Acute Asymmetric Sensorimotor Variant of Chronic Inflammatory Demyelinating Polyneuropathy Triggered by mRNA-1273 COVID-19 Vaccination

Chang-Jie Cheng[1,2], Chien-Jung Lu[1*]

Abstract

Purpose: Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) developing in the postvaccination period was distinctly unusual and its course was rarely well described. We aimed to clearly depict the clinical features of acute-onset multifocal acquired demyelinating sensory and motor neuropathy (MADSAM) caused by mRNA-1273 COVID-19 vaccination.

Case report: A 74-year-old man noticed weakness of hands 2-3 days after he accepted the second dose of mRNA-1273 COVID-19 vaccine. He soon became unable to walk within one week. Initially, muscle power of bilateral hand grasping was most severely affected. He had stayed on at the nadir for 3.5 months until the diagnosis of CIDP was made. Nerve conduction studies showed typical evidences of acquired demyelinating, but no sural spare pattern. He was treated with intermittent pulse steroid therapy. Two weeks after treatment, INCAT disability score improved from 10 to 4, but remained at 4 thereafter: arm disability score was 3 and that of leg was 1, which suggested muscles of upper limbs were more severely affected.

Conclusion: Diagnosis of acute-onset MADSAM was challenging at the beginning of this disease. For vaccine-triggered CIDP, time to symptom onset could be as short as 2-3 days. Delay in recognition may influence the remission of this disease. Muscles of upper limbs were more affected than those of lower limbs. Intermittent steroid pulse therapy would be an alternative to daily oral steroid therapy.

Keyword: chronic inflammatory demyelinating polyradiculoneuropathy, COVID-19 vaccination.

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INTRODUCTION

Typical chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) manifests as a chronic progressive course of weakness and sensory deficit symmetric in proximal and distal, generalized areflexia, and loss of large fiber sensation in length-dependent pattern[(1)]. Up to 16%-18% of CIDP patients the disease occurs acutely and mimics Guillain-Barré syndrome (GBS), which is termed acute-onset CIDP[(2)]. Although the clinical and electrophysiological features of acute-onset CIPD could be initially similar to those of GBS, the

From the [1]Department of Neurology, En Chu Kong Hospital, New Taipei City 237, Taiwan. [2]Department of Neurology, National Taiwan University Hospital, Taipei 100, Taiwan.
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Correspondence to: Dr. Chien-Jung Lu, MD. Department of Neurology, En Chu Kong Hospital, No. 399, Fuxing Rd., Sanxia Dist. New Taipei City 237.
E-mail: chienjung.lu@gmail.com

neurological deficits usually persist more than 8 weeks[2].

Asymmetric sensorimotor variant of CIDP, also known as multifocal acquired demyelinating sensory and motor neuropathy (MADSAM), is a well-described atypical variant of CIDP that accounts for 5 to 10 percent of CIDP cases. Patients often develop insidious onset of gradually progressive weakness and numbness which is characterized by asymmetry and affecting distal muscles more than proximal. Upper limbs are more severely affected than lower extremities[1]. MADSAM may eventually evolve into typical CIDP, and exhibit patterns of acquired demyelination on nerve conduction studies[1]. MADSAM is usually responsive to steroids and intravenous immunoglobulin (IVIg).

As COVID-19 vaccination programs commenced globally in late-2020, cases of new-onset autoimmune diseases triggered by COVID-19 vaccination have been reported in succession. Among them, GBS was one of the most often reported neuropathies[3-7]. Cases of CIDP were seldom reported as compared with those of GBS[4,8,9]. The COVID-19 vaccination campaign started in March, 2021 in Taiwan. People can receive mRNA-1273, BNT162b2, ChAdOx1, MVC COVID-19 Vaccine, or in combination in Taiwan. Here we present a rare case of acute-onset CIDP/ MADSAM triggered by mRNA-1273 COVID-19 vaccine.

CASE PRESENTATION

A 74-year-old man was normal except having osteoarthritis of both knee joints. He noticed weakness of hands and legs 2-3 days after he accepted the second dose of mRNA-1273 COVID-19 vaccine. He soon became unable to walk within one week. At that time, he was suffering quadriparesis: the powers of all proximal muscles were at grade 3 (of modified Medical Research Council scale), and those of bilateral hand-grasping were at grade 2. However, there was asymmetry between bilateral anterior tibialis muscles: grade 2 of right one and grade 4 of left one. Tendon reflexes were preserved, but mildly diminished. He also complained of paresthesia over bilateral C8 and T1 dermatomes. Spinal MRI revealed thecal sac compression at C4/C5 level (Figure 1) and spondylolisthesis at L4/L5 level. Because of acute-onset asymmetric weakness and retained tendon reflexes, acute compressive cervical radiculomyelopathy with pre-existing lumbar radiculopathy was considered. So, he accepted an anterior discectomy of cervical spines. Patient had got temporary improvement during perioperative days when he was treated with steroid.

Two weeks after that operation, however, disability reached the nadir where patient had stayed on for 3.5 months until he met the other neurologist who mad the diagnosis of CIDP. At that time, he had mild asymmetry

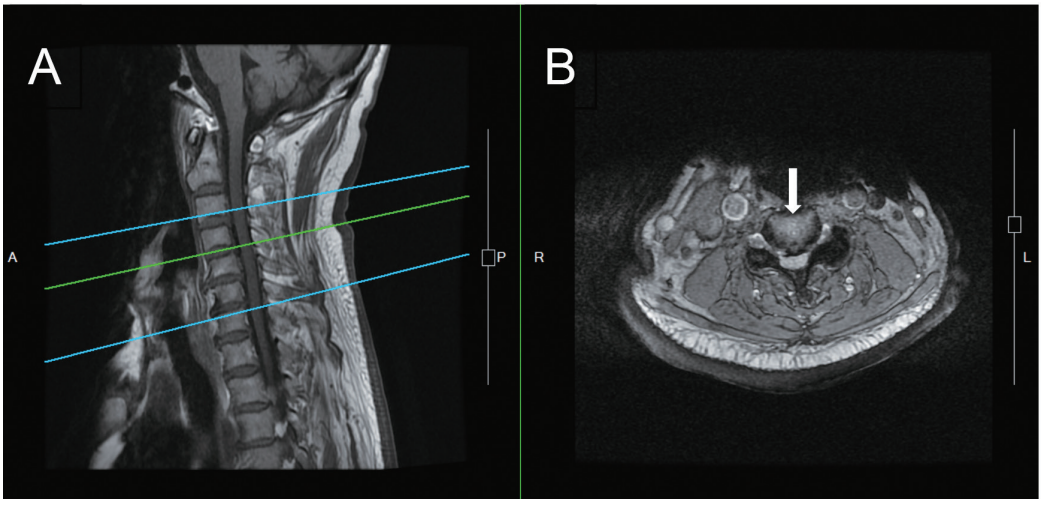

Figure 1. MRI of cervical spines. On Figure 1A, green line indicated the level was between C4 and C5. On Figure 1B, cerebrospinal-fluid space was obscured (white arrow), which suggested compression of thecal sac. There was no compression of cord because the shape of cord still appeared ovoid.

in weakness: muscle power of right side was generally weaker than that of left side. In upper limbs, powers of right proximal muscles were at grade 3, and those of left ones were at grade 4-. Distal muscles were more affected than proximal ones: bilateral hand-grasping power was at grade 2. The muscles of both lower limbs were less affected: powers of the right proximal and distal muscles were at grade 4-, and those of left ones were at grade 4. Patient, however, could not stand at all. By neurological examination, doctor discovered generalized areflexia, absent Babinski sign, intact sensation of pinprick and light touch, but impaired vibration and joint position sense in bilateral lower limbs. Cranial nerves and sphincter function were not involved. Nerve conduction studies showed typical evidence of acquired demyelinating and electromyography disclosed evidence of axonal degeneration; however, sensory action potentials of bilateral sural nerves were absent (Table 1).

Basic serum laboratory studies were performed, including hemoglobin A1c; complete blood cell count; electrolytes; liver, renal, and thyroid function studies; and vitamin B12 level. He was also screened for a monoclonal gammopathy with serum and urine electrophoresis, immunofixation, and free light chains. The results of the above tests were all normal. Cerebrospinal fluid study was not done.

Since power of bilateral hand grasping was most affected at the onset, he was considered as a patient who initially presented with MADSAM which eventually evolved into typical CIDP. He was soon treated with

Table 1. The nerve conduction study revealed slowing of conduction velocities in all evoked nerves; prolongation of motor latencies in bilateral median nerves, bilateral ulnar nerves, and left peroneal nerve; prolonged F-wave latencies in bilateral tibial nerves and left peroneal nerve; partial motor conduction block in bilateral median and tibial nerves. The absent signal from right peroneal nerve was probably due to right L5 radiculopathy.

Motor

Nerve	Stimulation site	Recording site	Latency (ms)		Amplitude (mV)		Velocity (m/s)	
			R	L	R	L	R	L
Median	Wrist	Abductor pollicis brevis	7.8	8.9	3.0	3.3		
	Elbow		13.9	15.8	2.1	2.3	35	34
Ulnar	Wrist	Abductor digiti minimi	4.4	3.8	5.9	8.0		
	Below elbow		8.4	8.3	5.2	6.9	23	25
	Above elbow		12.7	12.3	3.6	5.7	30	32
Tibial	Ankle	Abductor hallucis	5.9	4.9	8.0	11.2		
	Popliteal fossa		16.4	15.2	4.0	5.7	37	37
Peroneal	Ankle	Extensor digitorum brevis	NR	7.7	NR	3.1		
	Above fibular head		NR	15.8	NR	4.7		38

Sensory

Nerve	Stimulation site	Recording site	Latency (ms)		Amplitude (μV)		Velocity (m/s)	
			R	L	R	L	R	L
Median	Wrist	2nd digit	4.0	5.0	8.0	5.0	36	29
Ulnar	Wrist	5th digit	NR	2.8	NR	6.0		41
Sural	Lower leg	Ankle	NR	NR	NR	NR		

F-wave

Nerve	Latency (ms)	
	R	L
Median	NR	NR
Ulnar	33.5	33.4
Tibial	71.4	70.9
Peroneal	NR	69.5

intermittent pulse steroid therapy: methylprednisolone 1,000 mg every day for 3 days, followed by 1000 mg one day every week for 4 weeks. The inflammatory neuropathy cause and treatment (INCAT) disability score improved from 10 to 9 after he just accepted methylprednisolone 1000 mg for 3 days. INCAT score improved to 7 within one week, and thereafter maintained at 4: disability score of arms was 3 and that of legs was 1. As compared with the upper limbs, improvement was more significant in the lower limbs. Currently, he is regularly examined to see the effectiveness and side effects of intermittent pulse steroid therapy.

DISCUSSION

CIDP is a great imitator. The typical form usually progresses slowly. However, its onset could be acute and its progression could be rapid. Such acute-onset CIDP could mimic GBS, but both diagnoses were overlooked in this patient because the speed of onset and progression was so fast. CIDP could be mistaken for acute worsening of cervical compressive myelopathy because both disorders would get benefit by steroid therapy. As with this patient, asymmetric dorsiflexion of both feet was initially mistaken for a co-morbid L5 radiculopathy because of common morbidity of lumbar spondylosis.

CIDP consists of a variety of atypical variants. As to the atypical features of this patient, the first was acute onset. The second was asymmetric weakness which was significantly worse on upper limbs and distal muscles. Weakness of typical CIDP is present in a non-length-dependent pattern, affecting both proximal and distal muscles in similar degrees. As with this patient, upper limbs were more affected than lower extremities in MADSAM. The third was no "sural-sparing" pattern, which implied distal sensory involvement. The latter two atypical features pointed to the diagnosis of MADSAM. Therefore, the diagnosis of this patient was acute-onset MADSAM which combined acute onset with asymmetric sensorimotor features. The incidence of such "rare and rare" variant of CIDP was unknown.

Clinical diagnosis depended greatly on nerve conduction studies which showed evidences of acquired demyelination, including slowing of conduction velocities, prolongation of sensory and motor latencies, prolonged F-wave latencies, and motor conduction block. The unique finding of both acute and chronic acquired demyelinating neuropathies, the so-called sural sparing pattern, was not found in this patient. It may suggest sensory involvement of MADSAM was more than typical CIDP. EMG demonstrated reduced recruitment of normal morphology motor unit potentials with secondary axonal degeneration and reinnervation. Active denervation change was not found. CSF analysis was usually not necessary when the clinical manifestations and electrophysiological studies were consistent with CIDP, but it may be helpful for inconclusive case. When collected, albuminocytologic dissociation is anticipated. Basic serum laboratory studies were performed to exclude alternative or confounding diagnoses. The screening for a monoclonal gammopathy was also negative. Therefore, the occurrence of this atypical CIDP was supposed to be triggered by mRNA-1273 COVID-19 vaccination.

Cases of inflammatory demyelinating polyneuropathy after COVID-19 vaccination had been reported worldwide. Most of the cases were GBS characterized by facial diplegia occurring after adenovirus-vectored vaccines[4-7]. In some patients GBS deteriorated again after some weeks from onset, or several relapses occurred; in these patients a diagnosis of acute-onset CIDP was then considered. Therefore, diagnosis of acute-onset CIDP was challenging at the beginning of this disease. Only fewer cases of CIDP triggered by ChAdOx1 vaccines had been reported[4,8,9]. CIDP after vaccination was a rare event, accounting for about 1.5% of all patients with CIDP. Time of vaccination to symptom onset ranged from 2 days to 8 weeks. To the best of our knowledge, this is the first case of acute-onset MADASM after receiving mRNA-based COVID-19 vaccine in Taiwan.

For most treatment-naïve patients with CIDP, recommendations of immune-modulatory treatments consist of intravenous immune globulin (IVIg), plasma exchange, and glucocorticoids. Initial treatment with glucocorticoids appears more effective at achieving long-term remission[10,11]. In a retrospective study, 60% of patients were responsive to glucocorticoids, with 61% of treatment responders achieved remission[12]. Currently, we prefer the use of pulse rather than daily glucocorticoids for initiation and initial titration of dosing[13]. Although not confirmed by clinical trials, pulse dosing may have both

a greater chance for early efficacy, higher durability of response, and a better side effect profile. We typically start with an initial dose of IV methylprednisolone (1,000 mg/day) for three days, followed by 1,000 mg one day a week for four weeks[14]. Limited observational data suggest that IV therapy is associated with less weight gain and fewer cushingoid features but possibly more restlessness and sleep problems compared with oral therapy[14].

In sum, this was a case of vaccine-triggered CIDP. Diagnosis was delayed because the clinicians overlooked hyperacute-onset polyneuropathy. Delay in diagnosis may influence prognosis. As with this patient, he was a steroid responder, but did not get complete remission. In accordance with findings of electromyography, incomplete remission may suggest secondary axonal degeneration. We reported this case, and hoped the clinicians could early recognize this disease.

REFERENCES

1. Gwathmey K. Chronic Inflammatory Demyelinating Polyradiculoneuropathy and Its Variants. Continuum (Minneap Minn). 2020;26(5):1205-23.
2. Ruts L, Drenthen J, Jacobs BC, van Doorn PA. Distinguishing acute-onset CIDP from fluctuating Guillain-Barre syndrome: a prospective study. Neurology. 2010;74(21):1680-6.
3. Chen Y, Xu Z, Wang P, Li XM, Shuai ZW, Ye DQ, et al. New-onset autoimmune phenomena post-COVID-19 vaccination. Immunology. 2022.
4. Oo WM, Giri P, De Souza A. AstraZeneca COVID-19 vaccine and Guillain- Barré Syndrome in Tasmania: A causal link? Journal of Neuroimmunology. 2021;360: 577719.
5. Shao SC, Wang CH, Chang KC, Hung MJ, Chen HY, Liao SC. Guillain-Barré Syndrome Associated with COVID-19 Vaccination. Emerging infectious diseases. 2021;27(12):3175-8.
6. Su SC, Lyu RK, Chang CW, Tseng WEJ. The First Guillain-Barre Syndrome After SARS-CoV-2 Vaccination in Taiwan. Acta neurologica Taiwanica. 2022;31:46-51.
7. Pegat A, Vogrig A, Khouri C, Masmoudi K, Vial T, Bernard E. Adenovirus COVID-19 Vaccines and Guillain–Barré Syndrome with Facial Paralysis. Annals of Neurology. 2022;91(1):162-3.
8. Bagella CF, Corda DG, Zara P, Elia AE, Ruiu E, Sechi E, et al. Chronic Inflammatory Demyelinating Polyneuropathy after ChAdOx1 nCoV-19 Vaccination. Vaccines. 2021;9(12):1502.
9. Suri V, Pandey S, Singh J, Jena A. Acute-onset chronic inflammatory demyelinating polyneuropathy after COVID-19 infection and subsequent ChAd Ox1 nCoV-19 vaccination. BMJ Case Reports. 2021;14 (10):e245816.
10. Nobile-Orazio E, Cocito D, Jann S, Uncini A, Beghi E, Messina P, et al. Intravenous immunoglobulin versus intravenous methylprednisolone for chronic inflammatory demyelinating polyradiculoneuropathy: a randomised controlled trial. Lancet Neurol. 2012; 11(6):493-502.
11. Nobile-Orazio E, Cocito D, Jann S, Uncini A, Messina P, Antonini G, et al. Frequency and time to relapse after discontinuing 6-month therapy with IVIg or pulsed methylprednisolone in CIDP. Journal of Neurology, Neurosurgery & Psychiatry. 2015;86(7):729.
12. Van Lieverloo GGA, Peric S, Doneddu PE, Gallia F, Nikolic A, Wieske L, et al. Corticosteroids in chronic inflammatory demyelinating polyneuropathy. Journal of Neurology. 2018;265(9):2052-9.
13. van Schaik IN, Eftimov F, van Doorn PA, Brusse E, van den Berg LH, van der Pol WL, et al. Pulsed high-dose dexamethasone versus standard prednisolone treatment for chronic inflammatory demyelinating polyradiculoneuropathy (PREDICT study): a double-blind, randomised, controlled trial. Lancet Neurol. 2010;9(3):245-53.
14. Lopate G, Pestronk A, Al-Lozi M. Treatment of Chronic Inflammatory Demyelinating Polyneuropathy With High-Dose Intermittent Intravenous Methylprednisolone. Archives of Neurology. 2005;62 (2):249.