Letter to the Editor

SARS-CoV-2, periodontitis and brain inflammation: a putative role in epilepsy and neurological disorders

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Received: 06 August 2021; Accepted: 04 November 2021; Published: 10 December 2021.
doi: 10.21037/fomm-21-88
View this article at: https://dx.doi.org/10.21037/fomm-21-88

COVID-19 was first reported in December 2019 in Wuhan, Hubei Province, China. The severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) causes fever, dry cough, pain, headache, tiredness, anorexia, and loss of smell and/or taste. Patients infected with COVID-19 may also exhibit neurological alterations, such as delirium, ischemic and hemorrhagic strokes, and epileptic seizures. In accordance with the World Health Organization (WHO), in March 2020, COVID-19 became a new pandemic, affecting the lives of people, the health care system, the economy, and other aspects of life around the world (1). Epilepsy affects about 50 million people worldwide, and the whole mechanism of action of this pathology still unclear; however, it has been suggested that the increase of neuronal excitability in several areas of the brain can spread the seizures caused by the imbalance of many neurotransmitters (2). Currently, there has been an increase in the evidence indicating that astrocytes have a role in epilepsy, according to which this type of cell modulates neuronal excitation and inhibition in the brain, composing the tripartite synapse (3).

Several studies have revealed the presence of molecules responsible for the COVID-19 infection in oral tissues and cells, such as tongues, salivary glands, mucosa, junctional epithelium, oral gingival epithelium, and connective tissue (4). Furthermore, recent studies have shown a relationship between SARS-CoV-2 infections and other systemic disorders, such as hypertension, diabetes mellitus, obesity, and periodontitis (5,6). In addition, metagenomic analyses have shown a connection between SARS-CoV-2 and cariogenic or periodontopathic bacteria (7). Thus, poor oral hygiene can contribute to the pathogenesis of respiratory diseases, such as those implicated in COVID-19, and it is associated with several chronic inflammatory systemic diseases, as described above (7). Periodontitis is a chronic multifactorial inflammatory condition that affects the teeth, alveolar bone, soft tissues and may be related with systemic disorders (6). It is important to mention that periodontitis is associated with dysbiotic plaque biofilms caused predominantly by several species of microorganisms. In addition, these pathogens and their products, as interleukins, could move in the bloodstream and promote alterations in various organic tissues (6). Recently, the analysis of a three-dimensional human gingival model has showed that *Porphyromonas gingivalis*, the main pathogen of periodontal disease, migrates to the deeper epithelium through an intercellular rather than intracellular route, invading the circulation system (8). Scientific literature states that SARS-CoV-2 also penetrates into the human body via the oral epithelium and connective tissues, with the mediation of the angiotensin converting enzyme II (ACE2) receptors, expressed in epithelial cells of the tongue and salivary glands (6). From this point of view, the microorganisms that induce periodontitis, their products, and the SARS-CoV-2 virus may enter the oral blood vessels, reach the circulation of the system as a whole, and cause brain inflammation, leading to response of microglial cells and astrocytes (1,6).

When there is an invasion of microorganisms and viruses in the nervous system, astrocytes and microglial cells are activated and induce a large inflammatory cascade that causes hyper-excitability and neuronal loss in many areas

of the brain, such as the hippocampus and cerebral cortex, the main regions associated with epileptogenic seizures. Other alterations in the homeostasis of the brain are also produced by blood-brain barrier permeability, abnormal coagulation, mitochondria disturbances, and electrolyte imbalances, probably caused by cytokines arising from the systemic circulation to the CNS or by the release of several types of cytokines by activated microglia. Similarly, the presence of periodontal pathogens and their toxins can reach the bloodstream, penetrate into the brain, activate the inflammatory cascade, and initiate a neuroinflammation, which promotes the release of inflammatory cytokines (5), as described to SARS-CoV-2 infection.

The knowledge about COVID-19 and systemic disorders still needs several studies, and the complications associated with COVID-19, neurological disorders, and periodontitis should be considered as part of the clinical attention to be provided during this global pandemic. However, this letter to the editor aims to work as an alert, encouraging the discussion/reflection of a possible relationship associating COVID-19, periodontitis, and neurological disorders. This is not limited to epileptic seizures, since these may be closely associated to oral conditions that can "store" the SARS-CoV-2 virus and infectious oral diseases that can also cause inflammatory brain episodes, contributing for epileptic seizures and other neurological disorders to be triggered, including neurodegenerative diseases. Finally, it is important to mention that health professionals, mainly dentists, may be "opening the door" during dental care, since they work in an environment that is potentially infected by the SARS-CoV-2 virus, and several surgical or non-surgical interventions and blood vessels may be exposed in the oral cavity, facilitating the penetration of microorganisms and of the SARS-CoV-2 virus into the bloodstream.

Acknowledgments

We thank the University Center of North Paulista (UNORP) and São Paulo State University (UNESP) for supporting this study.
Funding: None.

Footnote

Provenance and Peer Review: This article was a standard submission to the journal. The article has undergone external peer review.

Peer Review File: Available at https://fomm.amegroups.com/article/view/10.21037/fomm-21-88/prf

Conflicts of Interest: Both authors have completed the ICMJE uniform disclosure form (available at https://fomm.amegroups.com/article/view/10.21037/fomm-21-88/coif). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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doi: 10.21037/fomm-21-88
Cite this article as: Tessarin GWL, Santos RMD. SARS-CoV-2, periodontitis and brain inflammation: a putative role in epilepsy and neurological disorders. Front Oral Maxillofac Med 2021;3:40.

https://fomm.amegroups.com/article/view/doi/coif

