

# Diagnostic Crossroads: To Highlight Diagnostic Confusion with Tongue Atrophy and Fasciculations Can Be a Manifestation of Neuropathy

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**Abstract:** *Peripheral neuropathy is a common neurological disorder with diverse etiologies, including metabolic, inflammatory, autoimmune, toxic, and endocrine causes. Among these, vasculitic neuropathy represents an important but potentially treatable cause of subacute to chronic progressive sensorimotor polyneuropathy. It typically results from inflammation of the vasa nervorum, leading to ischemic nerve injury and predominantly axonal degeneration. Clinically, patients may present with painful, asymmetric or symmetric sensorimotor deficits, often associated with systemic inflammatory features. Vasculitic neuropathy may occur as part of systemic autoimmune diseases, including rheumatoid arthritis and other connective tissue disorders, or as a nonsystemic vasculitic neuropathy confined to peripheral nerves. Nerve conduction studies typically show axonal sensorimotor polyneuropathy, and definitive diagnosis is often established by nerve biopsy demonstrating transmural inflammatory infiltrates and vascular changes. Early recognition is crucial, as timely immunosuppressive therapy can significantly alter disease progression and improve functional outcomes. In this case, we present a middle-aged female with hypothyroidism and chronic joint pain who developed progressive painful sensorimotor polyneuropathy with neurogenic atrophy and biopsy-proven vasculitic neuropathy, highlighting the diagnostic crossroads between inflammatory, and other neurogenic mimic etiologies.*

**Keywords:** Vasculitic Neuropathy, Sensorimotor Polyneuropathy, Axonal Degeneration, Nerve Biopsy, Immunosuppressive Therapy

## 1. Case Presentation

A 40/F with known Hypothyroidism and bronchial asthma developed insidious onset progressive weakness of both lower limb followed by upper limb (LL > UL, distal followed by proximal) for 3 years, in the form of H/o aware slippage of chappals, H/o difficulty in getting up from squatting posture and h/o Difficulty in climbing up stairs, H/o difficulty in carrying bucket of water and H/o difficulty in hooking jackets for past 2 years associated with H/o buckling of knees with no H/o falls and H/o flailness of lower limbs. H/o progression of weakness in the form of H/o difficulty in getting up from bed, uses support to walk for past 1 year. H/o cramps over thigh muscle and upperlimb muscle. However, there is no H/o twitching of muscles and no H/o thinning of muscles but however H/o swelling over both calves and both upper limbs present. No H/o Diurnal variation. & fatigability.

H/o paresthesias of both LL and UL for 2 years in the form of burning sensations of palms and soles, H/o reduced perception of temperature of water while bathing in distal upper limb and lower limb, H/o reduced perception of mosquito bite in distal upper limb and lower limb compared to other regions, H/o unaware slippage of chappals, H/o increased sensory perception of slight painful stimuli as severe pain when her children pinch and play with her which was bearable by her previously.

H/o early morning stiffness of small joint and large joint pain of UL and LL, dull aching in quality not associated with movements relieved with medications. H/o pain over bilateral Ankle and toes for past 1 week H/o aggravation of weakness symptoms for past 1 week for which attenders and patient came for medical attention.

On clinical examination there is presence of neurogenic tremor, EDB muscle wasting was present and there is presence of bilateral calves and brachioradialis hypertrophy. vitals were normal. cranial nerve examination revealed tongue atrophy with fasciculation. On motor system examination tone was normal with painful restriction of movement on examination and power was 4 in upperlimb muscles and 4- in lower limb muscles with marked reduction of power in distal muscles. Deep tendon reflexes were absent. Sensory system examination revealed Graded pattern of sensory loss of fine touch, pain and temperature till thigh in LL and till elbow in UL however joint position sense and vibration were normal. Examination of autonomic nervous system was normal. Other system examination was unremarkable.



Image (A): Tongue atrophy



Image (B): Calf muscle hypertrophy



Image (C): Brachioradialis hypertrophy

### Diagnostic Process and Treatment

Based on symptoms and clinical findings we dissociated and associated tongue atrophy and fasciculation with neuropathy. On Dissociating we narrowed down our differential diagnosis into Vasculitic Neuropathy and Hypothyroid neuropathy, On associating our differential diagnosis was Transthyretin Amyloid neuropathy. So, we proceeded for evaluation. Routine blood parameters were within normal range, peripheral smear was unremarkable. ESR, CRP was

elevated. ANA, ANCA, Complement levels were normal. Anti CCP and RA Factor were negative. Anti MUSK was negative. 2d echo and CSF analysis were normal. Electrodiagnostic study revealed mild motor axonopathy of Right ulnar, Moderate axonopathy of Left ulnar, Severe axonopathy of Left median/B/L Tibial /B/L peroneal, Sensory NCS revealed Moderate axonopathy of B/L median/ulnar and Severe axonopathy of B/L Sural. EMG-revealed Neuropathic pattern. MRI brain was normal and MRI C-spine with whole spine screening revealed subtle postero central disc bulge at C4. Since there was correlation of clinical neuropathy and investigation revealed supportive diagnosis of neuropathy we proceeded with Nerve biopsy which revealed Vasculitic neuropathy and no evidence of amyloid deposits in nerve and muscle biopsies. Muscle biopsy revealed neurogenic atrophy. Final diagnosis of Seronegative Rheumatoid Arthritis with Vasculitic Neuropathy mimicking MND and Hypothyroidism Was made. After available of reports of biopsy conclusion were made on vasculitic neuropathy and Investigations were done in lines of vasculitis Rheumatologist Review was obtained advised, Inj. cyclophosphamide 1g IV and prednisolone and thyroxine was started. Periodic review done and patient showed dramatic improvement on assessment.

## 2. Discussion

This case represents a diagnostic crossroads between inflammatory neuropathy, motor neuron disease mimics, endocrine neuropathy, and systemic autoimmune pathology. The patient presented with progressive painful sensorimotor polyneuropathy, distal > proximal weakness, generalized areflexia, tongue atrophy with fasciculations, and neurogenic pattern on EMG, raising an initial concern for lower motor neuron predominant disorders including amyotrophic lateral sclerosis (ALS). However, the presence of prominent sensory involvement, severe neuropathic pain, and biopsy-proven vasculitic changes strongly favored vasculitic neuropathy over a primary motor neuron disease.

Vasculitic neuropathy is a well-recognized but often underdiagnosed cause of subacute axonal polyneuropathy, resulting from inflammation of the vasa nervorum leading to ischemic nerve injury. It may present as asymmetric mononeuritis multiplex or as a symmetric sensorimotor polyneuropathy, particularly in systemic autoimmune conditions. Importantly, peripheral neuropathy can be the sole or predominant manifestation of systemic vasculitis, making early recognition clinically challenging [1].

A notable feature in this case was tongue atrophy with fasciculations and neurogenic atrophy on muscle biopsy, which are classical red flags for motor neuron disease. However, several reports have highlighted that vasculitic neuropathy can mimic motor neuron disease, especially when lower motor neuron signs predominate. In ANCA-related vasculitic neuropathy, patients may present with fasciculations, tremors, and denervation on EMG, leading to an initial misdiagnosis of MND. Luigetti et al. described a case where vasculitic neuropathy closely mimicked MND, emphasizing the need for caution in diagnosing ALS in the presence of atypical features such as sensory symptoms or inflammatory markers [1].

Similarly, tongue atrophy and fasciculations are not pathognomonic for ALS and can be seen in other neuropathic conditions including transthyretin amyloid neuropathy and inflammatory neuropathies. Reports have described tongue denervation with fasciculations in amyloid neuropathy acting as an ALS mimicker, reinforcing the importance of tissue diagnosis and electrophysiological correlation [2]. In our case, negative Congo red staining in nerve and muscle biopsy effectively ruled out amyloid neuropathy, further strengthening the diagnosis of vasculitic neuropathy.

Another important clinical dimension in this case is the background history of chronic joint pain with elevated inflammatory markers and hypothyroidism, raising the possibility of an underlying autoimmune rheumatological process. Rheumatoid arthritis-associated vasculitis is a well-documented entity and may occur even in seronegative patients. Cases of rheumatoid vasculitis in seronegative rheumatoid arthritis have been reported, where classical laboratory markers may remain negative despite active vasculitic pathology [3]. The elevated ESR, CRP, joint symptoms, and epineurial vascular inflammation seen on nerve biopsy in our patient support an immune-mediated vasculitic process possibly related to an underlying inflammatory rheumatologic spectrum disorder.

Electrophysiologically, the NCS findings in this case demonstrated severe axonal sensorimotor polyneuropathy involving median, ulnar, tibial, peroneal, and sural nerves, which is consistent with ischemic axonopathy typically seen in vasculitic neuropathy. Muscle biopsy showing neurogenic atrophy and nerve biopsy revealing transmural inflammatory infiltrates in epineurial arterioles with neovascularisation and luminal narrowing are diagnostic hallmarks of vasculitic neuropathy. The absence of onion bulbs, lack of amyloid deposits, and absence of primary myopathic features helped exclude CIDP, hereditary neuropathy, and amyloid neuropathy respectively.

Hypothyroid neuropathy was considered as a differential given the elevated TSH; however, hypothyroid neuropathy typically presents as a mild, length-dependent, predominantly sensory or sensorimotor neuropathy and rarely causes severe painful axonal neuropathy with biopsy-proven vasculitis. Moreover, the presence of marked inflammation in epineurial vessels and significant axonal degeneration is not characteristic of endocrine neuropathy, thereby making hypothyroidism an associated comorbidity rather than the primary etiology in this case.

This case also highlights the critical importance of nerve biopsy in atypical neuropathies with mixed lower motor neuron features. In patients presenting with tongue fasciculations, muscle wasting, and neurogenic EMG patterns, the presence of sensory loss, severe pain, and elevated inflammatory markers should prompt evaluation for vasculitic neuropathy before labeling the condition as motor neuron disease. Early identification is crucial because, unlike ALS, vasculitic neuropathy is a potentially treatable condition with immunosuppressive therapy such as corticosteroids and cyclophosphamide leading to significant clinical improvement.

Overall, this case underscores that vasculitic neuropathy can closely mimic motor neuron disease and amyloid neuropathy, particularly when lower motor neuron signs such as tongue atrophy and fasciculations are present. A comprehensive clinicopathological correlation including electrophysiology, inflammatory markers, and nerve biopsy is essential to avoid misdiagnosis and to initiate timely immunotherapy in this treatable neurological condition.

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