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Research Paper

SARS-COV 2 and Its Infiltration into Nervous System: A Review

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ABSTRACT
A new virus "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was isolated from current outbreak of COVID-19 patients. SARS-CoV 2 resembles the coronavirus (SARS-CoV) that lead to SARS epidemic in 2003. This new virus of the coronaviridae family is highly fatal causing pneumonia and high mortality rate in this pandemic across the world. The common symptoms of COVID-19 patients include fever, dry cough and difficulty in breathing. Many COVID-19 patients with respiratory distress had been treated in intensive care unit. There are patients who were found with rhinorrhea and sore throat considering upper respiratory tract infection. However some COVID-19 patient admitted in the hospital reported with cerebrovascular disease, altered consciousness along with injury to the muscle. Majority of patients complains of headache, nausea and vomiting. All these records and symptoms delineate involvement of nervous system in these patients. The experimental animal studies had proven that SARS-CoV infection infiltrates into the cerebrum and cerebellum. The involvement of brain stem is also seen during the infection in animal leading to its death. This signifies connection of respiratory centre in medulla of brainstem leading to respiratory distress and death. So, the infection of the nervous system by SARS-CoV2 should be taken into consideration as there is similarity of this virus with SARS-CoV.

KEY WORDS: *COVID -19, symptoms, infiltration, nervous system*

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I. INTRODUCTION

The diseases have different name caused by a virus. Their names are considered on genetic framework which accelerates the generation of vaccines, medicines and test for their treatment. The international committee of Taxonomy of Viruses (ICTV) provides title to these viruses. On 11th February 2020, ICTV come up with a name of a new virus "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) since it resembles coronavirus that causes SARS epidemic in 2003. On the basis of previous guidelines World Health Organization (WHO) declared COVID-19 as the name of this new disease on 11th February 2020 (1). These coronavirus belongs to coronaviridae family. They are enveloped RNA viruses with positive stranded genome and are responsible for manifestation of infection in gastrointestinal and respiratory tract infection. SARS-CoV-2 is a ß coronavirus (2). In 1960 two human coronavirus HCoV-229E and HCoV-OC43 were discovered which causes mild cough and common cold. However, ß-CoVs, SARS-CoV and Middle East respiratory syndrome corona virus (MERS-CoV) are responsible for deadly infection of the respiratory system (3). The researchers from China separate a SARS-CoV-2 from an infected patient on 7th January 2020. Due to rapid reproduction number (R_0) of SARS-CoV-2 there were increase pneumonia cases creating epidemic of COVID-19 (4). The target receptor of coronavirus SARS-CoV-2 and SARS-CoV is similar in the host cells after their entry (5). Their entry into the host cells is conciliated by angiotensin-converting enzyme 2 (ACE2) receptors which is exhibited in epithelium of the respiratory tract, in the endothelium of the blood vessels, cells of the nephron of the kidney and small intestine (6). The process of action of SARS-CoV-2 and SARS-CoV is almost same and increase number of case fatality due to acute respiratory distress arise curiosity regarding involvement of central nervous system. It is also verified that coronaviruses have a great affinity to attack neural tissues (7, 8). So it is necessary to come out with research to relate the involvement of central nervous system in COVID-19.

II. CLINICAL FEATURES OF SARS-CoV-2

The coronavirus manifest symptoms by involving the respiratory tract. In previous history of infection with coronavirus SARS-CoV and MERS-CoV , acute respiratory distress syndrome with severe pneumonia causes collective fatality of 10000 patients (9). The COVID-19 symptoms are very similar to the infection of previous two coronavirus. The cause of pneumonia was initially unknown in Wuhan China. The diagnosis was fully based on clinical features and imaging results. The majority of these patients complained of fever, dry cough and difficulty in breathing. The CT scan results demonstrates ground glass opacities with multiple areas of consolidation in subpleural areas seen as significant finding in both the lungs (10,11).

According to a report on 2nd January 2020 a total of 41 cases COVID-19 were detected confirmed in Wuhan China. Most of these cases presented with fever (40 patients,98%), cough (31 patients, 76%) , muscle pain with fatigability (18 patients, 44%), hemoptysis in 2 out of 39 patients (8%) and diarrhea in one out of 38 cases (3%). Headache is complained by 38 patients (38%). Apart from all these symptoms, dyspnea developed in 22 out 40 patients (55%). In SARS-CoV-2 infection some of the patients presented with rhinorrhea and sore throat reflecting upper respiratory tract infection. This symptoms are not part of presentation during SARS-CoV and MERS-CoV infection (12). In an under report from Wuhan China till 3rd February 2020, among 138 patients 26% of patients were transferred to ICU, 4.3% died and remaining 61.6% continuing treatment in the hospital. These patients were bought to the hospital due to onset of fever, dry cough, fatigue and myalgia. Finally symptoms got worsened by dyspnea. The period of onset of initial symptoms to dyspnea was 5 days and progression to acute respiratory distress symptom was 10 days. Patients in majority in ICU were given oxygen therapy and few required invasive ventilation (13). Italy reported 12462 positive cases till 11th March 2020 according to Instituto Superiore di Sanita. Majority of these patients developed acute respiratory distress syndrome ARDS due to pneumonia caused by SARS-CoV-2 (14).

Most of the symptoms related to SARS-CoV-2 are limited to respiratory system. However in a retrospective study from cases of three hospitals from Wuhan reported neurological symptoms in 78 (36%) out of 214 patients taken for the analysis. They have classified the symptoms according to central nervous system, peripheral nervous system and muscle involvement. The patients in their study were confirmed by SARS-CoV-2 detection kit which perform real-time RT PCR assay to detect the cases. The neurological symptoms were seen very common in critically ill patients 40 (45.5%). These patient include acute severe cerebrovascular disease 5 (5.7%), cerebral hemorrhage 1 (0.8%), impaired consciousness 13(14.8%) and muscle injury 17(19.3%). Immunosuppression and cerebrovascular disease is seen in this COVID-19 patients which is evidenced by low lymphocyte count and elevated dimer level. (15). There are also reports from Italy that the confirmed cases of COVID-19 had loss of smell and taste sensation as preliminary symptoms. Most of the patients that died are due to acute respiratory failure. The acute respiratory failure can be due to invasion of SARS-CoV-2 into the neural tissue of central nervous system. There is evidence that coronaviruses (CoV) are not confined to the respiratory system. They have the tendency to attack central nervous system (16, 17, 18). the involvement of the central nervous system should not be ignored in SARS-CoV-2 infection.

III. CHANCES OF INFILTRATION OF NEURAL TISSUE BY SARS-CoV-2

The ACE 2 closely resemble angiotensin- converting enzyme. It was found in the heart failure patients from the ventricles. They are obvious single peptide with transmembrane domain having an active site of metalloprotease. (19). This ACE 2 receptor has been isolated from SARS-CoV which form multinucleated cells that express S proteins (20). ACE 2 binds affectively with protein S1 that helps in the binding of virus particle with the cell membrane containing ACE 2 receptor (21). ACE 2 are located in epithelial cells of the alveolus, in the endothelial cells of the arteries and veins. They are also uncovered in renal, cardiovascular and gastrointestinal system (22). In middle eastern respiratory coronavirus (MERS-CoV) dipeptidyl peptidase 4 (DPP4 or CD26) serve as one of the main receptor (23). The DPP4 inhibitors hold a probable protective covering for neurons which leads to imbalance in memory and defective mitochondria (24). ACE 2 mRNA was found in brain in a research by utilizing quantitative real time RT PCR (25). In many studies perform in the year 2000 to 2003 corona virus was traced in brain. The expression of SARS-CoV antigen is detected in many neurons in a study on transgenic mice. The virus infects C57/BL6 mice brain indicating a secondary infection involving central nervous system. ACE2 activation due to SARS-CoV is also evidenced in cerebellum, cerebrum and brain stem (26). The two types of human coronavirus (HCoV) 229E and OCA3 has the ability to infect oligodendrocytes and neuroglial cells implicating multiple sclerosis (27).

The studies have proven that neurons are infected through intranasal route by SARS-CoV. This infection is evidenced to be due to expression of ACE2 receptors in the nervous tissue. The infection of the neurons is also cause by animal virus MHV and bovine coronavirus (CoV) (28). The brain is infected due to spread of this virus through the olfactory bulb from the olfactory neurons vial olfactory nerves. The effect of smell and taste sensation as initial symptom may be one of the reason behind infection due to SARS-CoV 2. Animal study in mice also demonstrated involvement of medullary cardiorespiratory centre in brainstem. This

has leads to suppression of the cardiorespiratory centre causing death of the animal. The cause of death was due to increase release of cytokines from the brain which increased permeability of blood brain barrier that promotes the binding of SARS-CoV with the ACE2 receptors (29). Majority of fatality is because of failure of respiratory system and probably it is linked to central nervous system which occupies a crucial place related to the death of the patients which is evidenced in a study in mice with ACE2 receptor involvement due to infection of SARS-CoV2.

IV. CONCLUSION

SARS-CoV and MERS-CoV infection are very similar with invasion of the central nervous system evidenced from many studies. The chances of neuroinvasion by SARS-CoV 2 should not be neglected. In the present infection with COVID 19 patients in Wuhan China neurological symptoms are seen related to the involvement of central nervous system. These patients complained of headache, altered consciousness, cerebrovascular infection and epilepsy. Some of them also had hyposmia and hypogeusia. There is infiltration of monocytes and lymphocytes in blood vessels tunics in the brain and muscles lead to edematous condition which explains the cerebrovascular and muscle involvement in SARS-CoV infection (30). A complete neurological inspection and exploration will illuminate the role of SARS-CoV 2 in infection of the nervous system in COVID-19 patients. The SARS-CoV isolation from cerebrospinal fluid and vascular endothelium of cerebral blood vessels will expose the involvement of nervous system. The autopsies of the deceased patient should be carried out to confirm the involvement of the nervous system. The concept of SARS-CoV 2 infecting the central nervous system and respiratory failure will lead the way for proper diagnosis and treatment of patients COVID-19.

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