*n*=126) |
|---|---|---|---|---|
| Age (years) | 55.3 | 61.4 | 44.1 | 47.4 |
| Male:female | 1.6:1 | 1.8:1 | 1.32:1 | 1.52:1 |
| Duration (months) | 6 | 5.5 | 18 | 9 |
| Mononeuritis multiplex (%) | 20.16 | 11.34 | 35.71 | 55.56 |
| Asymmetric polyneuropathy (%) | 0 | 6.34 | 17.46 | 23.8 |
| Symmetrical sensory neuropathy (%) | 0 | 3.9 | 0 | 3.9 |
| ANA | 0 | 20 | 4 | 24 |
| ANCA | 11 | 0 | 0 | 11 |
| Rheumatoid factor | - | 22 | 0 | 22 |
| Anti dsDNA | - | 12 | 0 | 12 |
| Anti-smith antibodies | - | 5 | 0 | 5 |
| Anemia | - | 6 | 1 | 7 |
| Eosinophilia | 4 | 0 | 0 | 4 |
| ESR (>20 mm/h) | 4 | 30 | 8 | 42 |

SVN=Systemic vasculitic neuropathy, NSVN=Nonsystemic vasculitic neuropathy, VN=Vasculitic neuropathy, ANA=Anti-nuclear antibody, ANCA=Antineutrophil cytoplasmic antibody, ESR=Erythrocyte sedimentation rate, dsDNA=Double stranded DNA

biopsies. The inflammatory infiltrate was predominantly composed of lymphocytes. Eosinophils were seen in four biopsies of SVN. The biopsies of SVN and NSVN patients also showed neutrophils in five cases and three cases, respectively. The biopsies showed features of active vascular damage characterized by fibrinoid necrosis in 21 cases (16.66%) and thrombosis in six cases (4.76%) [Figure 1]. Evidence of chronic vascular damage (neovascularization, intimal proliferation with luminal narrowing, and hemosiderin deposition) indicative of healed vasculitis was observed in 46 biopsies [Figure 2].

### Nerve fiber changes

All the biopsies showed the evidence of axonopathy in the form of fiber loss, endoneurial fibrosis, and regenerating clusters. The fascicular involvement was mostly nonuniform with sectorial loss of fibers. The fiber loss was mild in eight biopsies whereas severe in 21. The axonopathy was chronic in 122 biopsies; however, in four biopsies there were features of acute myelin breakdown and myelin ovoids indicating acute axonal damage.

## Discussion

Vasculitic neuropathy can be associated with systemic diseases (SVN) or can be limited to peripheral nerves (NSVN).[4] A total of 60%–70% of patients with systemic vasculitis may develop neuropathy.[5] In the present study, the predominant subtype was NSVN (51.58%) followed by secondary SVN accounting for 35.71%. Similar frequency has been reported in other nerve biopsy series.[6,7] In a series of 53 patients with vasculitic neuropathy, confirmed on nerve biopsy, 42% were NSVN, and 58% were SVN.[6] Collins compiled the prevalence of various types of vasculitic neuropathy and found NSVN to be the most common subtype accounting for 26% closely followed by PAN/microscopic polyangiitis (25%), RA (12%) and eosinophilic granulomatosis with polyangiitis (10%).[7] Table 3 shows the comparison of the frequency of vasculitis seen in our study with similar studies published in the literature.[6,7] Although vasculitic neuropathy can occur at any age, the mean age of the NSVN patients in the study was slightly lower than the other reported series. The mean age in other studies ranged from 58.4 to 61.8 years.[6,8,9] Studies have shown a female predominance in both NSVN and SVN patients.[6] Females are affected more than males in NSVN.[6,8,9] However, in this study, there was male preponderance except in cases of secondary vasculitis with underlying SLE where females outnumbered males. Inconsistent with the literature, the mean duration of symptoms was shorter with the presence of systemic features being much more common in the SVN group as compared to the NSVN group.[6]

The clinical features of neuropathy in the form of MNM, asymmetric, and symmetric polyneuropathy in our study is in correlation with the literature. Asymmetric polyneuropathy is the most frequent pattern of peripheral nerve involvement in vasculitic neuropathy. MNM is seen in 10%–15% of vasculitic neuropathy. A distal symmetric polyneuropathy is an infrequent form of presentation.[10] Similarly, Benett *et al*. in their series of vasculitic neuropathy found asymmetric sensorimotor neuropathy in the majority of the cases accounting for 45% followed by MNM in 20% of cases. Patients with symmetrical sensorimotor neuropathy were seen only in 11% of cases.[6] Although MNM was the most frequent pattern encountered in the study, distal symmetrical polyneuropathy was rare accounting for only 3.96% of cases. In contrast, Lawrence *et al*. in their study on 42 cases of vasculitic neuropathy reported a higher incidence of symmetric sensorimotor neuropathy accounting for 39.1% of cases.[11] Table 4 shows the comparison of clinical features of vasculitic neuropathy.

The primary SVNs are classified based on the size of the vessel involved. PAN involves medium-and-small-sized vessels and is frequently associated with VN (50%–75%).[10] It manifests as painful MNM or sensory ataxic neuropathy.[12,13] All the patients in the study presented with MNM.

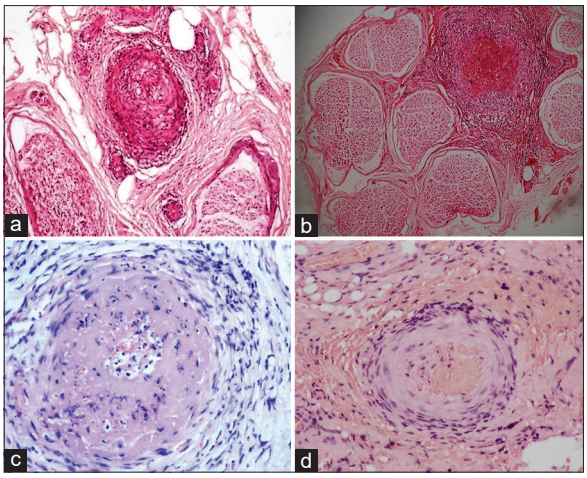

**Figure 1:** Definite vasculitis – active features (a) Vessel wall infiltrated by inflammatory cell infiltrate (H and E, ×100). (b) Disruption of endothelium and fragmentation of internal elastic lamina (H and E, ×40). (c) Fibrinoid necrosis (Masson trichrome, ×400). (d) Thrombus leading to luminal obstruction of the vessel (H and E, ×400)

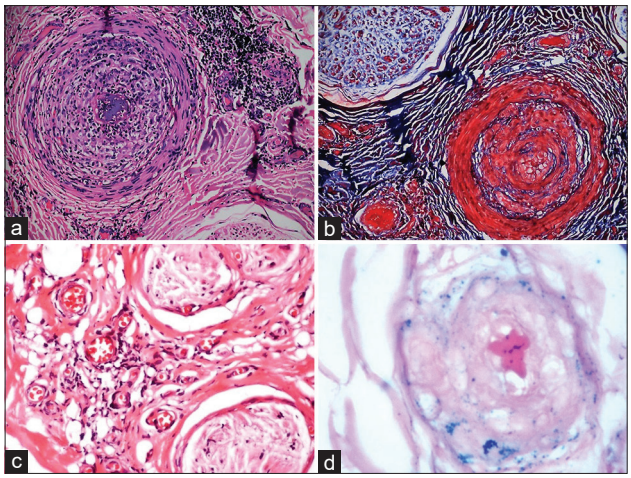

**Figure 2:** Definite Vasculitis - Chronic features (a and b) Intimal hyperplasia with luminal narrowing (H and E, ×400, Masson trichrome ×400). (c) Neovascularization (H and E, ×100). (d) Hemosiderin deposition (Perls stain, ×100)

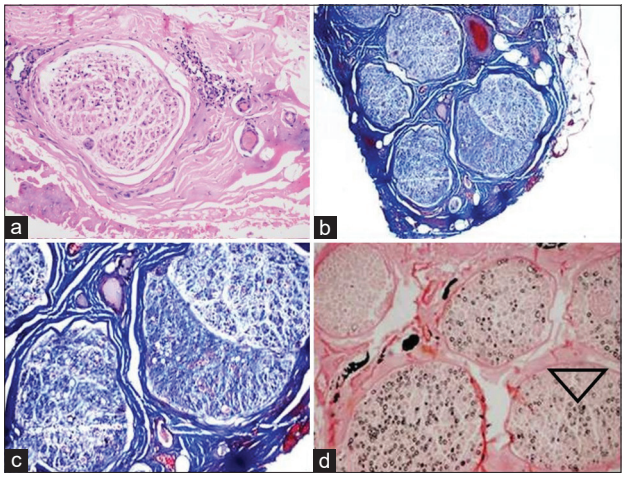

**Figure 3:** Probable vasculitis (a) Perivascular inflammation (H and E, ×100). (b and c) Endoneurial fibrosis indicating fiber loss (Masson trichrome, ×100 (b) and ×400 (c). (d) Asymmetric nerve fiber loss with sectorial involvement indicated by arrowhead (Kpal, ×100)

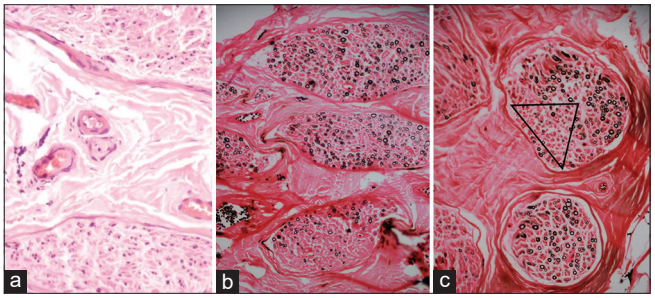

**Figure 4:** Possible vasculitis (a) The absence of perivascular inflammation (H and E, ×100). (b and c) Nonuniform involvement of the fascicles with sectorial loss of fibers indicated by arrowhead (Kpal, ×100 and ×400)

**Table 2: Histopathological classification of vasculitic neuropathy**

| Histopathology | Primary SVN (*n*=16) | Secondary SVN (*n*=45) | NSVN (*n*=65) | VN (*n*=126) |
|---|---|---|---|---|
| Definite vasculitis | 11 | 30 | 28 | 69 |
| Probable vasculitis | 5 | 10 | 37 | 52 |
| Possible vasculitis | - | 5 | - | 5 |

SVN=Systemic vasculitic neuropathy, NSVN=Nonsystemic vasculitic neuropathy, VN=Vasculitic neuropathy

VN in systemic vasculitis involves small–medium-sized vessels. Secondary SVN occurs in the context of underlying connective tissue disease, sarcoidosis, Behcet's disease, infection, drugs malignancy, inflammatory bowel disease, and hypocomplementemic urticarial vasculitis syndrome.[3] Neuropathy occurs in RA and SLE in 10% and 5% of cases, respectively, and presents as MNM or symmetrical sensory polyneuropathy.[14] The predominant causes of secondary systemic vasculitis in the study were RA and SLE.[6,7]

VN secondary to malignancy is seen most commonly associated with lymphoma, small-cell lung carcinoma, and gastrointestinal tract malignancy. The two cases of underlying lung carcinoma in the study showed adenocarcinoma on histology.[15]

NSVN was first described in 1938 by Kernohan and Woltman. The term nonSVN was coined by Dyck *et al*.[16] The diagnostic criteria as proposed by Collins include clinical and electroneuromyography features of axonal neuropathy in the absence of any identifiable etiology with histopathological evidence of vasculitis on nerve or muscle biopsy.[17]

NSVN has overlapping the clinical and laboratory features with SVN which includes constitutional symptoms, elevated ESR, anemia, leukocytosis, thrombocytosis, and the presence of auto antibodies.[18] There was the mild elevation of ESR in

**Table 3: Frequency of various vasculitic neuropathy**

| | Present study (*n*=126), *n* (%) | Bennett *et al*.[6] (*n*=53), *n* (%) | Collins and Periquet[7] (*n*=720), *n* (%) |
|---|---|---|---|
| NSVN | 65 (51.58) | 22 (41.5) | 197 (26) |
| PAN | 5 (3.96) | 10 (18.86) | 191 (25) |
| ANCA associated vasculitis | 11 (8.73) | CCS: 3 (5.67) | 79 (10) |
| | | WG: 3 (5.67) | 31 (4) |
| SLE | 12 (9.52) | 0 | 27 (3.5) |
| RA | 15 (11.90) | 3 (5.67) | 93 (12) |
| UCTD | 6 (4.76) | 2 (3.77) | 49 (6.4) |
| SS | 1 (0.79) | 2 (3.77) | 17 (2.2) |
| Paraneoplastic | 3 (2.38) | 3 (5.67) | 19 (2.5) |
| Cryoglobulinemia | - | 2 (3.77) | 17 (2.2) |

NSVN=Nonsystemic vasculitic neuropathy, PAN=Polyarteritisnodosa, ANCA=Antineutrophil cytoplasmic antibody, SLE=Systemic lupus erythematosus, RA=Rheumatoid arthritis, UCTD=Undifferentiated connective tissue disorder, SS=Systemic sclerosis, CCS=Churg-Strauss syndrome, WG=Wegener's granulomatosis

**Table 4: Comparison of the clinical features in vasculitic neuropathy**

| | Present study (*n*=126), *n* (%) | Bennett *et al*.[6] (*n*=53), *n* (%) | Lawrence *et al*.[11] (*n*=46) (%) |
|---|---|---|---|
| Age (years) | 47.4 | 56 | 69.8 |
| Gender | 1.52:1 | 23:30 | 2.8:1 |
| Mononeuritis multiplex | 70 (55.56) | 11 (20) | 9 |
| Asymmetric polyneuropathy | 30 (23.8) | 24 (45) | 10 |
| Symmetrical sensory neuropathy | 5 (3.9) | 6 (11) | 4 |
| Paresthesia | 82 (65.07) | - | 89 |
| Weakness | 39 (30.95) | - | 80 |
| Cranial nerve palsy | 2 (1.58) | 4 (8) | |

eight patients and anemia was seen in one patient. Although constitutional symptoms such as weight loss, fever, and malaise are more common in SVN, it is seen in 15%–40% of NSVN.[18] Similarly, in the study, fever and weight loss were seen in eight patients (7.65%). The serological evidence of ANA and high titers of rheumatoid factor is seen in 30% and 13% cases, respectively, in NSVN.[8,19] Diabetic radiculoplexus neuropathies is a subtype of NSVN occurring in 1% of diabetics characterized by proximal lower limb pain and weakness with a self-limited clinical course.[14] Similarly, was observed in four patients in the study.

Nerve biopsy has an important role in the diagnosis of vasculitis, especially in NSVN as there are no specific clinical or laboratory tests. Since is the disease is focal, the diagnostic yield of sural nerve biopsy is around 50%–60%.[3] In this study, the sensitivity of definite vasculitis on nerve biopsy was 54.76%.The nerve selected for biopsy depends on clinical and electrophysiologically affected sensory nerve. As the sural nerve is a distal branch of a long nerve, it is more prone to be affected. All the biopsies, in this study, were done from the sural nerve as it is a pure sensory nerve leaving no motor deficits after the biopsy. Moreover, it is easily accessible and can be readily tested electrophysiologically. All the patients in the study, had involvement of the sural nerve on NCS. A fascicular nerve biopsy is not indicated in clinically suspected cases of vasculitis as there are chances of missing the vasculitic changes in the perineurial space.[20] Therefore, a whole thickness biopsy of the affected sural nerve was done in all the cases. The epineurial involvement was most common. Endoneurial vessels are rarely involved. Only three biopsies showed endoneurial involvement.

Lymphocytes and macrophages are the predominant inflammatory cell infiltrate, and neutrophils are seen only in acute stages of vasculitis. Most of the lymphocytes in the inflammatory infiltrate are primarily CD4 positive and to a lesser extent, CD8 positive T cells.[21] This explains T-cell-mediated immunological reaction in the pathogenesis of vasculitic neuropathy. Studies have also revealed CD 68 positive macrophages along with few CD 22 positive B cells and CD 16 positive natural killer cells/neutrophils. Engelhardt *et al*. highlighted the use of immunohistochemistry (IHC) with CD4 and CD8 antibodies in cases of microvasculitis where the inflammatory infiltrate is inconspicuous on routine sections.[22.23] However, IHC was not done in the study to reveal inflammatory infiltrate since the inflammation was obvious in all biopsies. Oka *et al*., in their study, on vasculitic neuropathy have shown immunohistochemical expression of hypoxia-inducible factor 1alpha in early phase nerve damage and is a useful discriminatory marker, especially in cases where morphological features are not very well demonstrable.[24]

The classic definite evidence of vasculitis is comprising of transmural inflammation with destruction of the vessel wall with or without fibrinoid necrosis was evident in only 69 (54.76%)

**Table 5: Comparison of histological classification of vasculitic neuropathy**

| | VN | | | SVN | | NSVN | |
|---|---|---|---|---|---|---|---|
| | Present study (*n*=126) | Bennett *et al*.[6] (*n*=53) | Lawrence *et al*.[11] (*n*=46) | Present study (*n*=61) | Bennett *et al*.[6] (*n*=31) | Present study (*n*=65) | Bennett *et al*.[6] (*n*=22) |
| Definite vasculitis (%) | 54.76 | 36 | 26.08 | 32.53 | 48 | 22.22 | 18 |
| Probable vasculitis (%) | 41.26 | 62 | 21.73 | 11.9 | 52 | 29.36 | 77 |
| Possible vasculitis (%) | 3.96 | | 52.17 | 3.96 | | | |

SVN=Systemic vasculitic neuropathy, NSVN=Nonsystemic vasculitic neuropathy, VN=Vasculitic neuropathy

biopsies. This is similar to that reported in other series.[6,11] Table 5 shows the comparison of histological classification of vasculitic neuropathy. Features of definite vasculitis were identified more in systemic vasculitis. This suggests that vascular pathology in NSVN is milder and less necrotizing than in SVN. Perivascular inflammation without vascular damage is insufficient to make a diagnosis of vasculitis as this may be seen in many nonvasculitic inflammatory neuropathies.[25] Collins *et al*. have thus, tried to modify the diagnostic criteria and introduced the "probable" and "possible" categories.[3] This helps in increasing the diagnostic yield on nerve biopsies. Cases with evidence of vessel wall inflammation in the absence of necrosis but other features suspicious of vasculitis such as asymmetric nerve fiber loss and predominant axonal changes has been shown to increase the sensitivity from 61% to 86%.[26] Similar observation was seen in the study with 52 (41.26%) of the biopsies fulfilling the criteria for "probable" vasculitis. Five biopsies lacked classic histological features and were classified as possible vasculitis. The clinical and electrophysiological features were strongly in favor of vasculitis and thus were considered under the category of vasculitic neuropathy. The fiber loss may be centrofascicular or perifascicular based wedge-shaped regions. Multifocal axonal degeneration is characteristic of vasculitic neuropathy.[19]

## Conclusion

This is a large series from a single tertiary care center of vasculitic neuropathy diagnosed on nerve biopsy with clinical correlation. Nonsystemic vasculitis was the predominant type of vasculitic neuropathy in the study. Nerve biopsy is essential for the diagnosis, especially in cases, where neuropathy is the initial manifestation. The pathologic features of definite vasculitis were seen more commonly in systemic vasculitis compared to NSVN in the study indicating a milder form of vascular pathology in NSVN. The predominant involvement seen on histopathology was of epineurial vessels, with chronic axonal changes. The sensitivity increases when the diagnostic criteria of definite and probable vasculitis were applied taking into account perivascular inflammation accompanied by the vascular changes and axonopathy.

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Nil.

### Conflicts of interest

There are no conflicts of interest.

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