



## Vasculitic peripheral neuropathy

Mona Amini (MD)<sup>1\*</sup>, Reza Boostani (MD)<sup>1</sup>, Maryam Sahebari (MD)<sup>2</sup>

<sup>1</sup>Department of Neurology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

<sup>2</sup>Department of Rheumatology, School of Medicine, Mashhad University of Medical Sciences, Mashhad, Iran

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### ABSTRACT

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Primary systemic vasculitis in pre-capillary arteries is associated with peripheral neuropathy. In some types of systematic vasculitis about 60 % of patients have peripheral nervous system (PNS) involvement. In vasculitic peripheral neuropathies (VPN) a necrotizing and inflammatory process leads to narrowing of vasa nervorum lumen and eventually the appearance of ischemic lesions in peripheral nerves. Some features might be suggestive of VPN, like: axonal nerve degeneration, wallerian-like degeneration, and diameter irregularity of nerve. Peripheral nervous system (PNS) destruction during systemic vasculitides should be considered, due to its frequency and early occurrence in vasculitis progression. The first line treatment of non systematic VPNs is corticosteroid agents, but these drugs might worsen the VPNs or systemic vasculitis.

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## Introduction

Vasculitis is an autoimmune based disorder in which vessel walls have been destroyed by inflammatory events. These destructions lead to organic ischemic damage of different tissues and induce a wide spectrum of signs and symptoms (1). Systemic vasculitis is classified as primary (unknown etiology) and secondary (related to other pathological conditions such as connective tissue disease). Primary capillary arteries is associated with systemic vasculitis

categorization depends on the diameter of involved vessel. Primary systemic vasculitis in pre-peripheral neuropathy; these are included PAN (Polyarteritis Nodosa), Wegener Granulomatosis, etc (2). Some of secondary systemic vasculitis which lead to peripheral neuropathy are Systemic Lupus Erythematosus (SLE), Sjögren Syndrome and non-Hodgkin lymphoma, etc (3). In Figure1 the classification of peripheral vasculitic neuropathy has been shown.

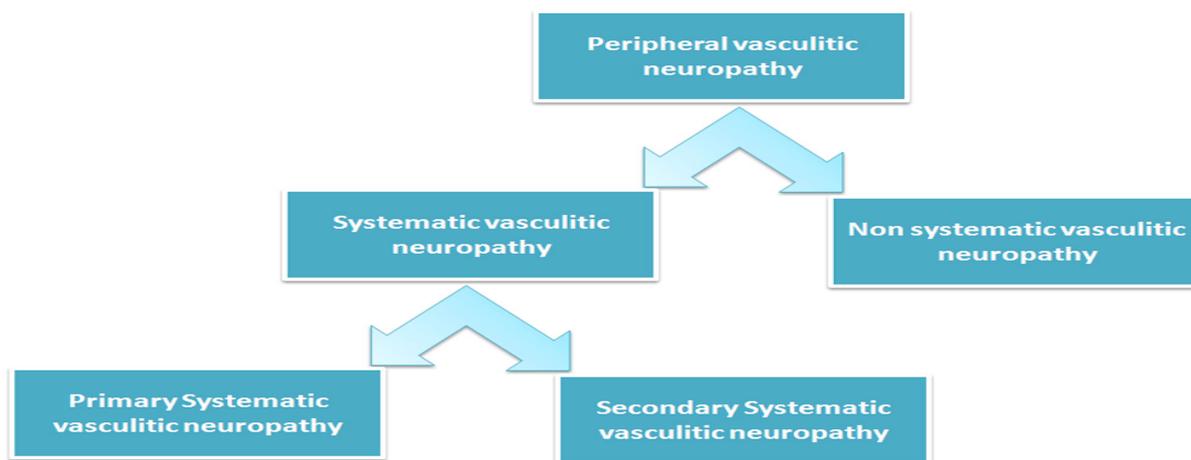
**\*Corresponding author:** Mona Amini.

Department of Neurology, School of Medicine,  
Mashhad University of Medical Sciences, Mashhad,  
Iran

**E-mail:** mona\_amini61@yahoo.com

**Tel:**09153139230

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**Figur1.** Classification of peripheral vasculitic neuropathy

In some types of systemic vasculitis about 60 % of patients have peripheral nervous system (PNS) involvement (4). In some patients peripheral neuropathy is the first or the only clinical manifestation of vasculitis. It can be concluded from various researches that about 30% of vasculitis causes limitations in PNS involvement. Peripheral neuropathy could be presented as a systemic vasculitis or as a non-systemic and isolated disorder in peripheral nervous system, without any serologic abnormality. VPNs (vasculitic peripheral neuropathies) have a heterogeneous etiology. In VPN a necrotizing and inflammatory process leads to luminal narrowing of the vasa nervorum and the appearance of ischemic lesions in peripheral nerves (5,6).

There are two theories for VPN mechanism, first one is the immune complexes deposition in vasa nervorum and the second one is the cell mediated immunity activation (7). Leukocytoclastic reaction has been known as the main mechanism for vessel injury in VPN, in recent years strong evidences have been found which have considered a more important role for immune mediated pathology. Antigen antibody complexes can activate the complement in circulation and lead to produce chemotactic elements. T cell-mediated reactions against endoneurial and epineurial are other parts of immune

mediated injury in VPN. VPN could be diagnosed by biopsy. Some features may be suggestive of VPN, like: axonal nerve degeneration, wallerian-like degeneration, and diameter irregularity of nerve. Though in some cases biopsy might not be diagnostic and only demonstrates the axonal damage (4-7).

## Discussion

Peripheral nervous system (PNS) destruction during systemic vasculitides should be considered due to its frequency and early occurrence in vasculitis progression (5). VPN affects both genders equally. Mean age of patients with VPN is 62 years. VPN clinical manifestations could be evaluated in two categories: neurologic and systemic features. Neurologic examination demonstrates dysesthesia, paresthesia and muscle weakness or pain, these signs and symptoms might be acute or chronic. First affected nerves are the longest one. The peroneal, tibial, ulnar and median nerves are the most involved nerves. Vasculitic peripheral neuropathies are sensory or sensory-motor neuropathies; pure motor neuropathy is very rare. Three patterns of PNS damage of VPN are: distal symmetric polyneuropathy, mononeuritis multiplex and asymmetric polyneuropathy (4).

Distal symmetric polyneuropathy is not

common and has a symmetric stocking-glove pattern in which distal parts of axons are involved firstly. Mononeuritis multiplex occurs in 10 to 15% of VPN and presents as hand or foot drop. It is important to diagnose this neuropathy, due to its leprosy, lyme and diabetes-like symptoms. Asymmetric polyneuropathy is the most frequent pattern (60%). Cranial and facial nerves involvements might happen in some patients as a part of VPN (8).

Imaging studies are not necessary for VPN diagnosis, but must be considered in suspected cases such as spinal nerve root lesion to roll out the differential diagnoses. There is no specific laboratory

test for peripheral neuropathy in vasculitis. Electrodiagnostic tests are a fundamental in diagnosis of any neuropathy, particularly VPN. These tests could localize and estimate nerve involvement distribution and degree (9).

There are some discriminating electrophysiologic manifestations for different types of neuropathies. Nerve or muscle biopsy is recommended in doubtful clinical or electrophysiological outcome, but in most cases electrodiagnostic test and physical examinations are sufficient to distinguish the VPN diagnosis (3). In Table 1 clinical features and treatment of VPN have been shown in different studies.

**Table 1.** Clinical features and treatment of VPN

Author	Asakura (10)	Collins (7)	Jamilloux (11)	Mathew (12)
<b>Publication year</b>	2013	2003	2013	2007
<b>Title</b>	Neurological involvement in Wegener's granulomatosis	Nonsystemic vasculitic neuropathy: insights from a clinical cohort	Immunological profiles determine neurological involvement in Sjögren's syndrome	Treatment of vasculitic peripheral neuropathy: a retrospective analysis of outcome
<b>Vasculitis type</b>	Wegener's granulomatosis	Nonsystemic vasculitic neuropathy	Sjögren's syndrome	—
<b>VPN</b>	Multiple mononeuropathy and multiple cranial neuropathy	Overlapping involvement of multiple nerves	Sensorimotor neuropathy and mononeuritis multiplex	—
<b>VPN treatment</b>	—	Corticosteroid monotherapy, cyclophosphamide for >6 months	Corticosteroids and immunosuppressive drugs	Prednisolone, cyclophosphamide

Corticosteroids, immunosuppressive drugs, plasmapheresis, penicillamine, infliximab, and immunoglobulin are the most used treatments in Sjogren's neuropathy, however in most cases the treatment depends on the vasculitis severity and activity. Axonal damage recovery needs a long time management which is not possible in all patients (12). In secondary VPNs, treatment is focused on treating the predisposing and confounder factors such as infections or

malignancies.

The first line treatment of non systemic VPNs is corticosteroid agents, but these drugs might worsen VPNs or systemic vasculitis. Cyclophosphamide with steroid combination is recommended as a useful remission induction treatment. In maintenance therapy period cyclophosphamide could be replaced by azathioprine or methotrexate. This treatment must be continued at least one year after the remission (7).

In primary or secondary vasculitis neuropathy treatment method depends on the systemic disease severity, but cyclophosphamide with steroid combination is the first line choice in many cases.

In infectious base VPNs short term corticosteroid therapy with at least 6 months anti viral drugs is recommended and plasmapheresis must be considered in resistant patients.

Anti-TNF alpha and Rituximab are the recommended agents in progressive disease.

Pain control medications and physical rehabilitation are necessary in many patients even after appropriate VPN management (13). Patients` prognosis is related directly to early diagnosis and management. It seems that neurologic outcome and deficits are worse in systematic vasculitis neuropathy (14).

In conclusion obtaining accurate and early preventive and therapeutic strategies in patients with systemic vasculitis could reduce the vasculitis peripheral neuropathy burden.

## Conclusion

Peripheral nervous system (PNS) destruction during systemic vasculitides should be considered due to its frequency and early occurrence in vasculitis progression.

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## Conflict of Interest

The authors declare no conflict of interest.

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