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Review Article

Threat of COVID-19 Infection Over the Human Brain: A Neurological Perspective

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Abstract

At present time the eruption of novel coronavirus allied COVID-19 disease has potentially spread and engrossed almost whole world. The world is reeling under the disaster caused by corona virus disease (SARS-CoV-2). In this review article we discuss and relate the some neurological disorder, fear and anxiety due to corona virus (SARS-CoV-2). The SARS-CoV-2 is the seventh virus of corona virus family known to infect human beings. Although the diseases have different clinical presentations, the infectious cause, epidemiological features, fast spread pattern, and deficient preparedness of health authorities to address the outbreaks are similar. So far, mental health care for the patients and health professionals directly affected. Several viral infections can cause severe harm to the structure and function of the nervous system, severe encephalitis due to viral infections in the CNS, toxic encephalopathy, and severe acute demyelinating injuries progressing after viral infections. COVID-19 virus exploits the angiotensin converting enzyme-2 (ACE2) receptor to gain entrance inside the human cells. This finding raises the curiosity of investigating the expression of ACE2 in neurological tissue and determining the possible contribution of neurological tissue damage to the morbidity and mortality caused by COVID-19. The SARS-CoV-2, like other coronaviruses such as SARS-CoV and MERS-CoV, could target the central nervous system, possibly infecting neurons in the nasal passage and disrupting the senses of smell and taste. The SARS-CoV-2 infects nerve cells, particularly neurons in the medulla oblongata, which is part of the brain stem that serves as the control centre for the heart and the lungs. Researcher have found the virus in the brain and cerebrospinal fluid (CSF), which probably causes different brain diseases such as cerebral haemorrhage, encephalitis, and nerve demyelination. The most prominent way to enter corona virus in the human body is the nasal pathway, which makes a channel to brain through olfactory tract. Hence, the COVID-19 may disrupt sense of smell (hyposmia) and becomes early symptoms of disease that also effects on the taste (dysgeusia). Pandemics can lead to heightened levels of stress; Anxiety is a common reaction to any tense situation.

Keywords: COVID-19; Dysosmia; Dysgeusia; Neurological Disease; Anxiety

Introduction

Coronavirus is an infectious disease caused by a newly discovered novel coronavirus and has recently spread throughout the world. On 11th February 2020, the coronavirus study group (CSG) of the international committee on taxonomy of virus finally designated as pneumonia associated SARS-CoV-2 (Severe Acute Respiratory Syndrome Corona virus-2), which was first reported in the Wuhan city of China in December 2019. On 30th January 2020, the World Health Organization (WHO) declared this outbreak as a public health emergency of international concern (PHEIC). On 11th February, 2020, the WHO named this disease as COVID-19 since it is caused by novel corona virus [1]. Coronavirus is an enveloped non-segmented positive sense single-stranded RNA virus belonging to the Coronaviridae family, in the order of Nidoviriales [2]. The

Coronavirinae sub-family consists of four genera in which Alphacoronavirus and Betacoronavirus infect humans and other mammals. Betacoronavirus include many pathogenic viruses including SARS-CoV, MERS-CoV and SARS-CoV-2, while Gammacoronavirus and Deltacoronavirus associate with infection in the birds [3]. The comparison of alpha and beta coronavirus identifies with two notable genomic features of SARS-CoV-2. On the basis of structural studies and biochemical experiments, SARS-CoV-2 appears to be optimized for binding to human receptor, Angiotensin converting enzyme-2 (ACE-2) [4]. It has unquestionably proved that SARS-CoV-2 is most deadly virus in comparison to SARS and MERS. The SARS-CoV-2 contains three structural proteins such as, Spike (S), Envelope (E) and Membrane (M) and these proteins form virus envelope [5]. The complete genome of novel corona virus has 29,903 nucleotides long single stranded RNA (ssRNA). The complete genome of SARS-CoV-2 from the city of Wuhan in China was submitted in early January 2020, to the NCBI database with ID NC-045512 [6,7]. The genetic similarity between SARS-CoV and SARS-CoV-2 is 79.5%, while the similarity of SARS-CoV-2 with bats coronavirus is much higher as almost 96% [8]. The COVID-19 patients have been reported to experience neurological problems including impaired consciousness, acute cerebrospinal fluid disease, cerebral venous sinuses and cerebral haemorrhage with participation of both central nervous system (CNS) and peripheral nervous system (PNS). These all symptoms appear in the patients suffering from severe infection and older age [3].

Categories of SARS virus and their effect

SARS-CoV-2 is the seventh coronavirus known to infect humans and is a zoonotic respiratory disease which may lead to neurological complications such as polyneuropathy, encephalitis and aortic ischemic stroke [9]. Sign of several oedemas and demyelination of nerve fibres has also been reported [10]. The MERS-CoV (Middle East respiratory syndrome) was originated from bats and its intermediate host was found to be camel. This virus shows neurological symptoms during infection period including infectious neuropathy, ischemic stroke, Guillain-Barre syndrome and sometimes paralysis [11]. The researchers have confirmed the presence of SARS-CoV-2 in cerebrospinal fluid by genomic sequence and virus may also cause nervous system damage. The other strains of novel coronavirus e.g. HKU1, NL63, OC43 and 229E are associated with mild symptoms in humans [2,4].

Route/mechanism of infection

The genetic material and even proteins of viruses can often be detected in nervous system tissue samples such as cerebrospinal fluid (CSF) of brain and directly invade the nervous system and may cause nerve damage [12]. There is an olfactory tract which channel between nasal passages to the central nervous system CNS) for the sense of smell. Novel coronavirus may enter in the brain though the olfactory tract in the early stage of infection [13]. When the virus enters into the lungs tissue cells through nasal passage, there it causes diffusion of alveolar and intestinal inflammatory exudation, oedema, and the formation of transport membrane. This leads to the alveolar gas exchange disorder causing hypoxia in central nervous system and increases anaerobic metabolism in the mitochondria of brain cells and then hypoxia condition induces the occurrence of acute cerebrospinal disease such as acute ischemic stroke [14]. Two categories of co-receptor for SARS-CoV-2 entry are ACE-2 receptor and transmembrane protease, serine-2 (TMPRSS2) [15] in which ACE-2 receptor is present in human brain (strongly expressed in ventrolateral medulla) and other organs of body made up of membrane bound proteins which provide the favourable site for the attachment with the host body. The structural protein encoded by coronavirus on the envelope, is spike protein that compactly binds with four motifs from 482 to 485 amino acid [5] to angiotensin-converting enzyme-2 (ACE-2) receptor with higher binding affinity and mediate subsequent fusion between envelope and host cells membrane to aid viral entry in to host cells [3,16].

Damage of cerebral by SARS-CoV-2

The presence of COVID-19 virus in the genome circulation understandably enables it to pass in to the cerebral circulation. Here the interaction of COVID-19 virus spike protein do happen with ACE-2 expressed capillary endothelium [17]. Subsequently budding of viral particles from the capillaries endothelium and damage to endothelial lining can favour viral access to the brain and interact to the ACE-2 receptor. Anticipated neuronal damage in the endothelial ruptures in cerebral capillaries accompanied by bleeding within the cerebral tissue can have severe consequences in patients with COVID-19 infection [7].

Intra cerebral haemorrhage by SARS-CoV-2

In order for the discovery the neurovirulence of SARS-CoV-2 in neurological tissue expression of ACE-2 receptors, the brain has

been reported to express ACE-2 receptors, that have been detected over glial cells and neurons, which make them a potential target of COVID-19 [7]**.** The coronavirus dock on the ACE-2 positive cells through spike protein and ACE-2 receptor express in cerebrovascular endothelial cells [17], that have role in multiple function regulation in brain include the regulation of hormonal functions and sympathoadrenal system water and sodium intake, vascular auto-regulation and cerebral blood flow [18]. Spike protein of coronavirus bind to ACE-2 receptor expressed in capillary endothelium and cause abnormal elevated blood pressure and increased cerebral haemorrhage, and also damage the blood brain barrier (BBB) and enter the central nervous system (CNS) by attacking the vascular system [7]. It is reasonable to hypothesize that brain ACE-2 could be involved in COVID-2 infection and its dysfunction leading to auto-regulation of disruption, high blood pressure spike and result of atrial wall rupture [19].

Damage of olfactory lobe by SARS-CoV-2

SARS-CoV-2 infects nasal cells and it can reach to the entire brain and cerebrospinal fluid (CSF) through the olfactory nerve and olfactory bulb within seven days and causes inflammation and demyelination [20,21]. The route intended for central nervous system infection with COVID-19 is peripheral trigeminal or olfactory cranial nerves. Based on studies it may be hypothesized that complications such as demyelination and stimulation of T-cell mediated autoimmune reactions may occur in the path of infection spreading with occurrence of dysosmia and dysgeusia can be considered potential consequences of the nerve injury [22,23]. Thus there is an altered sense of smell or hyposmia in an early stage of COVID-19 patients [2]. The loss of sense of smell and taste has been reported from the Iranian people as one of the heaviest involved countries with COVID-19 during the outbreak of diseases. However, the patients with reported dysosmia and dysgeusia along with other manifestations were found less severe and frequently recovered more quickly, may be because of early attention of disease onset [22].

Nervous system disease related to SARS-CoV-2 infection

The previous researchers have confirmed the presence of SARS-CoV-2 by genome sequencing in the cerebrospinal fluid (CSF). It has illustrated that COVID-19 has a potential to cause nervous system damage. Patients with COVID-19 develop neurological symptoms including headache, disturbed consciousness and paraesthesia. Encephalitis refers to inflammatory lesion in the brain parenchyma including neuronal damage and nerve tissue lesion. Early diagnosis of viral encephalitis is critical. Acute viral infection is also an important cause of this disease. Patients infected with COVID-19 often suffer from severe hypoxia, toxic encephalitis and the symptoms may include disturbed consciousness, brain dysfunction and headache [24,25]. Acute cerebrovascular disease is another infection of coronavirus especially SARS-CoV-2 leading to a cytokine storm syndrome [26]. Patients with COID-19 infection may have increased risk of shock, heart failure, arrhythmogenic cardiomyopathy, hypotension and embolic mechanism, and stroke [27]**.**

Psychiatric impact of COVID-19

This is existence done with best of intentions so as to comprise the spread of this viral disease; this is bringing about a significant negative impact on mental health of people. A Patient with confirmed or suspected COVID-19 may experience fear of consequence of infection with a potentially new virus. Those in quarantine might be experienced boredom, loneliness and anger. Symptoms of the infection, such as fever, hypoxia, cough as well as adverse effect of treatment such as insomnia caused by corticosteroid, could lead to worsening anxiety and mental distress [28]. Studies have also highlighted that the least amount of damage should be ensured when using psychotropic medicine, which will mainly decrease the harmful effects of any interaction with SARS-CoV-2 and its treatments [29]. Some methods used in the SARS outbreak could be helpful for the response to the SARS-CoV-2 outbreak. Multidisciplinary committees for mental health are established by health authorities at regional and national levels including psychiatrists, psychiatric nurses for better communication of treatment plans, progress reports, as well as for health status updates given to the patients and their families. Provide psychological counselling to affected patients, as well as their families and members of the public. Using safe communication channels between patients and families, suspected and timely psychiatric treatments should be provided for those presenting with more severe mental health problem. Psychotherapy techniques such as those based on the stress-adaptation model might be helpful in relief to the patients and health workers [30].

Anxiety due to COVID-19

What have not been recognized are the impact of this issue on existing patients of obsessive-compulsive disorder (OCD) and other anxiety disorders. Numerous patients' and care-givers' groups have perceived the trouble and are expressing their concerns about

the same. Distress of infection and too much washing of hands is possibly the commonest symptom of anxiety and now with so much of importance on washing hands in health advisories; it is probable that symptoms of OCD might worsen. Public were not willing to come to clinic or Hospital and have to be forced by her family to seek consultation. They acknowledged that he had settled extreme fear of getting infected with the virus after looking programs on TV set, listening to programs over radio and reading viewing messages on social media platforms like WhatsApp and Facebook about the virus [31,32].

Mostly peoples were worried with the COVID-19 pandemic over the past year. Like: unaffected peoples avoid contracting the Coronavirus infection people, worried for themselves and their close ones during pandemic, Sleeping difficulty due to being worried about the pandemic in the past year. Reduced social contact, people affirmed feeling scared when someone in their social circle became sick and using a mask without the apparent signs and symptoms of the infection and they frequently washed their hands [32].

Corona virus anxiety scale (CAS) is the important quality to measure anxiety of peoples, because many people who are not infected, but believe that they are infected with coronavirus due to the reason of mass hysteria, will seek unnecessary medical evaluations and care [33,34].

Conclusion

According to all previous research, a novel coronavirus has been identified as the cause of an outbreak of respiratory illness that originated from the city of Wuhan, China, and which has spread to several other countries around the world. It produces adverse effect on respiratory tract as well as nervous system. The public is being advised to stay aware of the latest information on the COVID-19 outbreak though national and public health authorities. According to the various researchers, increasing number of patients suffering with COVID-19, the SARS-CoV-2 may be considered as a new neuropathogen. As mental health professionals (MHPs), we need to evaluate as well as educate all patients of anxiety disorders and Provided that different channels of care like telephonic helplines and online consultations might also help. There is no specific treatment for disease caused by a novel coronavirus. However, many of the symptoms can be treated and therefore treatment is based on the patient's clinical condition.

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Conflict of Interest Statement

The authors have no conflict of interest to declare.

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