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Original Research Article

A Retrospective Study on Clinical Outcomes in Patients with SVN and NSVN

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Abstract

Introduction: One of the most prevalent illnesses of the neurological system is peripheral neuropathy. However, since more than 50% of them are classified as "idiopathic," there are fewer therapy choices. We attempted to assess the phenotypic, laboratory, and prognostic features of patients with biopsy-proven vasculitic neuropathy in this study.

Aim: To describe the clinical and analytical results of patients with vasculitic neuropathy confirmed by biopsy.

Patients and Methods: Review of the biopsy results revealed either definite or probable vasculitic neuropathy.

Results: There were 67 individuals in the cohort. There were 46 people with non-systemic vasculitic neuropathy and 21 people with non-systemic vasculitis (SVS) (NSVN). In 37 patients with definite vasculitis and 30 with possible vasculitis, the nerve biopsy revealed vasculitis. Paraesthesia and weakness were the primary symptoms at the time of beginning (68.7% and 28.4%, respectively). In 70.1% of individuals, diffuse polyneuropathy developed. For the vast majority of patients (80.59%), the course was chronic. 32.84% of patients had mononeuritis multiplex, and 67.16% had polyneuropathy, according to electrophysiology. 16.42% of the population had pure sensory neuropathy. The majority (71.05%) of the individuals who had completed bilateral nerve conduction testing had an asymmetric neuropathy. 80.59% of patients (mean 71.57 ± 30.81 mm/1 hr [in SVS] and 35.24 ± 21.62 mm/1 hr in NSVN]) had an increased erythrocyte sedimentation rate (ESR). Steroids, additional immunomodulators, and symptomatic drugs were all used in the treatment. 10.98 ± 9.58 months on average were spent following up. In 73.46% of patients, the outcome was favourable (43.8% with SVS and 87.88% with NSVN), with the NSVN group performing much better.

Conclusion: Peripheral neuropathy may have a curable underlying cause called vasculitis. The diagnosis and classification of patients into non-systemic and systemic vasculitic neuropathies may be aided by the clinical characteristics, electrophysiological, laboratory data, and nerve biopsy. Compared to patients with systemic vasculitis, NSVN patients had a better long-term prognosis.

Keywords: Electrophysiological evaluation, nerve biopsy, neuropathy, systemic vasculitis, vasculitis

Introduction

A fairly prevalent condition is peripheral neuropathy. This symptom turns out to have an unknown cause in around 60% of cases. In 50 to 70 percent of systemic vasculitic disorders, peripheral neuropathy develops [1, 2]. Systemic vasculitides (SVS) or non-systemic vasculitic neuropathy (NSVN) can cause vasculitic neuropathy [3–8]. The 50–300 mm vessels, or vasa nervosa calibre, are involved in the vasculitic process. Patients with so-called non-systemic vasculitic neuropathy, or vasculitis limited to the peripheral nervous system, have also been described in a number of cases [9, 10]. Because this group makes up one of the categories of reversible neuropathies, early diagnosis and therapy can significantly enhance quality of life [11, 12]. In this investigation, we discuss the clinical, biochemical, electrophysiological, and histological results of patients with biopsy-proven vasculitic neuropathy who were assessed at a single centre and belonged to different age groups.

Methods

The study was conducted between February 2021- January 2022 with the file review of biopsy proven patients of vasculitic neuropathy. All the patients were identified from the neuropathology archives of the records of patients who had undergone a nerve biopsy. Subjects who had evidence of definite or probable vasculitis were included in the study and a retrospective chart analysis was carried out. The study was approved by the institutional ethics committee.

The details of the clinical symptomatology, neurological deficits, and electrophysiological abnormalities were obtained from case records. The progression of symptoms was classified as acute, of less than 4 weeks duration; sub-acute, of between 4-8 weeks duration; and, chronic, of greater than 8 weeks duration.

Results of the laboratory investigations such as the hemogram, erythrocyte sedimentation rate (ESR), biochemistry, serology, and the autoimmune profile, which included the rheumatoid arthritis (RA) factor, antinuclear antibody (ANA), and anti-neutrophil cytoplasmic antibody (ANCA) were recorded, wherever they were available. Electrophysiological studies were carried out using standard protocols, and at least one motor and one sensory nerve each in the upper and lower limbs were examined.

Values beyond 2 standard deviations (SD) of laboratory control data were considered abnormal. Based on the available data, categorization of sensory/sensorimotor, axonal/demyelinating, mononeuritis multiplex/polyneuropathy, and symmetric/asymmetric neuropathies were made.

Definite Vasculitis

Transmural inflammatory infiltration with or without fibrinoid necrosis; Probable vasculitis: The presence of at least one vessel with an inflammatory cell rim or infiltrate, even in the absence of transmural infiltration; and the presence of additional supportive pathologic features, such as vascular changes (vascular thickening and sclerosis, lumen narrowing or obliteration, thrombosis with or without recanalization, epineurial capillary In this study, the presence of ten or more epineurial inflammatory cells or five or more endoneurial inflammatory cells was deemed indicative of severe inflammation. In the context of inflammation and sectorial myelin loss, a minimum of two vascular ***alterations were deemed significant.***

Statistical Analysis

The Statistical Package for the Social Sciences (SPSS) programme was used for the statistical analysis. For categorical data, frequencies were determined, and for continuous variables, means. The

categorical variables were compared between the groups using the chi square test or Fisher exact test, while the continuous variables were compared using the independent sample t test.

Results

76 individuals underwent nerve biopsy procedures with confirmed or suspected vasculitis during the research period. Nine people were not accepted because their medical documents were not full. Analyses were done on the remaining 67 patients' data. 37 patients had confirmed vasculitis, and 30 had suspected vasculitis, according to histopathology.

The majority (51%) of participants were in their fourth or fifth decades at the time of presentation. The age range at presentation was 18 to 69 years; the mean age was 42.67 ± 13.56 years. Male and female patients were impacted virtually equally, showing no gender preference (male: female = 33:34). In the majority of patients (86.6%), the lower limbs were where neuropathic symptoms first appeared. Paresthesias were the primary neuropathic symptom in 68.7% of patients and paresthesias and weakness were present in 28.4% of patients (Table 1).

Table 1: Clinical features of patients who present vasculitic neuropathy

Feature	Observation (*n*=67)
Presence of systemic/constitutional symptoms	26
Duration of systemic symptoms (months + standard deviation)	15.87 ± 13.76
Duration of neuropathic symptoms (months + standard deviation)	9.27 ± 13.73
Initial neuropathic symptom	
Sensory (paresthesias)	46
Sensorimotor (paresthesias and weakness)	19
Motor	2
Onset of neuropathic symptom	
Upper limb	9
Lower limb	58
Clinical pattern of neuropathy	
Mononeuritis multiplex	20
Diffuse polyneuropathy	47
Sensorimotor and sensory neuropathy (clinical)	
Sensorimotor	53
Pure sensory	14
Clinical course	
Chronic	54
Subacute	8
Acute	5

In 70.1% of patients, polyneuropathy and mononeuritis multiplex were the most prevalent clinical patterns. In 14 individuals, a pure sensory neuropathy was observed. In 54 (80.59%) individuals, the clinical course was chronic; in 8 (11.94%), it was subacute; and in 5 (7.46%), it was acute. 80.59% of the patients had an elevated erythrocytic sedimentation rate (ESR), with 50% of them having an ESR value of greater than 50 mm/hr. In 19 out of 59 patients, the rheumatoid arthritis (RA) factor was positive. 59 patients were screened, and 7 of them had antinuclear antibodies (ANA). Ro 52 was positive in 4 out of 29, ds DNA (double stranded deoxyribose nucleic acid) in 2 out of 29, anti- Sm (anti-Smith antibodies) in 2 out of 29, anti-RNP (ribonuclear protein) in 1 out of 29, p-ANCA (perinuclear anti-neutrophil

cytoplasmic antibodies) in 1 out of 25 patients. Three patients were found to be human immunodeficiency virus (HIV) reactive, one of whom was also HBsAg (surface antigen of the hepatitis B virus) reactive.

Of the 67 individuals, 38 had access to bilateral nerve conduction examinations, whereas the other 29 underwent unilateral motor and sensory studies. Only 4.48% of patients had a major demyelinating neuropathy; 95.52% of patients had axonopathy. 83.58% of individuals had sensorimotor neuropathy, while 16.42% had only sensory neuropathy. Polyneuropathy affected more than two thirds (67.16%) of the patients. Side to side asymmetry was also noted in 71.05% of patients with bilateral nerve conduction investigations. Sural nerve biopsy was performed on 61 of the 67 patients, superficial peroneal biopsy on 3, and dorsal cutaneous nerve of the ulnar nerve biopsy on 3. 37 patients had confirmed vasculitis, and 30 had probable vasculitis, according to the results of the nerve biopsy. Seven cases of rheumatoid arthritis with vasculitis were reported. Nine out of the thirteen patients who had muscle biopsies and five out of the seven who had skin biopsies both had vasculitis. Lip biopsies in three individuals with Sjogren's disease, three with HIV vasculitis, two with SLE vasculitis, one with Churg Strauss, and one with systemic sclerosis all had sialadenitis.

49 patients out of a total of 67 had at least a 6-month follow-up. Thirteen of these patients (1 patient died) had a poor prognosis, while 36 patients had a favourable outcome. The average follow-up time was 10.90 9.58 months. Systemic vasculitis had a significantly different prognosis from nonsystemic vasculitic neuropathy (87.88% good, 12.12% poor; 43.8% good, 56.2% poor).

Discussion

As the vasculitic process involves vessels of the size of 50 to 300 micrometres, which is the calibre of the vasa nervosa, peripheral neuropathy is a common symptom in both systemic and nonsystemic vasculitis. Vascular neuropathy can be an isolated occurrence or the result of a systemic illness that affects multiple organs. It accounts for 5.3%[17] to 13.8%[18] of peripheral neuropathies with biopsy evidence.

In this study, systemic vasculitis (21/67, 31.34%) was less common than nonsystemic vasculitic neuropathy (46/67, 68.66%). Studies from the West have shown that people with systemic vasculitis are more numerous than those with non-systemic vasculitic neuropathy. [19] Our results, however, are comparable to the series described by Murthy et al.[20], which included 43.75% patients with systemic vasculitis and 56.25% patients with nonsystemic vasculitic neuropathy. Referral bias is the most likely cause of this difference. As our centre is a tertiary care centre catering exclusively to neurological and psychiatry disorders, the proportion of cases of systemic vasculitides with multiorgan involvement is expected to be small, as most of these patients would be sent to other multi-speciality hospitals. The mean age at presentation of the cohort was 42.67 ± 13.56 years (range: 18-69 years). This study population was younger compared to the published studies from the Western literature. Collins et al.,[19] in their study reported a mean age of 62.1 ± 14.3 years, which is similar to that of Hawke et al. [21] However, our findings (42.67yrs) are comparable to a study from South India in which 42.37 years was the mean age at presentation.[20]

Twenty-six of the sixty-seven patients in the current investigation experienced systemic symptoms, including constitutional ones. Arthralgia, fever, and weight loss were the three most prevalent systemic symptoms (26.9%, 25.4%, and 13.4%, respectively). Systemic and constitutional symptoms are frequently present in systemic vasculitic neuropathy,

although they can also be present in nonsystemic vasculitic neuropathy. [19]

In the current study, 61 (91.04%) patients had their sural nerve most commonly biopsied. Three patients each had their superficial peroneal and dorsal cutaneous branches of the ulnar nerve biopsied. Based on clinical and electrophysiological data, the nerve to be biopsied was chosen. On the biopsy, 37 of these patients showed signs of definite vasculitis, and 30 showed signs of probable vasculitis. It was impossible to remark on the sensitivity of the nerve biopsy in suspected vasculitic neuropathy because the entrance point for our study was histopathologically verified vasculitis. The muscle biopsy revealed vasculitis in 69% of patients, with peroneus brevis having the highest yield. However, the sensitivity of muscle biopsy could not be ascertained in this study, as the number of cases in which muscle biopsy was performed was limited (n = 13). However, the additional yield of muscle biopsy has been described previously.[19,25,26] Lip biopsy revealed sialadenitis in three patients of Sjogren's syndrome. The utility of the lip biopsy in diagnosing the condition is well known.[27]

In the current investigation, vasculitic neuropathy caused by the human immunodeficiency virus (HIV) affected three patients. Peripheral neuropathy's characteristics and patterns have been previously discussed. [28,29] The majority of patients in the systemic vasculitic neuropathy subgroup had connective tissue diseases. Vascular neuropathy has been linked to a number of rheumatological conditions. [30 33]

Parenteral or oral steroids were given to the majority (90%) of the patients. They were given cyclophosphamide to a third of them. Highly active antiretroviral treatment (HAART) was administered by itself to three patients with HIV-related vasculitis. Only a tiny percentage of patients (9% and 6%, respectively) utilised azathioprine and methotrexate. 54% of patients in one of the largest series of vasculitic neuropathy were given cyclophosphamide. Even with nonsystemic vasculitic neuropathy, Collins et al. recommended a combined therapy (steroid plus cyclophosphamide). In 73.46% of cases, the outcome was favourable overall. Systemic (43.8%) and nonsystemic vasculitic neuropathy (87.88%) subgroups differed significantly from each other. Mathew et al.,[34] reported (in the subset of patients with positive nerve biopsies), an overall good outcome in 76% of those patients treated with cyclophosphamide and steroids. In their study, all the patients of nonsystemic vasculitic neuropathy had a good outcome irrespective of the treatment regimen. However, Collins et al., reported that in nonsystemic vasculitic neuropathy, a combination of steroid and cyclphosphamide was more effective than steroids alone, which was consistent with the result of the observational studies in systemic vasculitis.[35] Murthy et al., reported a good outcome in 8 out of 9 patients of nonsystemic vasculitic neuropathy, and in 5 out of 7 patients of systemic vasculitis. Corticosteroids were used in fifteen patients, and only one patient received cyclophosphamide. Hawke et al., also reported a poor long-term prognosis in systemic vasculitic syndromes.

Conclusion

Peripheral neuropathy has a possibly curable aetiology called vasculitis. In contrast to systemic vasculitis, the prognosis for isolated vasculitis of the peripheral nervous system is favourable. Planning treatment procedures, educating patients about medication compliance and adverse drug responses, and properly monitoring these patients all depend on the early diagnosis of these disorders. The few limitations of our investigation may be better addressed in prospective trials.

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