

CHAPTER 19

THE NEUROLOGICAL COMPLICATIONS IN PATIENTS WITH COVID-19

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INTRODUCTION

Coronaviruses are single stranded, enveloped, RNA viruses. In December 2019, an epidemic started related to a new coronavirus (2019-nCoV) that had never been detected before in humans. Later, the name of 2019-nCoV disease was accepted as COVID-19 and this coronavirus has been named SARS-CoV-2.

The common symptoms of infection include fever, cough, and dyspnea. In severe cases, pneumonia, severe acute respiratory failure, renal failure, and death may develop. The rate of neurologic complications is too high to ignore. In an observational study conducted in Wuhan, the rate of Covid-19 patients with neurological involvement has been determined to be 36.4% .

In fact, the coronavirus is not a neurotropic virus, it targets the respiratory epithelium. However, angiotensin converting enzyme 2 (ACE 2), the target receptor for virus binding and entry into cells, is also found in glial cells in the brain and spinal cord. Therefore, it can bind, multiply, and damage neuronal tissue. It can directly invade the brain parenchyma through the nasal mucosa, lamina cribrosa, olfactor bulb or retrograde axonal transport. Another

way to reach the nervous system is through the direct entry of the virus into the brain with the disruption of the blood brain barrier in the viremia phase of the disease. It is thought that SARS-CoV-2 is also affect the central nervous system (CNS) through these mechanisms. After Covid-19 invades the CNS, it causes neurological destruction, possibly due to hypoxia due to pneumonia and immune-mediated damage due to cytokine storm.

CNS involvement and complications of Covid-19 can be divided into two parts as central and peripheral.

CENTRAL NERVOUS SYSTEM INVOLVEMENT

Acute transverse myelitis

There are case reports of transverse myelitis associated with Covid-19. Valuiddin et al. have reported a 61-year-old female patient who completed numbness and weakness in the extremities about 1 week after a runny nose and tremor and an expansile lesion was found on cervical magnetic resonance imaging (MRI). The patient did not benefit from methylprednisolone, partially benefited from plasmapheresis. Munz et al. have detected a hyperintense lesion at T9 level in the T2 sequence in thoracic MRI approximately 1 week after the onset of Covid-19 symptoms in a 60-year-old patient. The common feature of MRI lesions in both patients is that they are in patchy style. The patients of Chow et al. who had transverse myelitis after Covid-19 have benefited from 1 g/ day methylprednisolone treatment for 3 days.

Postinfectious inflammation is probably responsible for the pathogenesis of transverse myelitis after Covid-19. There is no guideline on treatment, it has been seen that the reported cases had benefit mostly from methylprednisolone use.

Cerebrovascular events

Our knowledge of Covid-associated cerebrovascular disease is based on case series and retrospective observational studies. Although ischemic stroke is more common among the reported cases, intracranial hematoma and venous sinus thrombosis cases are also seen. Li et al have identified 11 patients with cerebrovasculer events, 10 ischemic and 1 hemorrhagic, in 219 patients with Covid-19 in a retrospective, single center, observational study.

Advanced age, Covid-19 disease severity, underlying diseases (hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, smoking and alcohol

consumption), high D-Dimer levels are risk factors for cerebrovascular diseases in patients with Covid-19. Renal failure is more common in cerebrovascular disease with Covid-19 than without. These patients should be evaluated carefully for renal function.

The choice of treatment (antiaggregant / anticoagulant) in terms of ischemic stroke should be made according to Trial of ORG 10172 in acute stroke(TOAST) classification, clinical syndrome and laboratory findings.

Dhamoon et al have detected Covid-19 infection in 38% of 277 stroke patients admitted during the Covid-19 epidemic period. National Institutes of Health Stroke Scale(NIHSS) scores at the beginning of the stroke have been found to be higher in patients with Covid-19. Accompanying inflammatory events, hypoxia due to pneumonia and further increase in cerebral edema may be factors that increase the severity of ischemic stroke.

The underlying etiology in cerebrovascular disease is thought to be endothelitis.

Headache and dizziness

Headache and dizziness are the most common neurological manifestation among the Covid-19 patient series. The frequency of headache has been found to be approximately 12-64% in studies and case series. Headache due to systemic viral infections can be seen. Although there is no definite information about the character of headache, it can be seen in migraine, tension headache, cough headache phenotype. The most common is the migraine phenotype. Pain usually begins on the first day of viral infection symptoms and it is bilateral, and in the migraine phenotype. It can be included in 9.2.2 Headache can be included in the attributed to systemic viral infection group, in the International Classification of Headache Disorders (ICHD-3).

The pathophysiology of headache is thought to be the invasion of trigeminal nerve endings by SARS-CoV-2 virus in the nasal cavity, trigeminovascular activation with increased ACE2 expression in endothelial cells, or the release of proinflammatory mediators such as IL-1 beta, PGE2, NO and cytokines.

Dizziness is a symptom that should not to be underestimated for Covid 19 patients. In a review of 141 patients, dizziness was found in all patients. It may accompany infectious conditions or be a symptom of cerebrovascular disease (cerebellar infarction or bleeding). Anamnesis should be taken well, neurological examination should be done in detail, imaging should be requested if necessary.

Encephalopathy

Encephalopathy is a diffuse brain dysfunction with different levels of impairment of consciousness. Infection is one of the encephalopathy etiologies. In addition, encephalopathy can be seen also in sepsis, electrolyte imbalance, hypoxia and renal failure, which are complications of Covid-19 infection. Severe underlying viral infection increases the risk of encephalopathy. The rate of encephalopathy reported in literatures is between 7.5-31%.

Correction of the underlying infectious, inflammatory, hypoxic and metabolic condition will help improve the encephalopathy picture.

Encephalitis / Meningitis

Viruses are the common cause of infectious encephalitis. Encephalitis cases related to other coronaviruses are encountered. Poyuiadji et al have published a case of acute necrotizing encephalopathy due to Covid-19.

Seizures

There are case reports about patients with covid 19 who had a seizure. These seizures may be due to electrolyte imbalance, hypoxia, CNS infection, renal failure and cerebrovascular events. There is no evidence that covid 19 infection causes an acute symptomatic seizure. However, there are case report. To determined incidence of new onset acute symptomatic seizure in Covid-19 patients, 304 patient were observed. They had no epileptic seizure during the follow up period.

Myoclonus

Generalized myoclonus cases developing after Covid-19 infection have been reported. Symptomatic drugs such as levetiracetam, clonazepam, valproic acid or immunotherapy such as corticosteroids and IVIG can be used in the treatment.

PERIPHERAL NERVOUS SYSTEM INVOLVEMENT

Guillanne Barre Syndrome

Guillain Barre Syndrome is ascending, symmetrical, inflammatory polyradiculoneuritis, which is mostly seen after bacterial and viral infections. There

are also cases seen after Covid 19 infection. Male gender and being over the age of 50 are risk factors for the development of Guillain Barré Syndrome. In Caress et al's 37 patients with Covid 19 and Guillain Barre series, two patients applied with Guillain Barre syndrome and Covid 19 was detected in their tests. For other cases, Guillain Barré Syndrome symptoms begin an average of 11 days after the onset of Covid-19 symptoms, with pain, paresthesia and weakness in the extremities, the most common initial finding. In the electrophysiological examination of these patients, the most common type of acute inflammatory demyelinating (AIDP), followed by Acute motor sensory axonal neuropathy (AMSAN), Miller Fischer syndrome, and acute motor axonal neuropathy (AMAN) were found, respectively. Thirty-three of 37 patients received 0.4 g/kg/day intravenous immunoglobulin (IVIG), three plasma exchange, and one symptomatic treatment. Plasma exchange (PLEx) was applied to two of the IVIG patients later. One patient died due to respiratory failure.

Myalgia / Myositis

Myalgia is one of the most common conditions in Covid-19 infection. There is a case series reporting its frequency as 52%. It is a finding that adversely affects the general condition of the patient, and care should be taken in terms of rhabdomyolysis complication. There are cases with rhabdomyolysis due to Covid-19 and it is a fatal complication. It is recommended that patients with myalgia should be followed up for rhabdomyolysis and evaluated frequently with renal function tests.

Anosmia/ Ageusia

Smell and taste disorders related to coronavirus have been reported frequently. When Covid 19 positive patients were compared with negatives, loss of sense of smell was found to be 68% to 16%, loss of sense of taste was found to be 71% to 17%. In the study, the viral load in the nasal cavity of both symptomatic and asymptomatic patients was found to be higher than the viral load in the pharynx. This suggests that the nasal cavity is the entry point of the virus. Viruses entering the nasal cavity, enter the CNS through the branches of the trigeminal nerve, causing anosmia and ageusia by damaging the peripheral extensions of the trigeminal and olfactory nerves. In one study, it was found that 27% of patients with anosmia who had Covid-19 recovered in an average of 7.2 days.

CONCLUSION

Sars-CoV-2 infection, which emerged in Wuhan in 2019, may have many neurological complications. These complications are too much to ignore. Both central and peripheral nervous systems are involved. Neurological complications may occur after the diagnosis of infection, or patients may present with neurological findings before Covid-19 infection is diagnosed. Every Covid-19 patient should be evaluated in detail in terms of neurological complications. In addition, Covid-19 infection should be considered while investigating the etiology of the neurological symptoms and diseases we encounter.

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