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Muscle, and Neuromuscular Junction Diseases During COVID-19 Pandemic: What Should We Know

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Abstract

Background

A New detected virus called COVID-19 reported by World Health Organization (WHO) as pandemic at March 2020 COVID-19 is affected mainly by respiratory illness, but it can also affect the brain. Neurological manifestations are recorded COVID-19 pandemics but are not effectively addressed how to deal and treat them.

Method

In this review, I try to discuss the postulated neuronal mechanisms of the coronavirus infection sequelae. After made midlines about this topic, I discuss prevalence, pathogenesis, and then put a proposal on how to deal with muscle disease, neuromuscular junctions' disorders.

Conclusion

This review aims to educate and update the neurologists and health team who work with patients

with muscle and neuromuscular junctions' disease among suspected cases of COVID-19 about the possible neurological presentations.

Introduction

At the end of 2019, at Wuhan, China new strain virus of CORONA group spread all over the world called COVID-19 [1,2]. This virus mainly affected respiratory system. However, about 36.4% (78/214) of patients with COVID-19 developed many neurological symptoms [3]. The affection of CNS occurred in severe cases rather than mild or moderate [4-9]. In general for more studies and researches in the past decades revealed coronaviruses had capacity to go beyond the respiratory system to enter the nervous system and establish persistent brain damage [4-9].

My aim in this review is to update according to my knowledge, the neurologists working with suspected cases of COVID-19 or with patents without respiratory symptoms about the possible muscle or neuromuscular. Also, I try to put a proposal to how to deal and treat patients with neurological disorders and COVID-19.

Search Strategy and Selection Criteria

I searched Medline, Egyptian Knowledge Bank, Scopus, Elsevier, PubMed, and Google Scholar. I collected data published between Jan 1, 2019, and June 25, 2020, using keywords "COVID-19", "Coronavirus", "pandemic", "SARS COV-2", management's strategy of neurological "neurology", "neurological", "muscle disease" myasthenia gravis" myositis" myalgia. My Search limited only to the English language.

How COVID-19 Affect Muscle and Neuromuscular

As previously known, Coronaviruses are not invading neurons primary. They invade respiratory epithelium first [3]. Then they invade CNS by a different mechanism. The coronaviruses invaded the nervous system either by direct or indirect pathways. In addition, it has a chronic phase in the affection of CNS. Affection of muscles and neuromuscular occur from indirect and chronic pathways.

Indirect mechanisms include hypoxic brain injury and immune-mediated damage to the CNS. hypoxic brain injury resulted from severe respiratory distress led to hypoxia, hypercarbia, hypoxia and anaerobic metabolism, accumulation of toxic compounds. These factors leaded to neuronal swelling and brain edema hence brain damage [10]. Immune mediated pathway resulted from cytokines storm which led to activations of T lymphocytes, macrophages, and endothelial cells. This then led to an accumulation of inflammatory substances including interleukin-6 (IL-6), alpha tumor necrosis factor (TNF-α), IL-10, IL-15, IL-1β, soluble TNF receptor, and interferon- gamma (IFN-γ). In addition to lymphocytes, in particular, natural killer cells (NK) CD56 that lead to brain injury by altering BBB by trypsin and matrix [4].

Chronic Phase: As The elimination of viruses is limited and depends on the role of cytotoxic T-cells and apoptosis of infected neurons which led to a lack of major histocompatibility complex antigen in nerve cells. So, it led to chronic existence of viruses and may facilitate exacerbation of neurologic damage and

degeneration [11-13]. Also, muscle and neuromuscular can affected from the late effect of drugs used in COVID-19 trials.

Prevalence of Neurological Disorders With COVID-19

One large study involved 214 confirmed COVID-19 cases. It revealed (36.4%) had neurological manifestations, including (24.8%) with the central nervous system (CNS)and (8.9%) with the peripheral nervous system (PNS). Also, (10.7%) with skeletal muscle affections, gustatory [5,14-17].

In a large study in china, fatigue occurred in 26%-51% of patients with COVID-19 in China, 36% of them had myalgia and increased creatine kinase (CK) was present in 33% of patients [18,19]. Myositis and rhabodomyolysis occurred In the last era of MERSA and SARS Viral affection [4,18].

How to Deal With Some Neurological Disorders During Pandemic

Neuromuscular Junction and COVID-19

Delly *et al*., reported the first known case of myasthenia gravis (MG)crises with COVID-19 [20]. Viral infections in general include Coronavirus have been reported to affect upon autoimmunity through augmentation of T cell signaling causing a pro-inflammatory environment due to a hyper-reactive antiviral immune response. Also, epitope spreading and also fever has an effect on neuromuscular junction function [21]. The scientists suggest the shared component between COVID-19 and MG crises are dysregulation of cytokine which promotes the increase of pro-inflammatory cytokines and chemokines that attack organ systems, particularly the lungs which can result in ARDS [20-22].

In trial to put protocol Guidance for the management of myasthenia gravis (MG) and Lambert-Eaton myasthenic syndrome (LEMS) during the COVID-19 pandemic, we studied different reports and different case reports [20,21,23-26] to conclude the following:

1. The MG expert pane suggests that decisions to manage every patient should be individualized according to the severity of illness and liability to get infections with COVID-19

2. More protections with extraordinary measures should be taken by the patients and their families as more distance, postpone blood tests if not necessary and used telemedicine and social applications for routine follow up.

3. MG/LEMS patients should take their treatment as there is no scientific evidence to suggest that Pyridostigmine or 3,4 Diaminopyridine increases the risk of infection

4. MG on immunosuppressive therapy should not stop it as that carries a potential for increased disease activity and/or MG exacerbation or crisis.

5. It is currently no evidence to suggest that the intravenous immunoglobulin (IVIG) or therapeutic plasma exchange (PLEX or TPE) increase the risk of getting infected with COVID-19? In which, IVIG uses pooled normal IgG that works through numerous mechanisms, which include: blocking both cytokine

production and pathologically activated the differentiation of Th1, Th17, and Tfh subsets, overwhelming the neonatal Fc receptor which in turn causes a reduction in endogenous and exogenous IgG leading to reduction of AChR antibodies, neutralization of autoantibodies by anti-idiotypic antibodies and inhibition of complement activation.

6. Hydroxychloroquine is reported to worsen MG as the combined use of hydroxychloroquine and azithromycin, a macrolide that aggravates MG, may have caused the worsening of MG, which may lead to the use an additional dose of IVIG.

7. However, the doctor should take care from the potential complication of IVIG is thrombosis and widespread thrombosis has also been reported in critically ill COVID-19 patients. Therefore, careful administration of IVIG is required in MG patients.

8. Delay initiation a B-cell depleting therapy4 (e.g., rituximab) as increasing the risk of worsening myasthenia or crisis and the risk of contracting the viral infection, until the peak of the outbreak is over.

Muscle Diseases With COVID-19

Fatigue occurred in 26%-51% of patients with COVID-19 in China [27], 36% had myalgia and elevated creatine kinase (CK) found in 33% of patients. There are no reports of EMG or muscle biopsy. Myositis due to virus infections reported during MERS [28] and SARS [29]. Also, myositis reported in patients with acute renal failure during SARS, and two reports of muscle involved during COVID [27,30]. Neuromuscular complications that may be directly or indirectly related to coronavirus infection include Risk of infection - causing a new myositis or critical illness myopathy.

In addition, the risk of exacerbating to unmasking previously unrecognized MG, myositis, muscular dystrophies, congenital myopathies, mitochondrial myopathies, metabolic myopathies. The risk of COVID-19 affection increased with the usage of immunosuppressant/immunomodulating therapies in patients with autoimmune neuromuscular disorders. Hydroxychloroquine and chloroquine can cause toxic neuropathy and myopathy [23].

As regard treatment guideline for patients with autoimmune muscular disorder Gudion and Amato, recommended Patients with NMD already on corticosteroids require doses adjustment according to stress. Other immunosuppression is stopped or continued based on the patient's clinical status from COVID-19 and the severity of their illness.

Chloroquine and hydroxychloroquine used as a possible treatment for COVID-19. They are associated with potential neuromuscular side effects. Unfortunately, patients taking chloroquine or hydroxychloroquine develop slowly progressive, painless, proximal weakness and atrophy in the legs more than the arms [23].

Myalgia

Myalgia and fatigue have been commonly reported during the infection process. fatigue recorded in 26%-51%, and 36% had myalgia [13]. Some patients showed fatigue, muscle soreness, and elevated muscle enzyme levels, which may be related to the inflammation and muscle damage caused by the virus.

Conclusion

There is a clear emerging group of neurological manifestations during and after SARS-CoV-2 infection. The COVID-19 pandemic is still affecting many people all over the world. Muscle and neuromuscular disorders occur due to indirect, or as chronic. Available treatment options might potentially lead to a wave of muscles and myasthenia gravis sequelae. Now we are facing unknown possible neurological complications of COVID-19. So, many types of researches should be developed to postulate this pointing.

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