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Coronavirus disease 2019 (COVID-19) in neurology and neurosurgery: A scoping review of the early literature

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is a devastating respiratory illness that has dramatically changed the medical landscape around the world. In parallel with a rise in the number of cases globally, the COVID-19 literature has rapidly expanded with experts around the world disseminating knowledge and collaborating on best practices. To date, the literature has predominantly consisted of case reports, case series, and systemic protocols for dealing with this deadly disease from a plethora of specialties with larger observational and randomized studies only now starting to emerge. This scoping review of MEDLINE, EMBASE, SCOPUS, and the Cochrane Library aims to evaluate and summarize the current status of the COVID-19 literature at it applies to neurology and neurosurgery. Neurological symptomatology, neurological risk factors for poor prognosis, pathophysiology for neuroinvasion, and actions taken by neurological or neurosurgical services to manage the current COVID-19 crisis are reviewed.

1. Introduction

Several cases of pneumonia occurring in Wuhan, China including several patients with exposure to a large seafood market selling live animals was announced by Chinese authorities in late December 2019 [1]. The pathogen was isolated as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) resulting in Coronavirus Disease 2019 (COVID-19). The disease has since spread rapidly to most countries around the world. The World Health Organization declared COVID-19 a global pandemic as of March 11, 2020.

Early reports have demonstrated respiratory predominant symptomatology including fever, cough, dyspnea, and fatigue [2]. However, as the prevalence of COVID-19 continues to increase globally, other disease manifestations such as those affecting the central nervous system (CNS) are reported [3]. Furthermore, the emergence of cases involving less commonly afflicted organ systems has necessitated rapid and dramatic changes in practice patterns and has significant implications for all specialties of medicine. This scoping review evaluates the current status of the COVID-19 literature as it relates to neurology and neurosurgery.

2. Methods

The 26-item 2018 PRISMA extension for Scoping Reviews (PRISMA-ScR) checklist was used as an outline for this study [4]. An a priori protocol was not pre-registered. A search of MEDLINE, EMBASE, Scopus, and the Cochrane Library (including the Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials, and the Cochrane Special Collections) from inception to April 7, 2020 was performed in order to identify articles evaluating both COVID-19 and neurology or neurosurgery. Variations of “COVID” AND “neuro OR brain OR spine OR peripheral nerve” related title/abstract/keywords and medical subject heading terms were performed with individual database search strategies outlined in Table 1. No language restrictions were applied. Database searches were combined and duplicates were removed.

Title and abstracts were then reviewed for relevance and articles evaluating COVID-19 with relevance to neurology and/or neurosurgery were reviewed in full text by two authors with 6 and 9 years of experience in the neurosciences. Studies not relating to COVID-19 or the clinical neurosciences were excluded from review. Relevant references were reviewed. Forward searching of key articles was also performed in Google Scholar. A gray literature search of conference abstracts was not

Abbreviations: SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; COVID-19, coronavirus disease 2019; SARS-CoV, severe acute respiratory syndrome coronavirus; ACE2, angiotensin-converting enzyme 2

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ACE2 is low in the brain, autopsy studies have previously demonstrated SARS-CoV particle presence brain tissue [20]. Moreover, neurological deposition has been demonstrated in most other beta-coronaviruses including SARS-CoV, MERS-CoV, HCoV-229E, HCoV-229E, mouse hepatitis virus, and porcine hemagglutinating encephalomyelitis coronavirus (HEV) [6]. Some authors have postulated a mechanism other than ACE2 epithelial or endothelial cell adherence as a route for CNS infiltration such as trans-synaptic viral transfer after initial peripheral nerve invasion [6]. This would then explain findings of some studies demonstrating the virus’ predominant presence in neurons [20–22]. However, the higher relative prevalence of SARS-CoV in the cerebrum (where glial cells are more common) compared to the cerebellum in autopsy studies has led others to postulate a glial presence of ACE2 [17,20].

Human cases of SARS-CoV-related polyneuropathy and encephalitis have been previously reported and a similar risk has been assumed for SARS-CoV-2 [8,23]. To date, at least three case reports of SARS-CoV-2 encephalitis have been reported [24–26]. The first case was reported in a Beijing hospital upon a SARS-CoV-2 RNA positive test of a patient’s cerebrospinal fluid (CSF) [8,16,24]. The second case was a 24-year-old Japanese man with sinustitis complicated by medial temporal lobe encephalitis and lateral ventriculitis [25]. The CSF also tested positive for SARS-CoV-2 RNA in the latter patient. A third case involving hemorrhagic necrotizing encephalopathy of the medial temporal lobes and thalami in a female airline worker in her fifties was recently reported in the United States [26].

The mechanism of action for SARS-CoV-2 neurological invasion is not yet specified. Several theories have been postulated including: direct invasion, blood circulation pathway, neuronal pathway, hypoxia injury, immune injury/cytokine storm syndromes, ACE2 receptor expression, among others [8,26]. As previously described, perhaps the leading current theory is direct seeding and trans-synaptic infiltration via the olfactory nerve or perineuronal cells. This route of invasion has been documented in animal studies for other coronaviruses [27–30]. For example, experimental studies in transgenic mice injected intranasally with SARS-CoV have demonstrated brain entry via the olfactory nerves with subsequent rapid spread to medial brain structures including the medial temporal lobe, basal ganglia, thalami, and midbrain [30]. These findings would be consistent with the limited case report data available to date.

Animal studies of other beta-coronaviruses have also suggested a link with some long-term neurodegenerative diseases [31]. Long-term persistent psychological distress has been shown in SARS survivors [32]. The potential long-term neurodegenerative and psychological effects of COVID-19 have yet to be determined.

3.3. Impact of COVID-19 on practice management

COVID-19 has dramatically altered practice patterns around the world. Early studies have been published with experiences and recommendations, predominantly from locations substantially affected by the COVID-19 crisis including China [9,12,13] and Northern Italy [10,11]. Thus far, early experience and recommendations in neurological [9–11,33], stroke [12], and spine [13,14] practices have been reported (Table 2). Included among these are algorithms pertaining to the deployment of healthcare personnel, and the prioritization, scheduling, and cancelling of surgical cases. Algorithms and protocols such as these have been created through interdisciplinary expert panel consensus with the goal of addressing critical neurological and neurosurgical issues and allowing for the safe and continued care of neurological patients in the context of the COVID-19 pandemic. Ongoing study of the effectiveness of these treatment algorithms will be necessary to ensure the implementation of optimum patient management strategies during this pandemic.

Preliminary consensus guidelines surrounding specific COVID-19 related management are also beginning to be published in...
At present, best practice regarding general anesthesia and monitored anesthesia care remains unclear and controversial, but more conservative measures with decreased risk of aerosolizing virus are favored when possible [34]. At present, best practice regarding general anesthesia and

subspecialties within neurology and neurosurgery based on pre-COVID-19 literature and expert consensus. For example, early guidelines are recommending strict precautions in patients with unknown or suspected COVID-19 requiring emergent endovascular thrombectomy [34]. At present, best practice regarding general anesthesia and
4. Discussion

Limited literature is available to date on the COVID-19 as it relates to the clinical neurosciences. This scoping review identifies several significant findings pertaining to the practice of neurology and neurosurgery, including:

1. Pre-existing cerebrovascular disease may be a risk factor for poor outcome in patients infected with COVID-19.
2. COVID-19 infection may manifest as neurological symptomatology, including: headache, dizziness, hypogeusia and/or anosmia, altered level of consciousness, acute cerebrovascular events, seizure(s), and ataxia.
3. Although the mechanism of invasion is not fully understood, COVID-19 appears to demonstrate neuroinvasive potential. Viral encephalitis +/- hemorrhagic necrosis involving mesial brain structures such as the mesial temporal lobes and thalami have been reported to date.
4. Long-term neurodegenerative effects of COVID-19 have yet to be elucidated, but are theorized based on past experience with other beta-coronaviruses.
5. Neurology and neurosurgical practice patterns are being changed dramatically and constantly updated with publications demonstrating early experiences and recommendations based on facilities and regions most affected.

As an early scoping review of available literature to date, this study has certain limitations. First, symptoms classified as neurological including headache, dizziness, and altered level of consciousness are non-specific with multiple potential causes. These symptoms may relate to an alternative system of origin, may be therapy related, and/or may be of psychosocial origin. The extent to which these symptoms may impact the practice of neurology and neurosurgery is uncertain. Second, the predominant limitation of this scoping review pertains to limited available early literature. As the number of COVID-19 cases continues to rise dramatically across the world, we anticipate that the literature will also continue to evolve. As the prevalence of COVID-19 increases, more cases reporting rare neurological presentations of COVID-19 are likely to be published. A better understanding of the mechanism and therapeutic options for invasive neurological cases may also evolve. Consensus statements and society guidelines will likely require continual refinement based on emerging COVID-19 specific data. Finally, optimal practice patterns will likely vary widely with nuanced configurations based on regional prevalence and available health care resources. In order to ensure optimum neurological patient management, ongoing study of treatment algorithms will be essential for updating and adapting these approaches as the COVID-19 pandemic evolves.

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