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Review Article

COVID-19 and Neurology. A Viewpoint

Gabriel Abudinén Adauy*

Neurologist, Neurology and Neurosurgery Department, Hospital Clínico Universidad de Chile, Santiago, Chile

***Corresponding Author:** Gabriel Abudinén Adauy, Neurologist, Neurology and Neurosurgery Department, Hospital Clínico Universidad de Chile, Santiago, Chile.

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Abstract

During this last time we have had to learn and investigate this new strain of coronavirus, which not only affects the respiratory tract, but also produces a systemic affection of different organs through diffuse endothellopathy and a severe systemic inflammatory response. In relation to the affection of the central nervous system, there is a direct relationship or neurotropism, through the receptors of the type 2 angiotensin converting enzyme (ACE2). This review tries to explain the neurological relationship and SARS-COV 2.

Keywords: Epidemiology; Neurology; SARS; COVID-19; Embolism Thrombosis

The world is at present in turmoil due to this pandemic caused by a new coronavirus. This virus family was studied in 2003, for the disease known as SARS (Syndrome of Acute Respiratory Distress). This new coronavirus, SARS-COV2 is a single-stranded RNA positive virus and its intermediary hosts are different from those of the previous SARS (in humans); it is believed that these vectors are bats *(Chiroptera)* and pangolins *(Pholidota*). These species live, and are consumed as food, in Chinese cities where the virus expansion started [1].

From the point of view of epidemiology, SARS-COV2t mainly affects men with classic risk factors: age, cardiovascular risk factors, smoking and obesity, which lead to a higher severity of the disease [2]. The most important factors impacting the severity of the symptoms are. Age (over 50 years), high blood pressure (arterial hypertension) and diabetes mellitus. In Europe, and now in Chile, another epidemiology feature began after the start in China, although affecting younger men with a history of obesity or smoking. Countries such as Spain and Italy showed the first case indexes: the south of Chile shows this clinical context now [3].

The new SARS-COV2

This new coronavirus shows a fundamental difference as regards SARS-COV, related to its viral structure, showing a higher infection rate and higher stability in the union with the angiotensin conversing enzyme receptor 2 (ACE2) [4]. Due to this, SARS. COV2 has a high infection rate (higher than that of SARS 2009) but less severity, since the viral antigen, called spike type protein 1 (SP1), shows a modification from the coronavirus studied in 2009. However, both coronaviruses use the ACE2 receptor -and its enzymatic cofactor TMPRSS2 [5] producing the same symptoms as in the 2003 SARS.

At the science level, there are evidences that SARS-COV2, which shows two different clinical infection contexts, could show two different strains: a less aggressive strain affecting 30% of patients and a mutation -called L, which is more aggressive and affects a larger number of people (70%) [6].

Pathogeny

The pulmonary disease is classically produced by the entry of Flugge droplets. Independently of the organ affected, two fundamental processes take place at the virus physio-pathology level:

- Cytokines storm. The virus replicates inside eukaryote cells causing cell lysis, and a profuse release of antigenic viral material. This causes an exacerbated inflammatory response, which depends more on the innate immune system, through the macrophage participation, with the consequent liberation of IL-6 [7]. On the other hand, there is an intrinsic factor that enhances the severity of this storm: an inhibition of the negative feedback for interleukins levels control. This, through the NOTCH pathway which has been found inhibited in COVID-19 cases [8].

- Procoagulant state. There are series of cases of COVID-19 patients that show increases of prothrombin, thrombocytosis, increase of coagulation factors and high D-dimer. This causes a pro thrombotic environment, with embolism in target organs and vascular periphery. It was believed at first that this was a local thrombosis process, but later on it was seen that it not only affected the lungs with a pulmonary thromboembolism, but that a process of similar characteristics also took place at the brain level (stroke-like), intestines (mesenteric thrombosis) and especially in children, with multiple distal embolisms [9]. Therefore, rather than a local thrombotic process, it is now recognized as disseminated intravascular coagulation, and COVID-19 patients show positive diagnosis criteria [10].

Entrance to the CNS

Coronavirus mainly affects the airways though the ACE2 receptors. These receptors are found not only in the breathing system, but also in other organs, mainly the brain, heart, intestines and kidneys.

Therefore, as the SARS-COV2 contagion advanced, different pathologies have been found associated to it. Furthermore, new research findings consider that there would be a viremia prior to the affection of other organs [11]. So, there could be a direct pathway for the infection of the central nervous system (CNS), through inoculation of the olfactory nerve, producing anosmia and secondarily ageusia [12] and though the haematogenous pathway by viremia, crossing the hemato-encephalic barrier [13].

SARS-COV2 neurotropism

There are evidences in previous detected cases that SARS and MERS-COV show neurotropism with infection of the olfactory bulb, thalamus and brainstem., At present SARS-COV2 has caused an impact at the CNS and periphery (PNS), with different neurologic manifestations (mostly hyposmia). Most appear together or later than other symptoms [12]. SARS-COV2 shows interaction with ACE2 receptors of the neuronal somas affecting the CNS but also causes axonal demyelination and multiple cranial neuropathies. Several brain pathologies, generally of the PNS are linked to infectious or post-infection states, mostly associated to pro-inflammatory and autoimmune processes (not necessarily direct neurotropism) [13].

Neurologic manifestations

There are reports of cases showing neurological affection around the world; the Spanish Neurology Society issued a report concerning the prevalence of these affections, ranging as follows: Encephalopathy (27%), Myalgia (27%), Anosmia/Ageusia (15%), Headache (10%), Stroke (CVA) (10%) and vertigo (11%) [14,15].

Different signs were evident during physical examination of patients who showed neurological manifestations: agitation, focused in the spinal cord and dis-executive syndrome) associated with alterations, both of the images (leptomeningeal capture, hypo perfusion and brain ischemia) as in laboratory tests (PCR SARS-COV2 in LCR-, oligo clonal banding) [14].

- Cerebro-vascular accident: trhough several pathogenic pathways (disseminated intravascular coagulation, cytokines storm and cardiac arrhythmia). This is generally evident in patients under invasive mechanical ventilation for COVID-19 in the ICU [15].
- PNS affection: by the immune process rather than by direct affection. Cases of Sd. Guillain-Barré and Sd. Miller-Fisher have been found with negative PCR in the cerebrospinal liquid (LCR) and poor evolution in spite of gamma-globulin therapy [16].
- Acute myelitis: the most probable cause might be post-infection (as for the majority of acute myelitis), since the PCR for SARS-COV2 is negative in LCR [17].
- Meningoencephalitis: there are reports of convulsive crises associated to SARS-COV2 (diagnosed by PCR), in some cases associated to Meningeal syndrome, febrile, deterioration of cognitive behavior and delirium. In images, the pattern of hippocampal atrophy is associated with a generally asymmetric involvement of the anterior temporal pole [18].
- Acute Necrotizing encephalitis: this is a rare post-infection complication, generally following influenza or post-viral and is related to a cytokines storm at the systemic and focal level, and breach of the HE barrier. Patients are admitted?? with breathing symptoms associated to encephalitis but the later prevails over breathing [19].

Conclusion

This review tries to capture the relationship on the coronavirus at the neurological level, identify the possible targets and the entry routes of SARS-CoV-2 into the central nervous system, in addition to describing the spectrum of neurological symptoms, the complications that have manifested so far in COVID-19 and its potential pathogenesis. This can lead to better clinical outcomes and better treatment algorithms. More studies are needed to understand the pathogenesis of the disease in the central nervous system, the post-recovery sequelae of COVID-19, and the natural history of COVID-19 in the central nervous system.

Bibliography

1. Zhang G., *et al*. "Clinical features and short-term outcomes of 221 patients with COVID-19 in Wuhan, China". *Journal of Clinical Virology* 127 (2020): 104364.

2. Richardson S., *et al*. "Presenting Characteristics, Comorbidities, and Outcomes Among 5700 Patients Hospitalized with COVID-19 in the New York City Area". *Journal of the American Medical Association* 323.20 (2020): 2052-2059.

3. Reportes Epidemiológicos de la Sociedad Chilena de Medicina Intensiva (2020).

4. YanweiLi., *et al.* "Physiological and pathological regulation of ACE2, the SARS-CoV-2 receptor". *Pharmacological Research* 14 (2020): 104833.

5. Hoffmann N., *et al*. "SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor". *Cell* 181 (2020): 1-10.

6. Tang X., *et al*. "On the origin and continuing evolution of SARS-CoV-2". *National Science* 7.6 (2020): 1012-1023.

7. Lipworth B., *et al*. "Weathering the cytokine storm in susceptible patients with severe SARS-CoV-2 infection". *The Journal of Allergy and Clinical Immunology: In Practice* 8.6 (2020): 1798-1801.

8. Rizo P., *et al*. "COVID-19 in the heart and the lungs: could we "Notch" the inflammatory storm?". *Basic Research on Cardiology* 115.3 (2020): 31.

9. Ranucci M., *et al*. "The procoagulant pattern of patients with COVID-19 acute respiratory distress syndrome". *Journal of Thrombosis and Haemostasis* (2020).

10. Song., *et al*. "Chinese expert consensus on diagnosis and treatment of coagulation dysfunction in COVID-19". *Military Medical Research* 7 (2020): 19.

11. Yan R., *et al*. "Structural basis for the recognition of SARS-CoV-2 by full-length human ACE2". *Science* 367.6485 (2020): 1444-1448.

12. Spinato G., *et al*. "Alterations in Smell or Taste in Mildly Symptomatic Outpatients With SARS-CoV-2 Infection". *Journal of the American Medical Association* 323.20 (2020): 2089-2090.

13. Baig A., *et al*. "Evidence of the COVID-19 Virus Targeting the CNS: TissueDistribution, Host–Virus Interaction, and Proposed Neurotropic mechanism". *ACS Chemical Neuroscience* 11.7 (2020): 995-998.

14. Helms J., *et al*. "Neurologic Features in Severe SARS-CoV-2 Infection". *The New England Journal of Medicine* 382 (2020): 2268-2270.

15. Aggarwal G., *et al*. "Cerebrovascular Disease is Associated with an Increased Disease Severity in Patients with Coronavirus Disease 2019 (COVID-19): A pooled analysis of published literature". *International Journal of Stoke* 5.4 (2020): 385-389.

16. Toscano G., *et al*. "Guillain–Barré Syndrome Associated with SARS-CoV-2". *The New England Journal of Medicine* 382 (2020): 2574-2576.

17. Zhao K., *et al*. "Acute myelitis after SARS-CoV-2 infection: a case report". *medRxiv* (2020).

18. Morigushi T., *et al*. "Meningitis/Encephalitis associated with SARS-coronavirus 2". *International Journal of Infectious Diseases* (2020).

19. Poyiadji N., *et al*. "COVID-19–associated Acute Hemorrhagic Necrotizing Encephalopathy: CT and MRI". *Radiology* 296.2 (2020).