Diagnostic challenges of functional neurological disorders after covid-19 disease or vaccination: case series and review of the literature

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Abstract
Background  Functional neurological disorders have rarely been described in patients recovering from Covid-19 or after vaccination but they are probably under diagnosed.

Material and methods  Six patients referred for rehabilitation of persistent symptoms and/or sequelae of Coronavirus disease 2019 (COVID-19) were diagnosed with functional neurological disorders. A literature review was conducted to identify reported cases of functional neurological disorders after Covid-19 infection or vaccination.

Results  In the current case series, patients diagnosed with functional neurological disorders presented high variability of clinical symptoms including hemiplegia, lower limb unilateral or bilateral paralysis, myoclonus, dystonia, tremor and sensory impairment. Four patients were young females with mild Covid-19 infection without hospital admission. Their neurological symptoms developed over the course of 4 weeks after the beginning of Covid-19 symptoms or vaccine administration with normal ancillary exams. One patient presented overlapping functional neurological symptoms and mild impairment of the left common peroneal nerve after prolonged ICU stay. In addition, all patients in our case series reported other non-motor symptoms such as fatigue, cognitive impairment and diffuse pain or dysesthesia, which are compatible with post Covid-19 condition.

Conclusions  It is important that clinicians recognize functional neurological symptoms and consider it as a differential diagnosis in patients with neurological complications of Covid-19 infection and vaccination.

Keywords  Covid-19 · Functional neurological disorders · Post Covid-19 condition · Vaccine

Introduction
Since the beginning of the Coronavirus disease 2019 (COVID-19) pandemic, an increasing number of functional neurological disorders (FND) have been reported in Covid-19 patients [1]. FND are characterized by common neurological symptoms such as movement disorders, paralysis, seizure, speech disorders and sensory impairment related to a functional, rather than a structural, disorder; symptoms are inconsistent and are incompatible with known neurological or medical conditions [2]. During the beginning of the COVID-19 pandemic, cases of functional movement disorders such as dystonia, gait disorders, tremor and non-epileptic seizure, more than doubled (9% versus 4% in previous years) in the Movement Disorders Unit of the Pitié-Salpêtrière University Hospital (Paris, France) [1]. Over 50% (10 out of 20) of patients admitted to the epilepsy monitoring unit in Texas hospital for urgent and emergent case evaluation during the first two months of pandemic presented psychogenic, non-epileptic seizures [3]. The prevalence of FND in the general population vary across studies, including approximately 12% of new neurology outpatient referrals in a large (3781 patients) prospective cohort study in the UK [4]. However, despite the global magnitude of Covid-19
pandemic and the high prevalence of neurological symptoms in patients with acute and long Covid-19, cases of FND have rarely been reported in this population [5–8].

The diagnosis of functional neurological symptoms may be specifically challenging in people with post Covid-19 condition, which is characterized by newly onset, fluctuating, or relapsing symptoms several months after initial recovery from Covid-19 [9].

Here we report 6 clinical cases of FND who were referred for rehabilitation of neurological symptoms of Covid-19 or complications of Covid-19 vaccine and discuss their common clinical traits, results of complementary neurological explorations and treatment/rehabilitation outcomes to facilitate their diagnostic and management.

**Materials and methods**

This case series included patients referred to the Institute Guttmann (Badalona, Barcelona, Spain) by a primary care physician or a specialist for evaluation of persistent symptoms and/or sequelae of COVID-19. All patients were evaluated by a Neurology or Physical Medicine and Rehabilitation specialist and a Neuropsychologist. When psychopathology was suspected, patients were also evaluated by a Psychiatrist. The diagnosis of functional neurological disorder was made according to the DSM-5 criteria [10]. Written informed consent for video publication was obtained from all patients.

A literature review was conducted in PubMed for articles on functional neurological disorders after Covid-19 infection or vaccination published from March 2020 to August 2022.

**Case description**

Sociodemographic characteristics, Covid-19 related clinical information, type of FND and results of complementary explorations are summarized in the Table 1.

**Case 1**

A 50-year-old male business person, developed severe Covid-19 infection and required ICU admission, mechanical ventilation for 20 days, and treatment with Methylprednisolone, Lopinavir/Ritonavir and Hydroxychloroquine. He presented with lower limb weakness, hypoaesthesia and neuropathic pain due to right lumbosacral plexopathy as a sequelae of the prolonged prone position but was able to walk with a walker after 2 months of rehabilitation. At 11 months after the acute infection, the patient developed a new episode of progressive bilateral lower limb weakness. He was able to stand but unable to walk due to a sensation of having his feet glued to the ground.

He required help for basic daily life activities and used an electric wheelchair to move around. He also complained of a burning sensation in his feet, sensation of full bladder without voiding desire, fatigue, and short-term memory alterations.

Neurological evaluation revealed bilateral lower limb weakness with inconsistent muscle strength at examination vs standing or transferring, trunk shaking and bilateral hand tremor at standing, distal symmetric hypoaesthesia, and impaired vibration in the lower limbs (Video 1). Neuropsychological evaluation revealed mild attention impairment, memory retrieval difficulties and executive function impairment. The complementary exams revealed mild lesion of the left common peroneal nerve, incongruent with the severity of motor impairment. He underwent rehabilitation and was able to walk with a walker after 2 weeks of training.

**Case 2**

A 30-year-old female nursing assistant, 1 month after mild Covid-19 reported insidious onset, progressive right-sided muscle weakness, slowness of gait, loss of balance, impaired sensory perception with burning and pressure-type pain in the right hemibody, bradykinesia of the right hand, dysphagia and 2 isolated episodes of bladder and bowel incontinence. Due to neurological impairment, she became dependent on others for basic daily life activities and started using a crutch for walking. In addition, she reported symptoms of persistent cough, severe fatigue, and episodes of severe shortness of breath which led to multiple emergency room visits.

Her neurological examination revealed right-sided hemiparesis and generalized bradykinesia. The motor impairment was inconsistent and disappeared during distraction: the patient kept her arm close to the trunk while walking or sitting (as if it was glued to the body) but was able to extend and lean on the arm. In addition, the Barre test was negative; she was lifting her paralyzed leg with the left arm to get on and off the examination couch but no weakness was observed during neurological examination or walking (Video 2). She also presented right-side hypoaesthesia with inconsistent midline boundaries on examination. The neuropsychological evaluation revealed impaired attention, memory, and executive functions, as well as symptoms of anxiety and depression. The complementary exams were normal. She was informed about the nature of FND and her motor symptoms spontaneously improved a few weeks later, being able to walk without crutches.

**Case 3**

A 43-year-old female pharmacist, developed progressive rubber leg and tingling sensation in the left leg, which led to
| ID | Age (years), Sex (M/F) | Medical history | Covid-19/Vaccine symptoms | Onset of FND after infection/vaccine | Type of FND | FND characteristics | Ancillary exams | FND treatment and evolution |
|----|------------------------|-----------------|---------------------------|------------------------------------|-------------|--------------------|-----------------|-----------------------------|
| 1  | 50, M                  | Obesity Benign prostatic hyperplasia | Severe infection (ICU admission and mechanical ventilation for 20 days) | Fatigue, cognitive impairment | 11 months | Bilateral lower limb weakness | Inconsistent muscle strength at examination vs standing or transferring, trunk shaking and bilateral hand tremor at standing | Head and spine MRI - normal. EMG: mild lesion of the left common peroneal nerve | Pregabalin, Lacosamide, Clonazepam, Sertraline without improvement Was able to walk with a walker after 2 weeks of physical rehabilitation but paraplegia persisted |
| 2  | 30, F                  | No Mild infection (no hospital admission) | Severe fatigue, persistent cough, episodes of severe shortness of breath, cognitive impairment, anxiety and depression | 1 month | Right-sided hemiparesis Right-sided hypoalgesia | Right-sided hemiparesia, disappeared during distraction Generalized slowness Inconsistent midline boundaries on sensory examination | Head MRI, EMG, MEPs, SSEPs - normal Tests for autoimmune disease – normal | Psychotherapy with motor improvement |
| 3  | 43, F                  | Migraine (untreated); Pericarditis (post-Covid-19) | Mild infection, second episode (no hospital admission) | Fatigue, cognitive impairment, anxiety and depression | 2 weeks | Unilateral lower limb weakness | Inconsistent weakness of left foot dorsiflexion muscles with normal toe raising and normal gait Inconsistent left-side dysmetria with slow movements and functional Romberg test | Head CT, EMG, MEPs, SSEPs - normal | Physical and neuropsychological rehabilitation without improvement |
| 4  | 46, F                  | Vocal cords polypectomy | Mild infection (no hospital admission) | Lower limb pain and emotional lability | 1 week | Head tremor Trunk and pelvis shaking Bilateral lower limb weakness Neck and shoulder dystonic movements | Intermittent, head tremor with a varying pattern, which decreased or ceased with distraction maneuvers or while walking Variable high amplitude flexion-extension movements of the pelvis, waddling gait, astasia-abasia without falling Dystonic movements with intermittent neck extension, scapular retraction and trunk rotation. Inconsistent bilateral lower limb weakness in supine position | Head and spine MRI, EMG, SSEPs - normal | Sodium valproate, Clonazepam with no effect on symptoms |
Table 1 (continued)

| ID | Age (years), Sex (M/F) | Medical history | Covid-19/Vaccine | Post Covid-19 symptoms | Onset of FND after infection/vaccine | Type of FND | FND characteristics | Ancillary exams | FND treatment and evolution |
|----|------------------------|-----------------|-----------------|------------------------|-------------------------------------|-------------|---------------------|----------------|--------------------------|
| 5  | 51, M                  | Mechanical neck pain Ludopathy | Mild infection (no hospital admission) | Cognitive impairment, anxiety and depression | 4 days | Jerky movements of upper and lower limbs | Jerky movements with variable amplitude and frequency, appeared in supine position during the early evening or later at night, disappeared during sleep and did not interfered with walking or driving | Head and spine MRI, MEPs and SSEPs, Polysomnography—normal, Metabolic analysis—normal, Jerk-locked back averaging EEG revealed presence of Bereitschaftspotential | Diazepam, Topiramate, Ropidolat, Amitriptyline without any improvement | Gradual resolution after his disability application was denied and returned to work |
| 6  | 20, F                  | Vertigo as a side effect of HPV vaccine; Transient unilateral visual impairment after an odontologic intervention; Mild Covid-19 | Vaccine, second dose | Fatigue | 1 week | Knee buckling | Sudden knee buckling and shaking legs while standing or walking and disappeared during monopodal standing or dragging the feet | Head and spine MRI, MEPs, SSEPs—normal | Diazepam with no effect on symptoms |

CT computer tomography, EMG electromyography, HPV human papillomavirus, MEPs motor evoked potentials, MRI Magnetic resonance imaging, SSEPs somatosensory evoked potentials
loss of muscle strength and gait impairment two weeks after Covid-19 reinfection (15 months after the first episode) with mild symptoms. She had been using crutches and a wheelchair for about 2 weeks. She also complained of fatigue, memory problems and paraphasias. The neurological evaluation revealed inconsistent weakness of left foot dorsiflexion muscles with normal toe raising while standing and normal gait; marked slowness of movement; inconsistent left-side dysmetria with altered finger-to-nose and heel–knee–shin test, functional Romberg test with excessive trunk sway and falling passively backward or lateral with normal proprioceptive sensation (Video 3). The neuropsychological evaluation revealed mild attention impairment and symptoms of anxiety and depression. The complementary exams were normal. She underwent rehabilitation without changes.

**Case 4**

A 46-year-old female factory worker, presented with sudden bilateral lower limb weakness and a sensation of having the feet glued to the floor and knee buckling, which developed during the first week of mild Covid-19 infection. She needed support for standing and required assistance while walking to avoid falling. During the following weeks she developed head tremor and pelvis shaking, lower limb pain, and emotional lability. She was taking Sodium valproate and Clonazepam without reporting any effects. The neurological examination revealed intermittent head tremor with a varying pattern, which decreased or ceased with distraction maneuvers (for example while performing coordination tests) and at walk. During standing and walking, she presented with variable high amplitude flexion extension movements of the pelvis, waddling gait which persisted during tandem and backward walking, astasia–abasia without falling, dystonic movements with intermittent neck extension, scapular retraction and trunk rotation. She also presented severe bilateral lower limb weakness in supine position without any limb weakness with negative Mingazzini test (Video 4). The neuropsychological evaluation revealed mild attention and executive function and severe memory impairment with incongruous learning and recalling abilities, anxiety and depression. Her complementary exams were normal. She was recommended psychotherapy and a follow-up visit within 3 months.

**Case 5**

A 51-year-old male taxi driver, 4 days after mild Covid-19 infection, reported bilateral, sudden onset jerky movement of lower limbs in supine position during the early evening or later at night, which did not interfere with walking or driving. After 4 months, the episodes became less frequent but increased in amplitude, and he also noticed similar movements in the upper limbs. He has tried several drugs which were ineffective. His neurological examination was normal, and analysis of the home recorded videos revealed jerky movement of lower limbs with variable amplitude and frequency (Video 5). The neuropsychological evaluation revealed evocative mnesic impairment and significant anxious and depressive symptoms. The jerk-locked back averaging EEG revealed presence of Bereitschaftspotential prior to the movement onset. After his disability application was denied, the symptoms gradually improved and he was able to return to work.

**Case 6**

A 20-year-old female student, during the first week after her 2nd dose of Pfizer/BioNTech vaccine administration, reported exacerbated post Covid-19 fatigue. Over a 3 day period, she developed bilateral leg weakness, shaking legs and impaired gait: therefore, she started using a wheelchair to move around (Video 6). She also had paresthesia in the upper limbs. The neurological examination revealed normal motor balance in supine position with sudden knee buckling and shaking legs while walking or standing. The buckling disappeared during monopodal standing or dragging the feet. Her complementary exams were unremarkable. She was recommended psychotherapy but no further follow-up was scheduled in our center.

To summarize, the FND in our series were very heterogeneous and included motor impairment (hemiplegia, lower limb unilateral or bilateral paralysis), movement disorders (myoclonus, dystonia and tremor), and sensory and cognitive impairment (Table 1). Most patients were young female with mild Covid-19 infection who did not require hospital admission. One patient presented with overlapping symptoms of functional paraplegia and lesion of the left common peroneal nerve after prolonged ICU. Complementary neurological exams were useful to confirm the presence of a positive functional sign and to evaluate Covid-19 related residual neurological impairment (Table 1).

**Discussion**

The current case series characterizes clinical phenotypes, diagnosis and outcomes of FND in post Covid-19 patients. In our case series, most patients were young females (66.66%, mean age 34.75 years) presenting with clinically heterogeneous motor and sensory FND (movement disorders, limb weakness, numbness or pain and gait disorder), which is line with previous reports on FND after Covid-19 infection or vaccine administration (Table 2). However, whereas post Covid-19 functional symptoms usually developed during the first weeks of infection, FND after Covid-19 vaccine
were commonly observed during the first 24 h after vaccine administration and included episodes of limb numbness and weakness mimicking polynuropathies, functional seizure, short lasting twitches and transient nerve palsy.

Demographic and clinical phenotypes of FND in our population are in line with FND characteristics in a recent large meta-analysis including 4905 individuals (non Covid-19), which revealed a high prevalence of FND in women (72.6%) with a significantly earlier age of onset of FND in women (39.1 years) versus men (40.1 years) and mixed FND (23.1%), tremor (21.6%) and weakness (18.1%) as the most common phenotypes [11].

In our study, functional paralyses (lack of movement, weakness) were observed in four patients (#1, #2, #3, #4). These were characterized by fluctuating muscle strength with impaired voluntary movements but normal motor function during neurological examination or distraction maneuvers; dissociation between severe motor impairment in the lower limbs in sitting or supine position and preserved walking ability, similar to previous reports [12]. Other functional motor symptoms described in post Covid-19 patients, such as external rotation of the foot and leg-dragging gait pattern functional hemiplegia [8], drift without pronation in functional upper limb paresis [7] may support the functional nature of motor impairment.

Functional paroxysmal hyperkinetic movements, dystonia and gait disorders where the most common functional movement disorders that required urgent admission to a specialized unit during the COVID-19 pandemic [1]. Repetitive, irregular jerky leg movement observed in the patient #5 and other post Covid-19 patients [5, 6, 13] differ from myoclonic jerky movement produced by structural lesions: the former usually vary in amplitude and frequency, appear in supine position, and decrease with distraction, standing or walking [14]. In contrast, functional negative jerky movement in patient #6 was observed during walking and disappeared during monopodal standing or walking without lifting their feet off the ground and, despite severe gait impairment, the patient did not fall. The knee-buckling in these patients is slower compared to negative myoclonus seen in patients with hypoxic or metabolic encephalopathy [15]. Diagnosis of more complex movement disorders resembling choreo-dystonic movements, similar to those observed in patient #4, may be challenging. Gait disturbance characteristics such as excessive slowness of movements; walking on ice; sudden knee buckling; uneconomic postures; swaying from side to side without falling; astasia-abasia, and functional Romberg may be the key to their diagnosis [16].

In post Covid-19 patients, functional sensory and motor impairment are frequently associated, therefore mimicking stroke, spinal cord injury or polineuropathy [8, 13, 17, 18]. Fluctuating limb dysesthesia or sensory impairment with inconsistent midline boundaries on examination with exact splitting of sensation in the boundaries of specific dermatome or nerve territory observed in patient #1 are suggestive of FND. Numbness in the four extremities associated with pain or weakness resembling polynuropathies, commonly beginning within 24 h of Covid-19 vaccine administration, were the most frequent phenotype of FND in a retrospective study in Japan [19]. Although uncommon, post-vaccination Guillain-Barré syndrome was reported as a major neurological complication of Covid-19 vaccine which generally appeared within 2 weeks of vaccine administration, as a result of molecular mimicry [20]. Therefore, nerve conduction studies, and CSF examination may be required for diagnostic purposes.

Although exhaustive instrumental examination is frequently conducted in patients with FND to exclude potential neurological damage, the results are usually normal or do not explain the neurological impairment. It is well known that over 20% of patients with FND may have and underlying neurological diseases [21, 22]. Therefore, instrumental diagnosis may be especially relevant in patients with suspected overlapping symptoms due to coexisting neurological diseases. In our study, complementary neurological explorations were normal in all patients, except for patient #1 who presented mild residual lesion of the left common peroneal nerve following prolonged ICU stay that did not explain his motor and gait impairment; therefore, pointing to overlapping symptoms of functional and structural neurological impairment. Other electrophysiological exams such as jerk-locking back averaging EEG with recording of Bereitschaftspotentials (indicating the involvement of the premotor cortex involvement in the preparation for movement) can be a useful diagnostic tools in patients with suspected functional myoclonus [23].

The diagnosis of non-motor FND in patients with long Covid-19 may be challenging. All patients in our study presented with other non-motor symptoms, such as fatigue, cognitive impairment and diffuse pain, which are common in post Covid-19 patients, regardless of the severity of acute infection [24]. However, their potential functional origin is not clear. The patient #4 reported severe memory impairment but the neuropsychological examination revealed incongruous learning and recalling abilities. Although “gold standard” diagnostic criteria for functional cognitive impairment are lacking, their functional nature is suggested by inconsistency between self-reported symptoms and objective cognitive deficits revealed by neuropsychological assessment [25].

Furthermore, four patients in our study presented with significant symptoms of anxiety or depression, which were exacerbated by or developed after acute Covid-19. FNDs are frequently comorbid with psychopathology such as anxiety, panic, depression, or posttraumatic stress disorders [2]. Although psychological comorbidity is not required for
Table 2  Review of the literature with case reports of FND after Covid-19 infection and vaccine

| Publication | Age (years), Sex (M/F) | Covid-19/Vaccine Post Covid-19 symptoms | Onset of FND after infection/vaccine | Type of FND | FND characteristics | Ancillary exams | FND treatment and evolution |
|-------------|------------------------|----------------------------------------|-------------------------------------|-------------|---------------------|----------------|---------------------------|
| Garg A, 2021 | 54, M                  | Moderate infection (hospital admission, no ICU) | Dizziness and lightheadedness, headache, throat numbness and brain fog, numbness and tingling in the arms and legs, muscle pain, fatigue, depression and poor sleep | 2 months | Jerky flexion movements of the head | Video EEG –head movements 150–200 ms, variable in frequency associated with movements artifacts, disappeared during sleep. Head CT, EMG, CSF analysis normal Metabolic, autoimmune, paraneoplastic negative | Levetiracetam with no improvement. Neuropsychological and physical rehabilitation with minimal improvement |
| Albu S, 2022* | 37, M                  | Moderate infection (hospital admission, no ICU) | Lower limb hyperesthesia | 2 weeks | Lower limb weakness | EMG normal Metabolic, autoimmune, infection–negative | Complete motor recovery after 2 months of physical rehabilitation |
|             |                        | Mild infection (no hospital admission) | Fatigue, joint pain, headache, cognitive impairment and major depressive disorder | 1 week | Left sided weakness Left sided hypoaesthesia Right hand tremor | Head and spine MRI, MEPs and SSEPs, EMG, CSF analysis–normal Metabolic, autoimmune, paraneoplastic negative | Physical and neuropsychological rehabilitation during 3 months without improvement |
| Piscitelli D, 2020 | 39, F                  | Mild Infection (no hospital admission) | NR | 1 week | Lower limb tremor, twisted movements and jerks | Head and Spine MRI, SSEP’s normal Autoimmunity and infection screening-negative | Benzodiazipines with no effect Tremor improvement after testing negative to SARS-CoV-2 |
| Publication   | Age (years), Sex | Covid-19/Vaccine | Post Covid-19 symptoms                                                                 | Onset of FND after infection/vaccine | Type of FND | FND characteristics                                                                 | Ancillary exams                          | FND treatment and evolution |
|--------------|-----------------|------------------|--------------------------------------------------------------------------------------|--------------------------------------|-------------|-------------------------------------------------------------------------------------|------------------------------------------|-----------------------------|
| Gilio L, 2021 | 23, M           | Mild infection (no hospital admission) | Fatigue, fluctuating limb dysesthesia, attention and memory difficulties, depression and anxiety | NR                                   | Left arm weakness | Arm weakness with extreme slowness and drift without pronation, variable and distractible | Head MRI, NCS, EMG, and EP were normal | Psychotherapy and physical therapy with resolution of dysesthesia and motor symptoms and cognitive improvement after 4 months |
| Ercoli T, 2021 | 41, M           | Vaccine, first and second dose | Immediate Bilateral facial palsy Right side weakness Left sided facial hypoesthesia | NA                                   | Bilateral arm weakness | Difficulties to blink and move facial muscles Transitory right-side weakness Left-side facial hypoesthesia with midline splitting of sensory deficit in the face | Head CT, head MRI, CA Doppler normal | No treatment Spontaneous resolution of facial palsy and hemiplegia within 40 min and resolution of sensory disturbance after 2 weeks |
| Butler M, 2021 | 38, F           | Vaccine, first dose | 20 min Left sided weakness Speech and cognitive impairment | Left sided weakness Progressive left-side weakness over 2 day with symptoms variability and positive Hoover's sign Intermittent word-finding difficulty and stammering and short-term memory impairment | Head CT and MRI –normal | Spontaneous improvement |
| 36, F         | Vaccine, second dose | NA | 2 h Alternating limb weakness | Right foot dragging with no arm swing while walking, variable pattern and excessive fatigue Fine movements impairment on the right hand New-onset left-sided weakness few weeks later | Head and spine MRI, EMG and NCS –normal | Physical therapy Evolution NR |
Table 2 (continued)

| Publication                  | Age (years), Sex (M/F) | Covid-19/Vaccine | Post Covid-19 symptoms | Onset of FND after infection/vaccine | Type of FND                          | FND characteristics                                      | Ancillary exams                        | FND treatment and evolution       |
|------------------------------|------------------------|------------------|------------------------|-------------------------------------|--------------------------------------|----------------------------------------------------------|---------------------------------------|-----------------------------------|
| Fasano A, 2021 NR, F         | Vaccine, 2 dose        | NA               | 20 min                 | Generalized tonic-clonic seizure     | Inability to move the body, preserved level of consciousness, no post-ictal period | EEG-normal                               | NR                                   |                                   |
| NR, F                       | Vaccine, dose NR       | NA               | 2 weeks                | Right-sided hemihypesthesia          | No sensory alteration on neurological examination | Head CT-normal                                | NR                                   |                                   |
| De Souza A, 2022 22, F       | Vaccine, first and second dose | NA              | 24 h                   | Involuntary movements of the head, neck, back and right shoulder resembling tremor | Brief twitches, increasing in frequency and amplitude on sitting or moving around, remitted when asleep. Tremors varied in amplitude and frequency, were entrainable, increased with weighting but decreased with distraction | Head and spine neuroimaging-normal | Diazepam | Nearly complete resolution after 1 week |
| 21, F                       | Vaccine, dose NR       | NA               | 6 weeks                | Head and bilateral upper limb tremor | Progressive irregular, jerky tremor; variable in frequency and direction, distractible and entrainable, spreading to other parts of the body on attempted voluntary suppression | Head MRI-normal | Metabolic, infection-negative | Recommended rehabilitation Evolution NR |
| 69, F                       | Vaccine, first and second dose | NA              | 1 week                 | Weakness of all limbs and reduced touch perception below the knees Jerky movements of the lower limbs Catatonic posturing in the lower limbs Catatonic posturing in the upper limbs | Weakness of the 4 limbs with impaired standing and gait Catatonic posturing with weak and flaccid muscles on examination with preserved movements in bed and was able to deflect her arm away from the face | Head and spine MRI, NCS, EMG-normal | Limb weakness improved after 5 weeks | Rapid motor improvement after rehabilitation Resumed ambulation with minimal support in 1 week |
| Publication | Age (years), Sex (M/F) | Covid-19/Vaccine | Post Covid-19 symptoms | Onset of FND after infection/vaccine | Type of FND | FND characteristics | Ancillary exams | FND treatment and evolution |
|-------------|------------------------|------------------|-----------------------|-------------------------------------|------------|--------------------|-----------------|-------------------------|
| Takahashi O, 2022 | 20s, F | Unknown | Fatigue | 24 h | Neuropathy-mimic | Numbness, pain and weakness in the 4 extremities, gait difficulties | NCS-normal Laboratory test-normal | Counseling and anxiolytics | Complete recovery |
| | 20s, M | Modena, dose NR | Fatigue | 24 h | Neuropathy-mimic | Numbness and pain in the 4 extremities and face, gait difficulties | Head and spine MRI, NCS-normal Laboratory test-normal | Counseling and anxiolytics | Complete recovery |
| | 20s, F | Unknown | NA | 24 h | Neuropathy-mimic | Numbness in the 4 extremities | Head and abdominal CT, NCS-normal CSF and laboratory test-normal | Counseling and anxiolytics | Complete recovery |
| | 30s, F | Modena, dose NR | NA | 24 h | Neuropathy-mimic | Numbness in the 4 extremities | Head CT, Spine MRI, NCS-normal Laboratory test-normal | Counseling and anxiolytics | Complete recovery |
| | 40s, F | Phizer, dose NR | NA | 1 week | Neuropathy-mimic | Numbness in the 4 extremities | NCS-normal Laboratory test-normal | Counseling and anxiolytics | Complete recovery |
| | 40s, F | Unknown | NA | 24 h | Neuropathy-mimic | Numbness in the 4 extremities | NCS-normal Laboratory test-normal | Counseling and anxiolytics | Complete recovery |
| | 50s, F | Unknown | Fatigue | 24 h | Neuropathy-mimic, Speech impairment | Numbness in the 4 extremities, weakness, difficult to speech | Head and spine MRI, NCS-normal Laboratory test-normal | Counseling and anxiolytics | Complete recovery |

*Not included in the current case series
CA carotid artery, CSF cerebrospinal fluid, CT computer tomography, EMG electromyography, EP evoked potentials, HPV human papillomavirus, MEPs motor evoked potentials, MRI Magnetic resonance imaging, NA not applicable, NR not reported, NCS nerve conduction study, SSEPs somatosensory evoked potentials
the diagnosis of FND, these are often triggered by stressful life events and physical injury [26]. During the Covid-19 pandemic, known patients with FND showed significantly higher levels of anxiety, perceived stress and symptoms related to post traumatic stress disorders compared to healthy controls [27]. Stressful life events related to infection and isolation by Covid-19, social media information suggesting neurological complications following Covid-19 infection may have contributed to appearance of FND. On the other hand, FND after vaccine may be triggered by psychological factors along with previous beliefs and expectations about vaccines. In 2021, in the context of videos circulating on social media which depicted individuals with continuous movements disorders and walking difficulties attributed to major neurologic adverse events after administration of the COVID-19 vaccine, with some of them diagnosed as FND, the US Centers for Disease Control and Prevention was warning that cases of FND may occur after administration of the COVID-19 vaccine but they are not the direct result of toxic vaccine effects and therefore do not mean the Covid-19 vaccines are unsafe. Rather, FND may be related to nocebo effects and negative expectations triggered by vaccine administration [28]. A systematic review by Amanzio et al. (2022) revealed that the adverse effects in the placebo group in patients enrolled in Covid-19 vaccine studies were more common in the younger population and in the first dose of placebo recipients of the mRNA vaccines, which accounted for over 70% of post vaccine symptoms, suggesting that negative expectation may play a major role in the occurrence of FND post vaccine [29].

Conclusions

There is a limited number of case reports of functional neurological disorders in post Covid-19 patients. The diagnostic of functional neurological symptoms in post Covid-19 patients may be specifically challenging in people with comorbid post Covid-19 condition and those with suspected non-motor functional symptoms. Is it important that clinicians recognize FND symptoms and to consider it as differential diagnosis in patients with neurologic complication of Covid-19 infection and vaccination.

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Declarations

Conflict of interest The authors have no competing interests to declare that are relevant to the content of this article.

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