



# SARS-CoV-2 associated Miller-Fisher syndrome or polyneuritis cranialis

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**Letter to the Editor:** With interest, we read the review article by Li et al. about 7 patients with SARS-CoV-2-associated Miller-Fisher syndrome (MFS) (Li et al. 2021). It was found that the most common clinical manifestations of SARS-CoV-2 associated MFS are perioral paresthesias (57.1%), ataxia (57.1%), blurred vision (42.9), ophthalmoplegia (42.9), and generalized areflexia (Li et al. 2021). The report is interesting but raises the following comments and concerns.

As per the end of March 2021 at least 13 patients with SARS-CoV-associated MFS or polyneuritis cranialis (PNC) have been reported (Dinkin et al. 2020, Garnero et al. 2020, Gutiérrez-Ortiz et al. 2020, Julio Caamaño and Alonso 2020, Kajani et al. 2021, Lantos et al. 2020, Lowery et al. 2020, Manganotti et al. 2020, Ray 2020, Reyes-Bueno et al. 2020, Senel et al. 2020). In a recent review about SARS-CoV-2 associated Guillain Barre syndrome (GBS) collected until the end of December 2020, 11 patients with MFS or PNC were identified (Finsterer et al. 2021). Of these 11 patients, 2 patients had MFS plus PNC and one patient MFS plus acute, inflammatory demyelinating polyneuropathy (AIDP) (Finsterer et al. 2021). In addition to these 11 cases, SARS-CoV-2-associated MFS was reported by Kajani et al. (2021) and Manganotti et al. (2020).

Age of these 13 patients ranged from 32 to 71 years (Table 1). Ten patients were male and 3 female (Table 1). Onset was identified after/before onset of non-neurological COVID-19 manifestations in 12/1 patients (Table 1). Latency between onset of COVID-19 and MFS/PNC ranged from 1 to 20 days. SARS-CoV-2 was not detected in the CSF in any of the patients (Table 1). Therapy of MFS comprised intravenous immunoglobulins (IVIG) in 9 patients, steroids in 1 patient, and three patients did not receive any therapy (Table 1).

Full recovery was achieved in 6 patients, partial recovery in 6 patients, and one patient died (Table 1). This review showed that the outcome of SARS-CoV-2-associated MFS/PNC is fair and that not only cranial nerves III, IV, and VI supplying the extra-ocular eye muscles can be affected in MFS but also other cranial nerves and also the peripheral nerves.

Concerning the methods of the study, it is unclear why PubMed was searched for appropriate hits only at a single day and not repeatedly. Searching the database only once can be associated with overlooking appropriate articles. Furthermore, application of only “MFS” as a search term is insufficient given the fact that MSF may be overlapping with other subtypes of GBS. Additional helpful search terms could be “ophthalmoparesis”, “polyneuritis cranialis”, “ptosis”, or “oculomotor nerve palsy”.

It is mentioned that COVID-19 was diagnosed in five of the seven patients prior to onset of MFS, suggesting that the diagnosis of COVID-19 in the two remaining patients was established after onset of MFS. If MFS developed before COVID-19 in two patients, it is conceivable that MFS in these two patients was not causally related to COVID-19 but may have another etiology. The statement that the temporal relationship between MFS and COVID-19 was not reported in three patients does not comply with the information that COVID-19 was diagnosed before/after onset of MFS in 5/2 patients.

A further shortcoming is that anti-GQ1b antibodies were detected in only a single patient. The fact that not all MFS patients were tested positive GQ1b is interesting as GQ1b antibodies are reported positive in up to 100% of the cases (Teener 2012). A further limitation is that the 7 cases included in the review were not referenced.

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**Table 1** SARS-CoV-2-associated MFS reported as per the end of March 2021

Age (y)	Sex	Onset	LOO (d)	Subtype	CIC	Comorbidities	IVIG	AV	Recovery	Country	Reference
50	M	A	3	MFS, PNC	No	No	Yes	No	Yes	Spain	Gutiérrez-Ortiz et al. (2020)
39	M	A	3	MFS, PNC	No	No	No	No	Yes	Spain	Gutiérrez-Ortiz et al. (2020)
61	M	A	10	MFS	No	No	S	No	Yes	Spain	Juliao Caamaño and Alonso (2020)
36	M	A	4	MFS	nr	nr	Yes	No	Yes	USA	(Lantos et al. 2020)
51	F	A	14	MFS	nr	nr	Yes	No	Partial	Spain	(Reyes-Bueno et al. 2020)
34	M	A	4	PNC	nr	Strabism	Yes	No	Partial	USA	(Dinkin et al. 2020)
71	F	A	Days	PNC	nr	AHT	No	No	Partial	USA	(Dinkin et al. 2020)
49	M	A	14	MFS	No	Crohn’s disease	Yes	Yes	Partial	USA	(Lowery et al. 2020)
55	M	A	20	AIDP/MFS	No	nr	Yes	No	Partial	Italy	(Gamero et al. 2020)
63	M	A	1	MFS	nr	nr	No	No	Partial	UK	(Ray 2020)
61	M	A	nr	MFS	No	nr	Yes	No	Yes	Germany	(Senel et al. 2020)
50	M	B	Days	MFS	No	DM, heroin, obesity	Yes	Yes	Death	USA	(Kajani et al. 2021)
50	F	A	16	MFS	nr	No	Yes	No	Yes	Italy	(Manganotti et al. 2020)

A onset of GBS after onset of non-neurological manifestations, *AHT* arterial hypertension, *AV* artificial ventilation, *B* onset of GBS before onset of non-neurological manifestations, *CIC* CoV2 in CSF, *DM* diabetes, *F* female, *LOO* latency between onset of GBS and COVID-19, respectively, vice versa, *M* male, *nr* not reported, *PNC* polyneuritis cranialis, *S* steroids

Overall, the review is appealing but has several limitations which should be accomplished before drawing conclusions as those presented.

**Author contribution** JF: design, literature search, discussion, first draft, critical comments

**Data availability** Not applicable

**Declarations**

**Ethics approval** The study was approved by the institutional review board.

**Consent to participate** Not applicable

**Consent for publication** Not applicable

**Informed consent** Informed consent was obtained.

**Conflict of interest** The author declares no competing interest.

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