Peripheral nervous system manifestation of COVID -19

DR Rahimi Jaberi

Neurologist

SUMS

Post– acute COVID-19 syndrome (PACS)

- Persistent symptoms after acute SARS-CoV-2 infection encompass a broad spectrum of alterations, and can be long-lasting.
- While numerous terms (e.g., persistent COVID- 19, post–COVID-19 syndrome) have been used to describe these symptoms, there is currently a degree of consensus that they may be grouped together under the term post– acute COVID-19 syndrome (PACS).
- Different studies define this entity as the persistence of symptoms and/or complications f acute SARS-CoV-2 infection beyond 4–12 weeks after onset of the initial symptoms.
- Common symptoms reported by patients with PACS include signs suggestive of peripheral nervous and muscular system involvement, such as myalgia, weakness, or exercise intolerance; sensory symptoms (mainly positive symptoms, such as paraesthesia and neuropathic pain); and dysautonomic symptoms.

Guillain-Barré Syndrome

- patients with GBS associated with COVID- 19
- **Age** : 8 to 94 years with a male preponderance (male:female = 2.18).
- ***The duration between the onset of GBS and COVID-19:***

From −10 days (preceding COVID-19) to +90 days (succeeding COVID-19 symptoms) with most patients (~95%) occurring after the onset of COVID-19 symptoms.

- **Variants:**
- Acute inflammatory demyelinating polyneuropathy (~75%)
- Acute motor axonal neuropathy (~11%)
- Acute motor-sensory axonal neuropathy (~7%)
- Other variants such as Miller–Fisher syndrome, polyneuritis cranialis, and the pharyngeal, cervical, and brachial variant, are uncommon to rare.
- **Outcome :**

relatively poorer outcome than GBS occurring otherwise

Mechanism of GBS in COVID

- **postinfectious process**:

Generation of antibodies lead to molecular mimicry and triggering an autoimmune process.

- **Parainfectious** :

Possibility of direct virus-mediated injury in COVID- 19-associated GBS

or

Different type of immune-modulation

Nerve Pain, Myalgia, and Skeletal Muscle Injury

- Nerve pain was found in 4 (4.5%) and 1(0.8%) of the patients with severe and non-severe COVID-19, respectively.
- Skeletal muscle injury was seen in 17 (19.3%) and 6 (4.8%) of the patients with severe and non-severe

COVID-19, respectively.

- **CPK**: It is important to consider that reports of creatine kinase (CK) elevation, as the only marker of muscle injury, are non-specific and may be related to prolonged bed rest and medications in severe COVID-19 cases more than a direct muscle injury from COVID-19.
- In the ALBACOVID registry, myopathy and myalgia were seen in 3.1% and 17.2% of the COVID-19 patients, respectively

Myalgias were reported in 15.79% to100% of COVID- 19 patients in other published studies

Myositis and myopathy

- Myositis as a rare manifestation of COVID-19 is only recently being reported.
- COVID-19 is associated with a viral myositis attributable to direct myocyte invasion or induction of autoimmunity.
- COVID-19-induced myositis may be varied in presentation, from typical dermatomyositis to rahabdomyolysis, and a paraspinal affliction with back pain.
- It may or may not present with acute exponential elevations of enzyme markers such as creatine kinase (CK)

Myositis

- **Acute Viral Myositis**
- cases of myositis attributable to COVID-19 have been described so far. COVID-19-induced myositis may vary in presentation, ranging from mild to frank muscle weakness
- **Rhabdomyolysis :**
- Rhabdomyolysis is one of the rare and severe complications of COVID-19 infection which can be an initial presentation in some cases .
- patients present with typical COVID-19 symptoms such as fever, cough, myalgia, and shortness of breath as well as manifest acute lower limb– dominant symmetric muscle weakness and subsequently go on to develop rhabdomyolysis associated with elevated CK levels. A study reported a peak CK value as high as 33,000 U/L .
- In this setting, they may present with frank muscle weakness, which is profound, proximal, lower limb–dominant, acute, and symmetric. At times, the patients are critically ill and requiring ventilatory support. The only manifestation of rhabdomyolysis in these may be myoglobinuria (dark urine) and acute kidney injury (AKI) needing hemodialysis with raised CK >5000 IU/L .

Dermatomyositis

- **Classic dermatomyositis** :
- rashes, muscle weakness, and interstitial lung disease. The latter two can occur in both COVID-19 and de novo myositis, making timely diagnosis challenging.
- However, the presence of typical rashes such as heliotrope with periorbital edema, malar erythema, or diffuse facial rashes may guide diagnosis of dermatomyositis.
- Sometimes, less specific erythematous rashes over the extensor surfaces of limbs (knees, elbows) and trunk may be the only clue.
- Muscle weakness is invariably present, being symmetric, proximal, and involving upper as well as lower limbs.
- Severe bulbar weakness is also reported
- CK is usually elevated but can occasionally be normal when muscle involvement is minimal.
- Myositis-specific autoantibodies can be an important clue to diagnosis, with recent reports demonstrating anti-Mi2 (n = 1), anti-MDA5 (anti-melanoma differentiation-associated gene 5) (n = 1), anti-SAE1 (anti small ubiquitin-like modifier-1 activating enzyme) (n = 2), or anti-nuclear autoantibodies (n = 1)

Myositis

- **Paraspinal Myositis**
- Involvement of the erector spinae and multifidus paraspinal muscles has been reported on MRI in those diagnosed with COVID-19 with back pain
- **Asymptomatic Rise in CK**
- **Other Rare muscle involvement :**
- isolated group of muscles may be inflamed in patients with COVID-19, resulting in myofascial compartment syndrome, which may even require amputation
- COVID-19-induced cachexia was also reported

Multiple Cranial Neuropathies

- Olfactory(70-75%)
- 5^{th} and 7^{th} cranial nerves involvement was also reported

Neuromuscular Junction Disorders

- New-onset antiAchR+ myasthenia gravis (MG) after COVID-19 infection can also occur and may also be due to molecular mimicry mechanisms as with other neurological manifestations.
- Acute respiratory distress (ARDS) seen in COVID-19 coupled with respiratory muscle failure in MG crises may result in a dire prognosis

COVID and PNS

- ARS-CoV-2 infection might be not only associated with the development of AIDP but could represent a precipitating factor for clinical exacerbations in patients with CIDP and other immune-mediated neuromuscular diseases, such as Myasthenia Gravis

Vaccine-Related Peripheral Nerve Syndromes

- **Guillain–Barrè syndrome**:
- several patients who developed a GBS following CoV-19 vaccinations, were described from different centers .
- In particular, most patients developed **bifacial weakness** with or without involvement of other peripheral nerves after ChAdOx1 nCoV-19 vaccination, suggesting this might represent a specific neuropathy phenotype associated with the vaccine.
- **Chronic Inflammatory Demyelinating Polyneuropathy(CIDP)** :

Was also reported

- **Personage turner syndrome**

Vaccine-Related Peripheral Nerve Syndromes continue…

- **Post COVID-19 vaccine small fiber neuropathy**
- **Facial palsy**
- **Nerve pain**
- **Myalgia**