Management of Neuromuscular Diseases in the Covid-19

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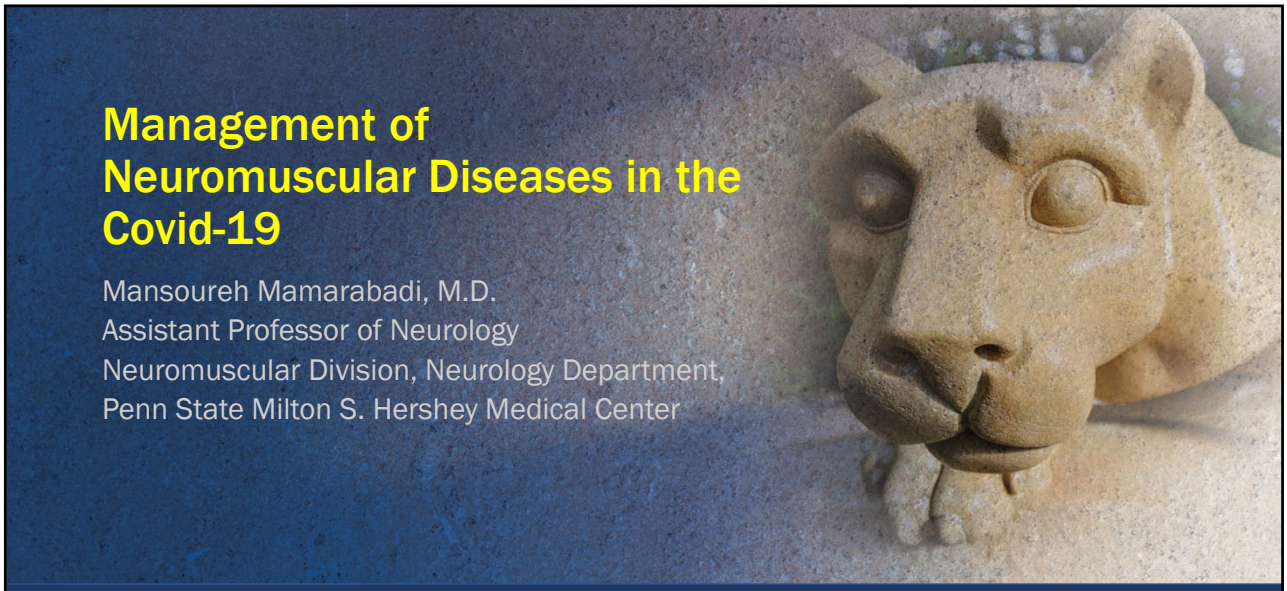

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Disclosure

- I have no financial relationship to disclose

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Introduction

- COVID-19 primarily causes a respiratory disease, but it has become apparent over time that the infection can affect various organ systems including peripheral nerve and skeletal muscle
- Physicians should be vigilant for neuromuscular complications that may be directly or indirectly related to coronavirus infection

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Potential neuromuscular complications of coronavirus 2019
1- Risk of infection causing a new neuromuscular disorder (NMD): a. Guillain-Barre Syndrome b. Myositis c. Critical illness myopathy or polyneuropathy
2- Risk of infection exacerbating known or unmasking previously unrecognized NMD: a. Autoimmune disorder such as CIDP, MADSAM, MMN, LEMS, myositis b. Degenerative disorders such as ALS, SMA, hereditary neuropathies, muscular dystrophies, congenital myopathies=, mitochondrial myopathies, metabolic myopathies, and others
3- Risk of immunosuppressant/immunomudulating therapies in patients with autoimmune NMD: a. Increased risk of COVID-19 infection and more severe disease b. Increased risks and severity of other infection in patients with COVID-19 in the setting of NMD treated with certain immunotherapies c. Immunotherapies might make vaccines less effective
4-Risks of treatment for COVID-19: a. Hydroxychloroquine and chloroquine can cause a toxic neuropathy and myopathy b. Antiviral treatments: lopinavir/ritonavir, remdesivir, others
5- Risks of vaccinations: a. Possible inflammatory neuropathy (e.g. Guillain-Barre syndrome, plexitis, mononeuritis)

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Assessment of overall risk from COVID-19 in patients with NMD

- Risks will depend upon the specific NMD, other comorbidities, age, and what immunotherapies the patients may be receiving
- We do not expect the majority of patients, even in the higher risk categories, to have severe complications of COVID-19
- We also can reassure patients that NMDs that spare swallowing and breathing muscles and where treatment does not involve immunosuppression are not considered to be high risk in COVID-19
- Patients may be in an overall higher-risk category due to other demographic factors or health considerations

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Coronavirus 2019 risk by neuromuscular disease

Disorder	Level of risk for COVID-19 or having severe COVID-19 disease course	Comments
Motor neuron disease	Moderate/high	Higher risk related to more advanced disease, use of ventilator or noninvasive ventilation, dysphagia, comorbid diseases
Neuropathies		
Inherited	All Levels	Low with uncomplicated neuropathy, High with autonomic involvement or cardiac involvement (e.g. amyloidosis), scoliosis with respiratory involvement
Immune mediated	All Levels	Related to degree of immunosuppressive therapy and respiratory/bulbar weakness
Idiopathic	Low	No appreciable increased risk
NMJ		
LEMS	All Levels	Consider underlying malignancy/chemotherapy
gMG	All Levels	Risk related to bulbar and respiratory weakness, immunosuppressive therapy
CMS	All Levels	Adult onset, stable for more than 10 years without bulbar or respiratory weakness likely low risk Actual or possible (based on mutation) bulbar or respiratory muscle weakness high risk
Muscle		
Inherited	All Levels	Related to bulbar and respiratory weakness, related diseases specific morbidities (i.e., diabetes, cardiac disease) influences risk
Inflammatory/immune mediated	All Levels	Immunosuppressive therapy determines risk

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Risk of infection causing a new NMD-Peripheral Nerve Complications, GBS

- Guillain-Barré syndrome (GBS):
  - ✓ Acute polyradiculoneuropathy characterized by rapidly progressive symmetric limb weakness and areflexia. Respiratory failure occurs in 20% to 30% of people with GBS. The main modalities of therapy are the administration of intravenous immunoglobulin (IVIG) and plasma exchange (PLEX)
- More than 60 published case reports on COVID-19-associated GBS, however, the causal relationship is debatable
  - ✓ Case reports assumed a relationship based on the fact that GBS occurred with symptoms and signs of COVID-19 or soon thereafter, suggesting a parainfectious (during the acute infection) or postinfectious process
  - ✓ Retrospective studies from Italy found a higher frequency of GBS in COVID-19-infected patients with an odds ratio (OR) of 4.6– 6.3.
  - ✓ Another study found that the incidence of GBS during the pandemic (0.202/100,000/month) was 2.6 times higher compared to the same period during the prior year
  - ✓ In contrast, a different study did not find a substantial increase in the number of patients hospitalized with GBS during the pandemic
  - ✓ The most extensive study to date, an epidemiologic study from the United Kingdom (UK):
    - Incidence of GBS was actually lower during the pandemic compared to prior years and found no correlation between the number of COVID-19 and GBS cases when comparing different regions of the UK.
    - No significant differences in clinical features of GBS, disease severity or outcomes between patients with or without COVID-19 except for a higher rate of mechanical ventilation in patients with definite COVID-19, which was attributed to pulmonary effects of COVID-19 rather than neuromuscular weakness from GBS.
- Potential mechanism:
  - ✓ Molecular mimicry between SARS-Cov-2 spike protein and host cell gangliosides and epitopes of the peripheral nerve gangliosides. However, studies to date have not consistently identified similar epitopes between SARS-CoV-2 and peripheral nerve that may cause cross-reactivity
  - ✓ Direct invasion of peripheral nerves: One autopsy study found SARSCoV-2 immunostaining in cranial nerves IX and X in 2 of 40 patients without GBS who died from COVID-19. However, There are no other reports of SARS-CoV-2 being detected in peripheral nerves

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Risk of infection causing a new NMD-Peripheral Nerve Complications, GBS

- literature review of published articles on patients with confirmed diagnosis of Covid and GBS
  - ✓ COVID-19-associated GBS seems to affect men and people more than age 65 more frequently
  - ✓ The latency between the onset of COVID-19 symptoms and time to onset of GBS ranges from 2 days to 4 weeks. In some cases weakness preceded typical COVID-19 symptoms
  - ✓ The frequency of respiratory failure is slightly higher in COVID-19-associated GBS compared with more commonly described GBS, likely a reflection of the concurrent pulmonary disease
  - ✓ Limb paresthesias or pain and weakness were the most common symptoms on presentation and most patients developed varying degrees of extremity weakness during the course of the illness
    - ✓ Miller-Fisher syndrome, a variant of GBS, has also been reported in association with SARS- CoV-2 infection
  - ✓ MRI of the spine was abnormal in ~50% of the patients
  - ✓ CSF analysis findings frequently show a typical albumin-cytological dissociation
  - ✓ Elector-diagnostics: Sensorimotor axonal, mixed axonal and demyelinating and demyelinating findings have also been observed
  - ✓ Management: most individuals have been treated with IVIG with variable outcomes. It is important to use caution with IVIG in those with COVID-19 because of the thromboembolic side effects of IVIG and the thrombotic complications of COVID-19 (none of the reports described thrombotic complications). The hemodynamic status in critically ill patients can be a limiting factor to the use of PLEX and also poses a significantly higher risk of exposure to healthcare providers. IVIG therefore remains the first line therapy for GBS

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Risk of infection causing a new NMD-Peripheral Nerve Complications, mononeuropathies

- Focal and multifocal mononeuropathies
  - In a cohort of 83 patients admitted to hospital with acute respiratory distress syndrome (ARDS) and COVID-19, 14.5% had mononeuropathies (sometimes multiple), most commonly in the ulnar, radial, and sciatic nerves.
  - This could be related to the use of prone positioning for management of ARDS, considering as 11 of 12 individuals with mononeuropathies had been placed in prone positions.
  - However, whether this finding is directly associated with the prone position, the viral infection, or the multiple comorbidities seen in this patient group is unknown.
- Cranial mononeuropathies (III,VI, VII)
  - have been reported in several case reports, but it is not clear whether they were caused by COVID-19 or arose coincidentally with COVID-19 infection
  - Ischemia due to endotheliopathy associated with COVID-19, immune-mediated injury and direct viral infection are potential mechanisms

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Risk of infection causing a new NMD-Peripheral Nerve Complications, Small fiber neuropathy and Autonomic dysfunction: an early experience

- New painful paresthesia and numbness within 2 months of SARS-CoV-2 infection has been observed, and some individuals with these symptoms also develop intense small fiber neuropathy (SFN) symptoms acutely and diffusely
  - ✓ In a study of 13 individuals with this presentation, NCS was normal in all, but skin biopsy showed reduced IENFD in 6 of 13, confirming SFN. Among the 6 persons with SFN confirmed by biopsy, 3 had preexisting but controlled associated conditions, whereas the others had no neuropathy etiologies identified. Neuropathy in some of these individuals was severe and did not respond well to symptomatic treatment
- Another case series reported 27 patients with autonomic symptoms 0 to 122 days after acute SARS-CoV-2 infection. Autonomic testing showed postural orthostatic tachycardia syndrome in 22%, mild orthostatic intolerance in 11%, and sudomotor dysfunction in 36%.
  - ✓ A case report also described a person who developed burning dysesthesias 1 week after receiving a second dose of COVID-19 vaccine, and subsequent skin biopsy showed reduced IENFD. The patient responded to symptomatic treatment very well with resolution of the symptom.
- These reports suggest that COVID-19 and COVID-19 vaccine reactions may represent new associated conditions for SFN. The neuropathy pathogenesis in these settings is not clear but may be immune-mediated, similar to post viral or post vaccination Guillain-Barré Syndrome.

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Risk of infection causing a new NMD-Muscle Complications

- Myalgia and fatigue: not specific for skeletal muscle injury, occur in 11–70% of patients
- Fatigue or muscle weakness are common lingering symptoms and are present in 63% as is myalgia in 2% of patients 6 months after acute infection
- Creatine kinase (CK) is elevated in 9–33%
- Rhabdomyolysis:
  - To date, there are more than 30 published case reports on rhabdomyolysis occurring in patients with COVID-19
  - One study found that rhabdomyolysis occurred in 1.1% of patients hospitalized with COVID-19
  - Patients with COVID-19 infection may be prone to known causes of rhabdomyolysis, such as severe electrolyte imbalance, ischemia, prolonged immobility or myotoxicity from medications, but immune-mediated damage or direct invasion of myocytes by the virus are additional possible mechanisms
  - Management: Careful monitoring for renal failure and hydration

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Risk of infection causing a new NMD-Muscle Complications

- Myositis:
  - Has been documented with MRI in a person with interstitial pneumonitis, suggesting an autoimmune-mediated mechanism
  - Muscle biopsy in some case reports showed evidence of perivascular inflammation with endomysial extension, and abnormal sarcolemma and sarcoplasmic expression of major histocompatibility antigen 1 (MHC-1) suggestive of dermatomyositis
  - Patients responded to steroids with clinical improvement and decrease in CK over couple of weeks
  - Whether SARS-CoV-2 directly infects muscle is unclear

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Risk of infection causing a new NMD-Muscle Complications

- ICU acquired weakness (ICUAW): CIM and critical illness polyneuropathy (CIP)
  - ✓ Not specific to COVID-19
  - ✓ Risk factors include prolonged immobility, sepsis, systemic inflammatory response syndrome and multiorgan failure, which can complicate severe COVID-19 infection
  - ✓ In published cases, ICUAW was suspected when critically ill patients with COVID-19 had diffuse weakness and/or difficulty weaning from mechanical ventilation
    - ✓ CK was normal or mildly elevated, and nerve conduction studies/electromyography showed myopathic features in CIM or axonal sensorimotor polyneuropathy in CIP
    - ✓ In patients who survived, strength improved over weeks to months
  - ✓ Features of CIM/CIP following severe COVID-19 infection appear to be comparable to CIM/CIP from other severe illnesses
  - ✓ Single-center study reported that people with COVID-19 who required mechanical ventilation had ICUAW upon awakening (72%), at ICU discharge (52%), and at the time of hospital discharge (27%). Those who developed ICUAW had longer times on ventilation and in the ICU, higher morning glucose levels, and received more dialysis, corticosteroids, sedatives, analgesics, and neuromuscular blockade

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Risk of COVID-19 infection exacerbating known or unmasking previously unrecognized NMDs

- Infection is a common trigger of exacerbation or disease progression and many NMDs, both inherited and immune mediated
- Considerations for exacerbation in acquired and inherited disorders are primarily related to degree of baseline cardiac and respiratory dysfunction, bulbar weakness, underlying pathophysiology of disease, and related comorbid conditions
- Patient with motor neuron disease (e.g. ALS, spinal muscular atrophy) and hereditary neuropathies with ventilatory muscle involvement may be particularly susceptible to infection
- Those with metabolic myopathies (or lipid storage diseases and mitochondrial disorders) are at increased risk of rhabdomyolysis with fever, infection or fasting (attributable to loss of appetite).
- Patients with various muscular dystrophyies, including myotonic dystrophy and metabolic diseases (e.g. Pompe disease) who have ventilatory muscle weakness or cardiomyopathy are likely at increased risk for severe COVID-19.
- Patient who developed COVID-19 may not return to their prior baseline

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Risk of COVID-19 infection exacerbating known or unmasking previously unrecognized NMDs: Neuromuscular Junction disorders

- An interim analysis from an international, physician-reported registry found that 36 of 91 (40%) MG patients with COVID-19 experienced worsening of MG requiring rescue therapy. Most patients were treated with IVIG and/or corticosteroids. Twenty-four percentage of patients died, whereas 43% had complete recovery and/or were discharged home.
- The true incidence of COVID-19 infection in patients with MG is unknown, but a large American database study found that 380 of 40,392 patients with MG (0.94%) were diagnosed with COVID-19 as of December 2020
- Similarly, a French database study found that the cumulative incidence of symptomatic COVID-19 among MG patients was 0.96% (34 of 3,558 patients)
- The rate of hospitalization ranged from 27 to 69%. In total, 10–26% of patients required ICU admission, and the mortality rate ranged from 7 to 24%
- A few papers reported new onset of myasthenia gravis (MG) in patients infected with COVID-19. However, perhaps a more likely explanation is that these cases represent patients with subclinical MG or subtle symptoms whose symptoms became unmasked in the setting of an infection or the use of antibiotics (Azathioprine) or antimalarials (Hydroxychloroquine)

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Risks of immunosuppressant and immunomodulating therapies inpatient with autoimmune NMDs

- Patient with NMDs who use immunosuppressive therapies (IST) are likely at increased risk of contracting COVID-19 or having a more severe course of the virus
- The risk is variable even among patients on ISTs and with the same disease

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Factors increasing risk of contracting corona virus 2019 (COVID-19) or having more severe disease
Underlying immunotherapy
Immunosuppression with multiple agents
Additional factors
✓ High doses of immunosuppressive therapy o cell/antibody depleting therapies
✓ Multiple immunosuppressive therapies, concurrently or sequentially
✓ Highly active immune mediated neuromuscular disease
✓ Swallowing or respiratory muscle weakness
✓ Other medical comorbidities
Pulmonary disease
Pulmonary hypertension
Renal impairment
Neutropenia or lymphopenia
Liver disease
Diabetes mellitus
Ischemic heart disease
Older age

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Risks of immunosuppressant and immunomodulating therapies inpatient with autoimmune NMDs

- A few retrospective studies examined the impact of IST for MG on the risk of COVID-19 infection and outcomes
- One study showed that IST did not increase the risk of COVID- 19 infection in patients with chronic autoimmune neuromuscular disorders, including those with MG. Patients with chronic autoimmune neuromuscular disorders on IST were more likely than those not on IST to be hospitalized (OR 2.86) but were not at increased risk of being admitted to an ICU. However, this study had several limitation
- Another study showed that severe baseline MG status, but not IST use, was associated with severe COVID-19 infection (defined as requiring ICU care or resulting in death)

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Risks of immunosuppressant and immunomodulating therapies inpatient with autoimmune NMDs

- In terms of managing immunosuppressive :most outpatient without infection should continue to take their medications, with instructions to call their neurologist and temporarily hold the medication if they develop symptoms of infection
- In some cases, after discussion of risk and benefit between the patient and provider, some patients may be able to continue immunosuppressive therapies or be treated with a different less immunosuppressive option.
- This involves a discussion of potential risks and benefits related to COVID-19 and underlying neuromuscular disease when adjusting doses or stopping immunosuppressant or immunomodulating therapies. Examples of risk include age, comorbid medical problems, geographic location, household or occupational risk factors, and underlying neuromuscular disease severity.
- Avoiding abrupt cessation of medication that may participate a flare of the underlying condition, which could in turn necessitate higher doses of prednisone, immunosuppressive therapy or hospital admission is difficult. Holding or suspending prednisone is not recommended.
- Some therapies are not expected to increase the risk of COVID-19 or severe disease including immunoglobulin therapy (i.e. intravenous or subcutaneous), complement inhibitor therapy (e.g. eculizumab), therapeutic plasma exchange or neonatal Fc receptor (FcRn) antagonists (various forms are now being assessed in clinical research trials)

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Risks of immunosuppressant and immunomodulating therapies inpatient with autoimmune NMDs

- Guidelines for the management of NMJ disorders during the pandemic, namely, MG and Lambert-Eaton myasthenic syndrome (LEMS), recommend continuing treatment without alteration with strict social-distancing measures:
- For patients considering B-cell depleting therapy (e.g. rituximab), delaying initiation until after the peak of the outbreak in the patient's region is advised. In our opinion, the local incidence and prevalence ofCOVID-19, ability to strictly socially isolate, and vaccination status should be considered at a minimum. In unvaccinated patients, postponing the initiation of B-cell depleting therapy to at least 2 weeks after vaccination may be advisable to allow for a sufficient antibody response.
- IVIG is thought unlikely to affect the antibody response to vaccination, thus there is no recommended minimum interval between IVIG treatment and vaccination at the time of writing this review. Although not definitively known, PLEX is likely to remove antibodies that form in response to vaccination. Reduction in antibodies against COVID-19 was observed in a patient with severe COVID-19 infection who underwent PLEX . Therefore, in patients with MG on maintenance PLEX or requiring rescue therapy, the risk of COVID-19 must be carefully weighed against the benefit of PLEX over alternative treatment options for MG.
- For patients with MG or LEMS who develop COVID-19 infection, guidelines suggest that current therapy should be continued, but a temporary pause may need to be considered in patients with severe infection especially if there are concurrent infections or sepsis

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Recommended adjustment of immunotherapy in neuromuscular patients

Medication Class	Examples	Patients initiating treatment	Patients already on treatment
Corticosteroids	Prednisone, Methylprednisolone, Deflazacort	Treat at lowest effective dose	Continue therapy regimen If treated with intravenous corticosteroids, consider home infusion, intramuscular or oral dosing.
Immunosuppressive Therapy	Azathioprine, Mycophenolate mofetil, Methotrexate, Tacrolimus, Cyclosporine	Consider delaying initiation in stable patients with mild disease. Consider spacing-out lab monitoring	Continue therapy regimen
Immunomodulatory Therapy	IVIG/SCIG, Plasmapheresis	Consider initiating home infusions for immunoglobulin	Consider home infusions, reducing frequency in stable patients.
Cell depleting Therapy	Rituximab, Cyclophosphamide	Avoid initiating unless no alternative	Consider postponing infusions, spacing out dosing or switching to subcutaneous therapy
Complement Inhibitors	Eculizumab	Consider need for immunizations, exposure to facilities during infusions	Likely does not increase COVID-19 risk
Non-immunomodulatory infusions, gene therapy	Edaravone, Nusinersen/zolgensma, Patisiran/Inotersen, Lumizyme/myozyme	Consider initiating home infusions. SMA1&2 should not delay initiation of Nusinersen/Zolgensma. SMA3&4 could consider delay	Consider home infusions, risk of exposure in facilities versus risk of treatment interruption. Recommend not delaying Nusinersen/Zolgensma infusions in children, could consider delay in adolescent or adult patients.

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Neuromuscular Complications of COVID-19 Therapies

- Lopinavir and ritonavir, 2 protease inhibitors, were studied as potential therapeutic agents for COVID-19 however, failed to show clinical improvement for COVID-19 compared with standard of care alone
  - ✓ Lopinavir/ritonavir does not increase the risk and may actually reduce risk of distal sensory polyneuropathy in HIV-infected individuals. Given the duration of treatment in patients with COVID-19 infection, we would suspect the likelihood of inducing or worsening of preexisting polyneuropathy with them is likely to be low.
  - ✓ Lopinavir and ritonavir, used in combination with a statin and particularly in patients with impaired renal function, have been associated with toxic myopathy and rhabdomyolysis
- Remdesivir: no definite MND is associated with remdesivir in a trial for Ebola, though pain in the arms and legs was noted as a common complaint in healthy controls
- Hydroxychloroquine and chloroquine: were proposed as possible therapeutic agents for COVID-19, although no clinical evidence for this was found and emergency authorization was withdrawn in the US. It is widely known that these 2 drugs have neuromuscular side effects, including toxic myopathy and neuropathy and exacerbation of myasthenia gravis
- Azithromycin: At the beginning of the pandemic, it was proposed as a treatment option for COVID-19. Although this drug is not currently used to treat COVID-19, it has also been identified as a trigger for myasthenia exacerbations

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COVID Vaccine and NMD

- With regards to vaccination patient with neurologic disease, several concerns arise:
  - What is the risk a particular vaccine might precipitate or worsen neurologic disease
  - Patients with neurological diseases are increasingly treated with therapies that either modulate or suppress the immune system, concerns arise regarding a) the risk that vaccine might produce active infection; and b) whether vaccine efficacy might be reduced in the context of these therapies.

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COVID Vaccine and NMD

- The approval of 3 vaccines Pfizer, Moderna and Johnson & Johnson by FDA for emergency use results in the potential to significantly reduce the incidence of symptomatic disease in this vulnerable populations
- None of the currently the currently approved COVID-19 vaccines utilize live attenuated SARS-CoV-2 virus and thus none have the potential to produce SARS-CoV-2 infection

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COVID Vaccine and NMD

- Much of our knowledge about the safety and efficacy of vaccination any neurologic patient comes from the results of previous vaccine studies and our understanding of the mechanisms of action of commonly used immunotherapies
- Prior studies have shed the light on the likelihood of neurological complications following vaccinations.
- For example AIDP is the most common neurologic syndrome and has been described in case reports following vaccination for flu, polio, rabies, meningococcus, measles, mumps and tetanus. This cases occurred between 1 and 6 weeks following immunization.
- The current guidelines by the advisory committee on immunization practices of the CDC, lists AIDP within 6 weeks of previous influenza as better" precaution" for immunization against influenza. This means that while the risks may be elevated, individual risks versus benefits should be considered before recommending immunization.
- Vaccination has been associated with the development of chronic inflammatory demyelinating polyneuropathy in 1.5% of CIDP patient within 6 weeks of administration and the worsening symptoms were also reported after tetanus vaccination in 8.7% of patients
- Though neurological side effects were not more commonly observed following active vaccine over extended follow up period for any of the vaccines, a number of neurological complications of these vaccines are now being reported in the most comprehensive registry, the vaccine adverse events reporting system (VAERS) database. These include strokes, cranial neuropathies including Bell's palsy, tinnitus and trigeminal neuralgia, peripheral neuropathies, dysautonomia, acute disseminated encephalomyelitis, transverse myelitis and AIDP. Most recently, the possibility of increased risk of AIDP in the weeks following vaccination was formally added to the label for the Johnson & Johnson vaccine. These complications are rare and comparable to the larger number of vaccinated individuals, however, it is too early to know the true incidence and to risk factors for this complications.

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Vaccine in Immunocompromised NMD patients

- Studies of COVID-19 vaccine efficacy and patient receiving immunotherapies are currently limited
- A recently published real world study of the Pfizer COVID-19 vaccine found that 2 doses of vaccine reduce SARS-CoV-2 infection by 71% in immunosuppressed patients compared to a 90% reduction among the non-immunosuppressed.
- In general, immunomodulatory therapies have less impact on vaccine response than immunosuppressive or B- cell depleting therapies
- Important to note that partial immunity might still be achieved even with those therapies that blunt measured vaccine responses
- For those patients treated with immunosuppressive therapies known or suspected to decrease response, patient should be counseled to remain vigilant about infection mitigation efforts even after vaccination due to the possibility of absent or diminished immunity
- Some providers may choose to measure post Covid vaccination antibody levels against the SARS-CoV-2 spike protein to assess vaccine response and aid in counseling this patient's, although the clinical significance of such testing with regards to COVID-19 risk remains uncertain

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AANEM recommendations:

- All individuals with NMDs who are not taking IS agents should be encouraged to receive COVID-19 vaccines because the risk of COVID-19 infections likely outweighs the potential risks of the vaccine.
- Individuals with NMDs who are taking IS/IM agents should be counseled that there are no data currently regarding the safety or efficacy of COVID-19 mRNA vaccines in this population, but the vaccine benefits of reducing COVID-19 infection likely outweigh the potential risks. Even reduced efficacy may confer benefits against COVID-19 infections.
- Individuals with autoimmune NMDs should be counseled that no data are currently available on the safety and efficacy of mRNA COVID-19 vaccines in this population. An increased risk of developing autoimmune or inflammatory disorders was not observed in clinical trial participants who received an mRNA COVID-19 vaccine compared with placebo. There are no data regarding the risk of exacerbation of autoimmune NMDs by the COVID-19 vaccine.
- Persons with autoimmune conditions who have no contraindications to vaccination may receive an mRNA COVID-19 vaccine
- Persons with a history of GBS and autoimmune conditions may receive COVID-19 mRNA vaccines unless they have other contraindications to vaccination.
- Individuals should be counseled that the vaccine does not carry the risk of inducing systemic COVID-19 infection, and that it does not alter their DNA.
- Known adverse effects of the vaccine should be discussed and patients should be encouraged to participate in vaccine safety tracking programs such as V-safe by the CDC.

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Take home points

- Although numerous case reports suggested a potential association between COVID-19 and Guillain-Barre´Syndrome, a recent large-scale epidemiologic found no link
- To date there is unclear evidence of increased risk of Guillain-Barre´ syndrome with COVID-19 vaccination
- COVID-19 infection may be more severe in patients with myasthenia gravis than the general population.
- COVID-19 appears to be associated with a range of skeletal muscle symptoms and conditions, including rhabdomyolysis, critical illness myopathy, and myositis.
- Retrospective studies suggest that while the incidence of symptomatic COVID-19 in patients with MG is low, the risk of hospitalization, ICU admission and death are relatively high. The use of IST appears to increase the risk of hospitalization, but not the risk of ICU admission or death.

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