

## Neurology & Vasculitis – A Complex Convergence

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### Abstract

#### *Presentation*

A 61-year-old female patient developed left ulnar neuropathy and right foot drop over 3 days.

#### *Diagnosis*

Nerve conduction studies (NCS) showed left ulnar and right common peroneal neuropathy. Inflammatory markers were raised and Anti-Neutrophil Cytoplasmic Antibodies (ANCA) positive in a peri-nuclear pattern, evident by antibodies against myeloperoxidase (MPO). Bone marrow biopsy revealed an acute inflammatory response. Cerebrospinal fluid analysis and neuro-imaging were non-diagnostic. Right sural nerve biopsy inconclusive, but demonstrated mild macrophagic infiltration nearby unmyelinated axons, raising the possibility of early peripheral nerve demyelination.

#### *Treatment*

Sensory symptoms improved post-intravenous high-dose methylprednisolone. Inflammatory markers and anti-MPO antibody titres decreased after Rituximab infusion. Following a five-day course of intravenous immunoglobulins (IVIG) and regular physiotherapy, right foot power and left hand motor function subjectively improved.

#### *Discussion*

Diagnosis of mononeuritis multiplex secondary to MPO-vasculitis was supported by nerve biopsy, responsiveness to immunotherapy and antibody positivity.

## Introduction

Mononeuritis multiplex(MNM), defined as progressive dysfunction involving two or more non-contiguous peripheral/cranial nerves<sup>1</sup>, is a recognised neurological manifestation of systemic vasculitis, reported in 65% of cases<sup>2</sup>. This report describes a diagnostically challenging presentation of MNM as the initial manifestation of anti-myeloperoxidase (MPO) ANCA-associated vasculitis (AAV), in the absence of classical systemic features.

## Case Report

A 61-year-old right-handed woman presented with 3 days of asymmetric limb weakness and numbness affecting the left hand and right foot. Past medical history notable for hypertension and significant tobacco use. Four months prior, she developed bilateral lower limb stiffness, pain, fatigue, myalgia and raised inflammatory markers. Her condition deteriorated over eight weeks, culminating in wheelchair dependence. She was treated with oral prednisolone 40mg daily for polymyalgia rheumatica (PMR), which improved mobility and pain.

One month later, she re-presented with new and very rapid-onset weakness, muscle wasting and sensory deficit to regions innervated by the left ulnar and right common peroneal nerves. Examination revealed right foot drop and clawing of the left hand with hypothenar and intrinsic muscle wasting. Weakness of left abductor digiti minimi (MRC 3/5) and positive Froment's sign were evident. Sensory loss confined to the ulnar distribution of the left hand. Right lower limb examination showed reduced tone, severe weakness of right ankle joint dorsiflexion and eversion (MRC 1/5), and sensory loss over the dorsum of the right foot and lateral calf. Reflexes preserved except for diminished right ankle jerk. No signs of cranial neuropathies, upper motor neuron signs, myelopathy, or cerebellar dysfunction.

Investigations revealed leucocytosis (WCC  $17 \times 10^9/L$ ), normocytic anaemia, thrombocytosis, and elevated inflammatory markers (CRP 140 mg/L, ESR 38 mm/hr). Bone marrow biopsy excluded haematological malignancy and demonstrated a reactive inflammatory picture. Serology positive for p-ANCA with anti-MPO antibodies (titres 33 and 16 U/mL on repeat testing). CSF analysis normal, no albumino-cytological dissociation. Nerve conduction studies(NCS) and electromyography(EMG) confirmed severe axonal neuropathies in the left ulnar and right common peroneal nerves, consistent with MNM. MRI brain and spinal cord unremarkable. Sural nerve biopsy revealed mild macrophage infiltration around unmyelinated axons, suggestive of early immune-mediated peripheral nerve demyelination, though not diagnostic for vasculitis.

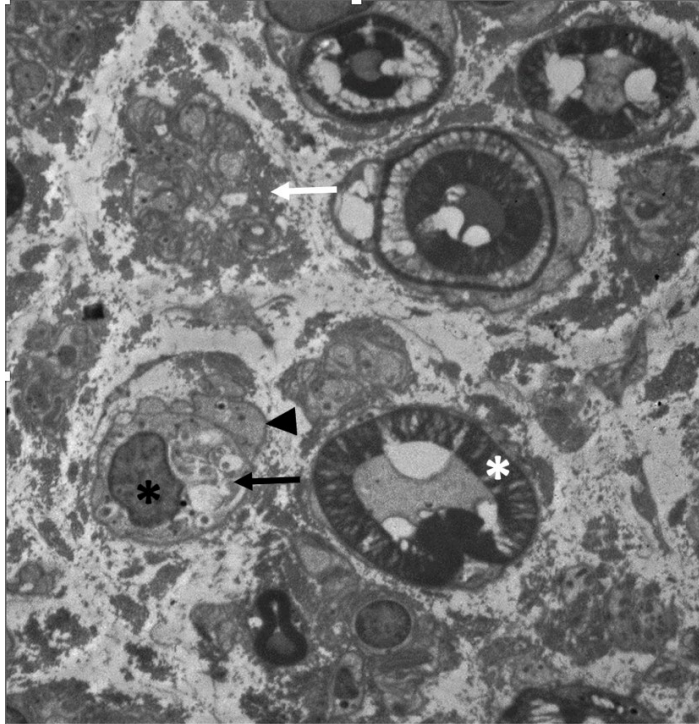


*Figure 1: Electron Microscope image. Black asterisk is the nucleus of a macrophage which contains myelin debris in its cytoplasm (black arrow showing debris). This is in close approximation to an axon without myelin (black arrowhead). White asterisk shows an intact myelinated axon. White arrow shows cluster of unmyelinated axons.*

### Motor Nerve Conduction Studies

| MNCS                                |           |           |           |               |
|-------------------------------------|-----------|-----------|-----------|---------------|
| Nerve                               | Lat<br>ms | Amp<br>mV | CV<br>m/s | F-M Lat<br>ms |
| <b>Medianus Motor Left</b>          |           |           |           |               |
| Wrist - APB                         | 3.44      | 3.6       |           | 24.0          |
| Ulnar <u>stim</u> - APB             | --        | --        |           |               |
| Elbow-Wrist                         | 7.77      | 3.6       | 53.1      |               |
| Ulnar <u>stim</u> -Elbow            | --        | --        | --        |               |
| <b>Medianus Motor Right</b>         |           |           |           |               |
| Wrist - APB                         | 3.29      | 7.6       |           | 23.8          |
| Elbow-Wrist                         | 7.63      | 6.7       | 53.0      |               |
| <b>Peroneal - EDB Motor Left</b>    |           |           |           |               |
| Ankle - EDB                         | 3.96      | 0.18      |           |               |
| <b>Peroneal - EDB Motor Right</b>   |           |           |           |               |
| Ankle - EDB                         | 0.050     | NR        |           |               |
| <b>Peroneus Motor Left</b>          |           |           |           |               |
| Bl. fib. head - TA                  | 2.77      | 4.4       |           |               |
| Ab. fib. <u>head</u> -Bl. fib. head | 4.48      | 3.8       | 49.7      |               |
| <b>Peroneus Motor Right</b>         |           |           |           |               |
| Bl. fib. head - TA                  | 2.93      | 0.66      |           |               |
| Ab. fib. <u>head</u> -Bl. fib. head | 4.15      | 0.66      | 77.9      |               |
| <b>Tibialis Motor Left</b>          |           |           |           |               |
| Ankle - <u>Abd hal</u>              | 3.67      | 5.1       |           | 49.4          |
| <b>Tibialis Motor Right</b>         |           |           |           |               |
| Ankle - <u>Abd hal</u>              | 3.42      | 7.3       |           | 47.6          |
| <b>Ulnaris Motor Left</b>           |           |           |           |               |
| Wrist - ADM                         | 2.77      | 0.58      |           |               |
| Bl. elbow-Wrist                     | 6.65      | 0.48      | 47.7      |               |
| Ab. elbow-Bl. elbow                 | 8.95      | 0.46      | 45.7      |               |
| <b>Ulnaris Motor Right</b>          |           |           |           |               |
| Wrist - ADM                         | 2.31      | 8.5       |           | 25.0          |
| Bl. elbow-Wrist                     | 5.71      | 7.1       | 52.9      |               |
| Ab. elbow-Bl. elbow                 | 7.56      | 7.2       | 59.5      |               |

### Sensory Nerve Conduction Studies

| SNCS                                          |                |           |           |
|-----------------------------------------------|----------------|-----------|-----------|
| Nerve                                         | Peak Lat<br>ms | Amp<br>uV | CV<br>m/s |
| <b>Medianus Sensory Left</b>                  |                |           |           |
| Wrist - Dig II                                | 3.11           | 20.4      | 57.8      |
| Wrist - Dig III                               | 3.29           | 15.3      | 55.8      |
| <b>Medianus Sensory Right</b>                 |                |           |           |
| Wrist - Dig II                                | 3.08           | 17.7      | 60.9      |
| Wrist - Dig III                               | 3.27           | 17.2      | 60.9      |
| <b>Peroneus <u>superfic</u> Sensory Left</b>  |                |           |           |
| Lower leg - Ankle                             | --             | --        |           |
| <b>Peroneus <u>superfic</u> Sensory Right</b> |                |           |           |
| Lower leg - Ankle                             | --             | NR        |           |
| <b>Radialis Sensory Left</b>                  |                |           |           |
| Forearm - <u>Dig I</u>                        | 1.56           | 26.6      | 72.8      |
| <b>Radialis Sensory Right</b>                 |                |           |           |
| Stim - <u>Dig I</u>                           | 1.69           | 26.7      | 68.4      |
| <b>Suralis Sensory Left</b>                   |                |           |           |
| Mid. lower leg - Ankle                        | 2.75           | 4.4       | 58.7      |
| Mid. lower leg - Ankle 2                      | 2.69           | 5.1       | 57.6      |
| <b>Suralis Sensory Right</b>                  |                |           |           |
| Mid. lower leg - Ankle                        | --             | BIOPSY    |           |
| <b>Ulnaris Sensory Left</b>                   |                |           |           |
| Wrist - Dig V                                 | --             | NR        |           |
| <b>Ulnaris Sensory Right</b>                  |                |           |           |
| Wrist - Dig V                                 | 2.74           | 20.8      | 61.0      |

Figure 2: Peroneal motor studies recording from Extensor Digitorum Brevis (EDB) show an absent response on the right. The response recording from the right tibialis anterior is severely attenuated in amplitude in keeping with axon loss without slowing or conduction block around the fibular head. Ulnar sensory response is absent on the left. Ulnar CMAP amplitude is severely attenuated on the left in keeping with axon loss with diffuse slowing in the axonal range throughout the nerve.

## Discussion

Intravenous methylprednisolone (1 g/day for 3 days) led to 30% subjective improvement in sensory symptoms. Rituximab infusion reduced inflammatory markers and ANCA titres. A five-day course of IVIG and physiotherapy, resulted in 75% improvement (self-reported) in right foot strength and 30% improvement in left hand function. At six months post-IVIG, neurological examination demonstrated no appreciable change in muscle strength compared to baseline. Repeat NCS/EMG pending. Quantitative Muscle Assessment (QMA) not performed due to unavailability of specialized neurophysiotherapy services at the Model 3 centre.

Anti-MPO antibodies are present in 50% of patients with microscopic polyangiitis and its specificity for ANCA-associated vasculitis (AAV) is above 90%.<sup>3</sup> Although AAV typically presents with renal, pulmonary, cutaneous, or joint involvement<sup>4</sup>, MNM can occasionally serve as primary manifestation. The clinical constellation of asymmetric sensorimotor

neuropathy, MPO-ANCA seropositivity, steroid responsiveness and histology supported the diagnosis.

The most common aetiologies of MNM are vasculitic neuropathies, including polyarteritis nodosa, eosinophilic granulomatosis with polyangiitis, granulomatosis with polyangiitis, cryoglobulinaemic vasculitis (typically Hepatitis C-related), rheumatoid vasculitis and vasculitis associated with Sjögren's syndrome or systemic lupus erythematosus<sup>5</sup>. Other causes include diabetes mellitus, autoimmune thyroid disease, infections, neurosarcoidosis and drug-induced neuropathies<sup>1</sup>.

This case underscores the importance of considering systemic vasculitis in patients presenting with rapidly progressive, asymmetric neuropathies despite the absence of classical systemic features.

**Declarations of Conflicts of Interest:**

None declared.

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