COVID-19 infections may lead to neurologic complications

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Overview

COVID-19 may affect brain function in some people who become infected. In fact, **studies show that between 36.4% to 84.5% of COVID-19 patients show neurological symptoms.**[1-3] Neurological symptoms can present at any time during the illness or even after infection has been definitively diagnosed.[3-4] These symptoms may be seen in mild forms of the illness but seem to be more common in severe cases.[1,3-4] The most frequent neurological symptoms include muscle ache/pains (myalgia), headaches, encephalopathies, dizziness, and loss of sense of smell and taste.[3] Recent data have shown that COVID-19 can infect neuronal cells, which may explain the higher than normal rate of neurological symptoms seen with this illness and emphasizes the need for a full neurological workup in patients with COVID-19 infection.[5]

See the table on page 3 for relevant test offerings that may assist in the diagnosis of these patients.

Literature Review: Neurologic manifestations of COVID-19

A recent study evaluated the neurological symptoms, risk factors, and outcomes for 509 patients from a large health system. **Data show that 42.2% of patients had neurological symptoms at COVID-19 onset, 62.7% at hospitalization, and 82.3% at any time during their illness.** Among the most frequent of these symptoms was encephalopathy. Encephalopathy was independently associated with worse functional outcome and higher mortality within 30 days of hospitalization, regardless of respiratory symptom severity. Risk factors for encephalopathy included a history of any neurologic condition and chronic kidney disease. Further, risk factors for developing any neurologic manifestation included more severe infection and younger age.[3]

The study also showed that patients with neurological symptoms had longer hospital stays, worse functional outcomes at 30 days after discharge, were associated with male sex, severe COVID-19 disease, older age, and previous neurological illness.

This study underscores the importance of a full workup for patients presenting with neurological symptoms due to COVID-19 infection.

Who is at increased risk?

Individuals at increased risk include pediatric and elderly patients with severe disease[3]; patients of any age with a history of obesity, hypertension, ischemic or hemorrhagic stroke, dementia, or certain autoimmune conditions; and pediatric patients who have had multisystem inflammatory syndrome.

Parkinson Disease (PD) has been known to occur in patients after infection with other viral illnesses, such as influenza, HIV, West Nile Virus, and varicella zoster. In fact, 5 years after the Spanish flu pandemic during the 1910's there was a 3-fold increase in the incidence of PD. Recently, new onset PD after COVID-19 infection was detailed in the literature.[6] Patients diagnosed with PD before COVID-19 infection may be at risk of worsening illness after recovery. Studies show that up to 75% of PD patients can experience new or worsening motor and non-motor PD symptoms after COVID-19 infection.[7-8]

A recent review article details the effects of disease-modifying therapy (DMT) on the immune system and examines the literature regarding its use in patients with multiple sclerosis (MS) and COVID-19. The authors conclude that MS patients receiving DMT are NOT at an increased risk for contracting symptomatic COVID-19 infection, nor are they at a higher risk for severe complications from COVID-19 if infected.[9]

What can I do as a clinician?

Monitor patients' risk for coagulopathies (PT, aPTT, D-dimer, fibrinogen, ADAMTS13, APOE). COVID-19 infection causes a hypercoagulable state and patients with COVID-19 infection are at an increased risk of stroke, especially those with severe disease.[1]

Even after the acute infection, patients can be at risk for neurological complications such as Guillain-Barré syndrome or myasthenia gravis.[10] As such, conducting a symptom-driven neuroimmunologic evaluation and monitoring with appropriate laboratory testing, neuroimaging studies, and physical and mental assessments is prudent.

How can clinicians incorporate this information into patient care?

Blood- or CSF-based biomarker assessments (AChr, NMDAr, titin, RyR, Musk, MOG, NfL, etc) may assist with the differential diagnosis of a patient's presenting/emerging neurologic symptoms and inform appropriate clinical interventions and risk mitigation.

Evidence shows that patients with neurologic complications from COVID-19 usually lack typical autoantibody signatures in serum and CSF (except for NfL), but do show increased levels of CSF proteins, lactate, or white blood cells indicative of autoimmune encephalitis. Additionally, antineuronal autoantibodies in the CSF (IgG) have been identified that are not normally included in standard assays.[11]

What are the psychiatric complications of COVID-19?

Pre-COVID-19 estimates of depression and anxiety range between 6% and 18%; however, the rates of anxiety and depression in the general population during the pandemic range from 28% to 33.7%.[12-13] In fact, a separate survey conducted during the COVID-19 pandemic confirmed these estimates by showing a depression prevalence rate more than 3 times higher during the COVID-19 pandemic than before the pandemic.[14] Additionally, patients with current or past COVID-19 infection also seem to be at a higher risk for psychological symptoms with the prevalence of anxiety and depression ranging between 29.2% and 65% and the rate of PTSD symptoms was as high as 96.2%.[13-16]

The COVID-19 virus may directly affect the brain by entering through the olfactory bulb and increase blood brain barrier permeability through pro-inflammatory cytokines.[17] Recent research has shown that worse inflammation (as measured by systemic immune-inflammation index) at baseline diagnosis of COVID-19 may correlate to greater risk of depression and anxiety at 1 month follow-up.[18]

Appropriate treatment of these psychiatric conditions can result in improved quality of life and finding the right medication can be made easier through using pharmacogenomics. Pharmacogenomics can help a clinician to know which medications are more appropriate for a person, based on their genetics.[19] Quest offers a Pharmacogenomics Panel of over 40 genes that may be useful in guiding prescribing for certain medications.

Table: COVID-19-related neurological phenotypes and associated tests

Neurological phenotypes	Symptoms, findings, and associated conditions	Related testing
Encephalopathies/ Neuroinflammatory syndromes	Encephalitis—delirium, psychosis, confusion, disorientation, acute demyelinating encephalomyelitis, seizures, myelitis, numbness, various CT and/or MRI findings suggestive of other neuroinflammatory illnesses	• Encephalitis Antibody Evaluation with Reflex to Titer and Line Blot, Serum • NMDA Receptor (NR1-subunit) Autoantibody • Autoimmune Neurology Antibody Comprehensive Panel with Reflexes, Serum
Peripheral nervous system	Guillain-Barré Syndrome—weakness and tingling in the feet and legs or paralysis, muscle weakness, difficulty moving eyes or face, chewing, talking or swallowing	• Sensory Neuropathy Antibody Panel (Ganglioside) • Sensory-Motor Neuropathy Complete Antibody Panel • SensoriMotor Neuropathy Profile with Recombx®-Complete • Sensory-Motor Neuropathy Antibody Panel (Ganglioside) • Sensory Neuropathy Complete Antibody Panel
Myasthenia gravis (MG)	May include droopy eyelid/ mouth, weakness in the arm and leg muscles, double vision, and difficulties with speech and chewing. Onset of symptoms is generally gradual but can sometimes be acute following viral infection or pregnancy	• Myasthenia Gravis Panel 2 with Reflex to MuSK Antibody • Myasthenia Gravis Panel 2

Healthcare providers should use their clinical discretion, based on patient exams and presenting symptomology, to guide appropriate diagnostic testing.

For more information, go to **QuestDiagnostics.com/COVIDCare**

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