

Expert consensus on clinical prevention and control of new coronavirus infections of neurology (first edition)

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The COVID-19 pneumonia has received extensive attention since December 2019, which first appeared in Wuhan of Hubei Province, and has quickly spread to the other provinces throughout China and many other countries in the world. The novel coronavirus has been identified as the pathogen of this pandemic. On February 11th, WHO announced that the disease caused by the new coronavirus would be named Coronavirus Disease 2019 (COVID-19). If the first clinical symptoms are neurological symptoms, they have often been misdiagnosed, which cause delay in treatment. Also, these patients can be latent spreaders. To help our colleagues to understand the development, progression, and outcome of COVID-19, as well as prevention and treatment, we summarized the current clinical findings into this guidance.

In addition to systemic and respiratory symptoms, what neurological symptoms may patients with COVID-19 have?

1, General and respiratory symptoms

While COVID-19 patients often have fever, dry cough, and fatigue as the main manifestations, some patients may present with sore throat, abdominal pain, diarrhea, and conjunctivitis. Even if the symptoms are mild, they must be watched closely.

2, Neurological symptoms

Some patients have neurological symptoms. At present, neurological symptoms of COVID-19 includes, but are not limited to, acute cerebrovascular disease symptoms such as sudden onset slurred speech and unilateral paralysis, symptoms of intracranial infections such as headache, seizures, impaired consciousness, and myalgias. A few patients developed symptoms of neuropathy, e.g. paresthesia, and bowel/bladder function disturbance. Neurologists need to pay close attention when caring for these patients, watch for neurological symptoms related to COVID-19, and take measures in a timely manner to prevent further damage.

3, Imaging and laboratory testing

Most patients with COVID-19 have low-grade fever. Importantly, some patients do not have fever, even at the time the chest CT manifestations are very significant and shortness of breath has occurred. Additionally, some patients have return of their temperature to normal, despite progression of pneumonia. It is crucial to have a low threshold to repeat the chest CT if there is any worsening of the clinical picture.

For the laboratory tests, it is worth noting that some patients had leukopenia even before the onset of the symptoms, suggesting that we should pay great attention to the changes of lymphocyte count. At present, some companies have developed tests for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) coronavirus antibodies, which may be applied for the purposes of diagnosis and follow up in the future.

Currently, the detection of the viral RNA with PCR is the standard for diagnosis, though the sensitivity of the test is not high. Some patients need several consecutive tests to show a positive result. Therefore, there is an established clinical consensus that even if the nucleic acid test is negative, combined travel or contact history, clinical manifestations, and chest CT with characteristic changes warrant a presumptive diagnosis. Treatment should not be delayed in those patients while waiting for repeated nucleic acid test results, or even though it comes back negative.

What are the possible causes and the treatment precautions in COVID-19 patients with neurological symptoms?

1. Acute cerebrovascular disease related symptoms

The elderly composed of the majority COVID-19 patients, especially in patients with a critical condition and elevated D-dimer levels, which led to an increased risk of embolic vascular events. These patients may already have comorbidities for cerebrovascular disease risk factors at baseline, so medical personnel need to watch for related neurological symptoms (e.g. acute ischemic stroke symptoms) in COVID-19 patients. Secondary stroke prevention measures should also be applied as clinically indicated. Patients will be treated in an isolated unit by a multidisciplinary team composed by related subspecialties. Some patients with underlying hypertension and concurrent COVID-19 may have much elevated blood pressure due to the binding of SARS-CoV-2 virus to the ACE2 receptor, which increases the risk of cerebral hemorrhage. In addition, critically ill patients with COVID-19 often have severely reduced platelets, which may also contribute to acute cerebrovascular events in these patients.

Some studies have shown that ACE inhibitor (ACEI) and angiotensin II receptor blocker (ARB) antihypertensive drugs may increase the expression of the ACE2 receptor. Caregivers should discontinue ACEI and ARB antihypertensive drugs and replace them with calcium channel blockers (CCB), diuretics, and other categories of the antihypertensive drugs for blood pressure control in these patients.

2. Symptoms associated with intracranial infection

Evidence shows SARS-CoV-2 virus can infect the central nervous system. Previous investigations detected SARS-CoV-2 nucleic acid in patients in both cerebrospinal fluid and brain tissue at

autopsy. Additionally, some COVID-19 patients may present with CNS infection signs and symptoms with headache, seizures, and impaired consciousness. Sometimes these symptoms are their initial clinical manifestations. Brain MRI with gadolinium contrast, lumbar puncture, and CSF analysis for detection of 2019-CoV-2 virus nucleic acid are recommended as clinically indicated. These patients need emergent treatment for CNS infections, as well as supportive care e.g. fluid resuscitation, seizure control by AEDs, and antipsychotics.

3. Symptoms associated with muscle injury

Some patients may have the symptoms of muscle injury, such as fatigue, limb soreness, and elevation of muscle enzymes, which may be related to the inflammatory response to the 2019-CoV-2 virus or the direct damage caused by the virus. Recommendations include strengthening nutritional support therapy in these patients while they receive ongoing COVID-19 therapy. In cases of severe muscle damage, gamma globulin therapy should be considered as soon as possible (0.25g/kg/d or 15-20g/d, a course of treatment for 3-5 days).

As a Neurologist, when caring for a COVID-19 infected patient, how to take precautions?

Neurologists may care for COVID-19 patients who develop neurological symptoms in different settings. Based on the "Technical Guidelines for the Prevention and Control of New Coronavirus Infection in Medical Institutions (Trial Version)" enacted by the National Health and Health Commission, we categorize some regimens according to the relevant situations.

1. Precautions for the Neurology Outpatient Clinic

Patients with neurological symptoms as their first clinical manifestations may come to a neurology outpatient clinic. The following recommendations should be considered:

- (1) Wear disposable caps, medical protective masks, isolation gowns, and disposable latex gloves, and carry hydrogen peroxide hand sanitizer with you.
- (2) Before entering the clinic, patients and their family members should have their temperature taken at a pre-screening, triage station. All patients and their accompanying family members (to reduce cross-infection, try to reduce family members entering the clinic) should wear disposable

masks. If there are symptoms related to pneumonia, it is mandatory to go to a fever clinic first, and then consult a neurologist if indicated.

(3) For neurology patients without emergent conditions, avoid hospitalization as much as possible, and postpone any hospitalization until after the pandemic is under control.

(4) After seeing the patient, remove the protective equipment, following the procedures of “putting on and taking off protection equipment” strictly. Leaving the contaminated area while wearing protection equipment is prohibited, in order to prevent cross-contamination.

2. Precautions in emergency rooms

(1) In areas with a high incidence of COVID-19, protection equipment for the neurology team should be Level III protection.

(2) Strictly separate the neurology areas (including the exam room, CT/MRI room, interventional operating room, etc.) from the other areas in the emergency department and the fever clinic to ensure that there is no cross infection with COVID-19 patients.

(3) Before entering the exam room, the physician should screen patients and their family members for COVID-19 related symptoms such as fever and sore throat within 14 days. They should also confirm whether patients had a contact history with confirmed diagnosed COVID-19 patients or suspected patients. If there is any concern of potential infection, the patient should be sent to the fever clinic, and hospitalized in an isolation unit if indicated. If the potential infection is ruled out, the patient can be transferred to the neurology ward.

(4) Patients receiving IV tPA and/or interventions for acute stroke should be watched closely in a single room.

(5) Medical staff should strive to balance their professional duty obligations with their personal health, insuring they stay healthy to provide the highest quality care.

3. Precautions in the Neurology ward

- (1) In areas with a high incidence of COVID-19, protective equipment for medical staff of the Neurological Ward Unit should be Level III protection. Medical staff in general wards should wear disposable caps, medical protection masks, and isolation gowns.
- (2) Apply a strict access control system to reduce stays and visits, arrange special personnel at the entrance to the ward, check the temperature of the entering personnel, and all patients and their families should wear disposable medical masks to avoid cross infection.
- (3) Implement a real-time temperature reporting system. Notify the COVID-19 prevention and control team of the department immediately if there is any febrile case in the ward. The COVID-19 prevention and control team will assist in isolation and ward disinfection.
- (4) Once a highly suspected patient is identified, an in-house COVID-19 infection consultation should be ordered immediately. At the same time, other patients and their family members and exposed medical staff should be isolated. The temperature of all contacts and COVID-19 related symptoms should be closely monitored. Suspected patients should be transferred to the isolation unit as soon as possible. If the patient cannot be transferred immediately due to the shortage of beds, a separate room should be temporarily arranged. The patient should be transferred to another designated hospital as soon as possible.

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