Coronavirus 2019 and neurological impairments: A review.

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Abstract

Coronaviruses have been known for long primarily to cause severe respiratory damage and systemic infection. However, interest of scientific community on coronaviruses increased as a result of the recently identified species (2019-nCoV). The novel coronavirus 2019 pandemic as declared by the world health organization has done more damage than thought. It is no more a news that COVID-19 affects human's breathing however; it is also associated with lot of complication

COVID-19. This thus translates to impaired neurological functions. This has been attributed to expression of angiotensin converting enzyme II receptor in the brain. Therefore in this review, highlight would be given on neurological complications associated with COVID-19 infection.

Keywords: Coronavirus infection, Neurologic complications, COVID-19, Alzheimer's disease.

Introduction

The primary target of coronavirus is well known to be the human respiratory system. In late 2019, a novel species of coronavirus was identified in patients admitted in hospital based in Wuhan, China [1]. Shortly after the first case in China, it was declared a global pandemic by the world health organization. It has since then been a public heath challenge. Unfortunately there is no approved therapy for 2019-nCoV till date.The pathogenesis of 2019-nCoV is initiated by attaching to the host cell membrane. This is made possible *via* the spike protein which binds the host cell Angiotensin Converting Enzyme II (ACE2); host cell surface receptor that facilitates viral entry [2,3].

The pulmonary system expresses ACE2 in abundance which makes it prone to 2019-nCoV infestation [4]. It is therefore imperative to be worried about other organs that express ACE2 protein. This forms the basis of arguments on 2019-nCoV disease and multi-organ damage [5]. Interestingly, ACE2 is also expressed in the brain and its inhibition is a classical approach in neuroprotection and Alzheimer's disease prevention [6]. Currently, over 1.5 billion people are neurologically impaired [7]. Neurological disorders are diseases that cause abnormalities in the brain and neural connections [8]. It entails structural, electrical or biochemical alterations resulting in array of symptoms. These include paralysis, muscle weakness, confusion, seizure, poor nervous coordination, loss of sensation (smell), pain and memory impairment [9].

Causes of neurological problems vary but nevertheless, viral infection is known to be a common etiology of neurological diseases such as encephalitis which is characterized by inflammation of brain [10]. Encephalitis is the most common cause of brain inflammation. Mostly, patients are presented with change in consciousness coupled with seizure, movement dysfunction and focal neurological deficit [11]. Since the genesis of 2019-nCoV, multi-organ damage complication has become an interest in the scientific society but unfortunately not much is known yet due to novelty of the virus. In this review, highlight would be given on the 2019-nCoV infection and its neurological complications.

Literature Review

2019-nCoV and central nervous system penetration

Middle East Respiratory Syndrome Corona virus (MERS-CoV) has been reported to cause severe neurologic syndrome. Brain MRI of three patients revealed severe brain alterations with the patients presenting altered level of consciousness and motor deficit [12]. Although, this raised certain questions on the mechanism of MERS-CoV invasion into the brain cell of the subjects. 2019-nCoV and MERS-CoV share lot of similarities [13]. Therefore, 2019-nCoV may also have the tendency of causing neurological deficits. Several molecular probing techniques have revealed the presence of coronavirus in the brain [14]. Although, the mechanism by which 2019-nCoV infiltrates nervous system has been fully elucidated.

Possible mechanisms of coronavirus brain infiltration

Although the pulmonary system is the primary target of Coronavirus, it has been reported to invade other organs to cause multiple organ damage [15]. Route of organ invasion could follow different mechanisms.

ACE2 receptor is expressed on olfactory cilial cells. This is a proximate route for viral attachment which makes it possible

for the virus to penetrate the brain and cerebrospinal fluid within 7 days. This can cause inflammation of the nervous system. The hematogenous route is also an important mechanism of viral invasion. The process involves virus entry into the blood stream and then penetrate through the blood brain barrier by tranendothelial means [16].

The virus can also travel along the neuronal axon to block biochemical communication within the neurons. This mechanism is referred to as the axonal transport. The mechanism ensures a neuron to neuron viral transmission that bridges interneuronal communications [17].

Cytokine mediated invasion is a postulated mechanism of virus brain infiltration. This mechanism involves increased infiltration of pro-inflammatory cytokines. This inflames the blood brain barrier and causes virus-mediated Neuroinflammation. This process could be likened to cytokine storm in 2019-nCoV patients.

Evidences from experimental models

Published an interesting animal model on multiple organ damage associated with 2019-nCoV. The scientists developed a transgenic animal model that permits MERS-CoV susceptibility then monitored viral infiltration in various organs. In this model, the brain showed high virus titers with 2 and 6 days. Brain disease was also seen to be peculiar to thalamus and brain stem [18]. Also reported a similar model showing ability of Coronavirus to penetrate brain cells.

It severe acute respiratory syndrome corona virus infection does not only infect the brain but also neuronal cells [19]. However, we have not been able to lay our hands on 2019-nCoV model in this respect. It is then imperative for scientists to delve into this research path to unravel the unknown.

Discussion

Clinical evidences of 2019-nCoV and neurological complications

Mounting evidences are coming up on neurological complications associated with 2019-nCoV. The report of a retrospective study by Pleasure indicated neurologic complications in about 36% of 314 2019-nCoV patients with these subjects showing neurologic symptoms ranging from mild to more pronounced ones including seizure and stroke [20]. This report is in line with where the author categorized neurologic manifestations of 2019-nCoV into central nervous system manifestation, peripheral manifestation and skeletal muscular injury manifestations.

It has been revealed recently that one of five 2019-nCoV patients in a study showed neurologic complications. In the report, the author reported neurological manifestations in about 57% of 841 hospitalized 2019-nCoV patients. The author hypothesized that 2019-nCoV may possess special tropism towards posterior circulation and endotheliopathy [21].

Stages of Neuro-Covid infection

An interesting publication by proposed the classification of 2019-nCoV neurological complications (Neuro-Covid) into three categories. This will be a useful tool for patients' stratification. Neuro-Covid falls into three stages and it could be linked to viral invasion brutality. The stage I is the initial stage of NeuroCovid infection in which the viral damage is restricted to the epithelial cells in the nose and mouth. This is characterized by loss of smell and taste sensations.

The second stage (II) involves the initiation of neuronal inflammation as a result of cytokine storms and extrapulmonary dissemination of viral particles. This is characterized by blood clots in small and large vessels which could cause stroke. The final stage is a more critical stage. The stage III involves the damage of the blood brain barrier in response to cytokine storm from stage II which permits viral infiltration into the brain to impair the neurological functions [22].

Conclusion

Currently, it is obvious that lots of research works are needed to better understand the pathology of 2019-nCoV in multi-organs. In this review, we have been able to shed certain lights and create awareness on possibility of 2019-nCoV triggering neurological complications. Although we have not been able to lay our hands on animal reports showing this claim but however, we have shown certain reports on MERS-CoV. Therefore, it is possible that 2019-nCoV shares this pathology due to their similarities.

In addition, we have highlighted certain reports showing clinical manifestations of neurological complications in 2019-nCoV patients. This is a call to emergency medicine practitioners and clinicians that 2019-nCoV should be given a wider view rather than being seen as just a mere infection. The multi-organ damage of 2019-nCoV may be more severe with chronic health implications.

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