A case of atypical Miller Fisher Syndrome with stroke-like onset

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AIM: describing an atypical case of Miller-Fisher Syndrome (MFS)

CASE PRESENTATION: a 62-year-old man, with a history of hypertension, dyslipidemia, previous ischemic stroke without sequelae, was admitted to Neurology Department of Policlinico Tor Vergata in October 2024 with an **acute progressively worsening postural instability**.

Neurological examination at admission: ataxic gait with retropulsion; spontaneous, right-beating inexhaustible nystagmus; vertical up-beating nystagmus in the Rose position; leftward deviation at past-pointing test, preserved deep tendon reflexes

➡ suspected posterior circulation stroke

He subsequently developed **binocular diplopia** on right lateral gaze, rightward **deviation of the soft palate**, **hypersialorrhea** with progressively worsening mixed **disphagia**, nasogastric tube feeding needed. Deep tendon reflexes became absent. No previous infection was reported.

Diagnostic workup

- Brain MRI: negative for acute ischemic lesions (Fig.1)
- Cerebrospinal fluid (CSF): white cells 12 mmc, proteins 38 mg/dL
- Anti-ganglioside antibodies: negative in both serum and CSF
- Onconeural antibodies, Serum tumor markers: negative
- Whole body FDG PET-TC: negative
- Repetitive nerve stimulation, serum AchR Ab, MuSK Ab: unremarkable
- **Electroneurography (ENG) on 31th October 2024**: bilaterally reduced sensory nerve action potential (SAP) amplitude of the ulnar and median nerves, F-wave latency prolonged in both upper and lower limbs

  ➡ **Non–length-dependent sensory neuropathy of the upper limbs** (Fig. 2)
- **ENG on 8th November 2024:** severe reduction in SAP amplitude in the right sural nerve and median nerves, the lower limbs consistent with ***Miller Fisher syndrome*** (Fig. 3)
- **Electrochemical skin conductance (ESC)** measured with Sudoscan: severe sudomotor dysfunction

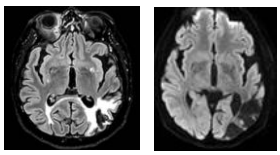


Fig 1. Brain MRI. FLAIR and DWI

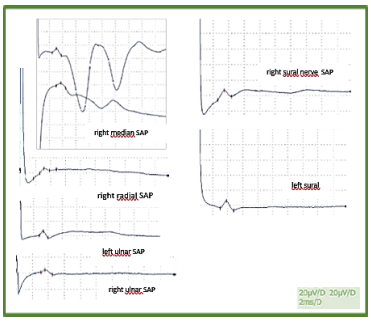


Fig 2. ENG 31th October 2024

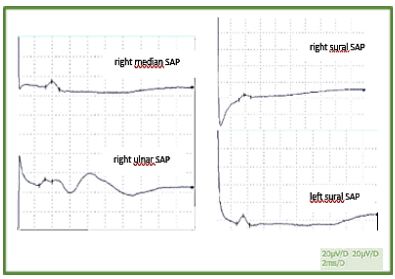


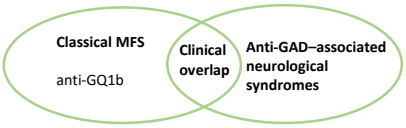
Fig 3. ENG 8th November 2024

Considering the atypical presentation with both peripheral and central signs (e.g. central nystagmus), an extended autoimmune antibody panel was performed on serum and CSF, revealing elevated **serum anti-glutamic acid decarboxylase antibodies titer** (159,3 UI/ml – nr < 5) [1]

Clinical and neurophysiological findings suggested MFS; intravenous immunoglobulin was administered for 5 consecutive days (0,4 g/kg/die), with progressive clinical improvement.

But…what underlies the patient's symptoms?

The Anti-GAD Antibodies



Autoimmune comorbidities linked to anti-GAD antibodies were excluded

Open questions: in anti-ganglioside seronegative cases

- Could anti-GAD Ab reflect an underlying systemic autoimmune background that promotes other pathogenic processes (e.g. through unidentified antibodies or inflammatory mechanisms) involving both central and peripheral nervous system? [2]
- Could anti-GAD Ab play a pathogenic role impairing central Gabaergic transmission? → it has been postulated that anti-GAD Ab may cause reduction of GABA synthesis in the nerve terminal as well as dysfunction of GAD-expressing neurons in the brainstem and cerebellum [3]
- Could anti-GAD Ab serve as an immunological marker, suggesting exposure to other, yet unidentified, antigens? [3]

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