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EXPLORING THE LINK BETWEEN SARS COV-2 INFECTION AND RHABDOMYOLYSIS

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Novel coronavirus disease (COVID-19), caused by infection with severe acute respiratory syndrome coronavirus-2 (SARS CoV-2), was identified in late 2019 in Wuhan, China.[1] It has rapidly spread around the world, and was named a pandemic by the WHO on March 11, 2020. The most common symptoms of coronavirus (COVID-19) in humans include; cough, fever, shortness of breath, headache, sore throat, diarrhea, and muscle aches.[1] Here we discussed unusual association between infection SARS COV 2 and creatine kinase elevation and reviewed the literature in this topic.

The main associated risk factors of rhabdomyolysis are alcoholism, lesions caused by compression, overexertion, heat intolerance, sunstroke, low phosphate levels, convulsions and drug use or overdose.[2]

Numerous bacterial, viral and fungal infections can lead to rhabdomyolysis. Viral infections in particular have a recognized association with a wide spectrum of muscle disorders, ranging from acute non-specific myalgia to severe myositis and rhabdomyolysis.[3] Influenza is the most common viral etiology followed by HIV infection and enteroviral infection.[4, 5]

Recently, few cases of rhabdomyolysis associated with COVID-19 were reported, the first was a report of a COVID-19 patient from Wuhan, China, who developed rhabdomyolysis during hospitalization and the second case in New York, USA of an elderly male who presented with rhabdomyolysis and later was diagnosed with COVID-19.[6, 7, 8, 9, 10, 11, 12]

Frank rhabdomyolysis may be rare, elevated CK levels were identified in 13.7% of patients in one large cohort of COVID-19 disease from China, suggesting some component of muscle injury may be relatively common. Additionally, evidence of myocardial injury is being frequently reported in COVID-19 patients and may represent a common underlying mechanism.[8, 13]

The prevalence of acute kidney injury in SARS-CoV-2 is 15%. A study of 701 SARS-CoV-2 patients by Cheng and colleagues demonstrated that in-hospital mortality increased by almost three-fold in those who had acute kidney injury.[14, 15]

Furthermore, a report by Wang et al.[16] describes 3 cases of 2002 severe acute respiratory syndrome (SARS) related to coronavirus, who developed rhabdomyolysis during their disease course. The authors concludes that rhabdomyolysis-associated renal failure may be another unusual but severe presentation of SARS.

The proposed pathophysiological mechanisms of rhabdomyolysis in patients with viral infection include direct viral invasion of skeletal muscle, Immunologic reaction "cytokine storm" resulting in collateral muscle damage and generation of viral toxin causing direct muscle injury.[7, 5]

The risk of developing rhabdomyolysis after drug use is possible. The drug-induced, myopathy is defined as the acute or subacute manifestation of myopathic symptoms such as muscle weakness, myalgia, creatine kinase (CK) elevation, or myoglobinuria that can occur in patients without muscle disease when they are exposed to certain drugs.[17] Symptoms of myopathy typically occur weeks or months after administration of the drug and usually improve or resolve within weeks after discontinuation of the offending agent. Elevated CK levels are not sufficient for a diagnosis of toxic myopathy, and muscle biopsy is often necessary to document evidence of myotoxicity and eliminate other causes of weakness and/or elevated CK in the differential diagnosis. Drug-induced myopathies are often a diagnosis of exclusion, as the differential diagnosis for muscle symptoms can be quite broad.[17]

For this association, the most likely etiology is viral infection, but the drug etiology cannot be excluded,

especially with the association of several drugs providing this disorder, such as: anti malarics (hydoxychloroquine), corticosteroids (methylprednisolone), macrolides (azithromycin), and azoles (fluconazole) was among agents inhibiting CYP3A4.

The previously reported Chloroquine / hydroxychloroquine-related myopathies cases may shed light on the possible causal relationship between Chloroquine / hydroxychloroquine and myopathies, and suggested discontinuation of antimalarials in any patient with suspected antimalarial agent–related myopathy.[17]

Glucocorticoids are among the most recognized myotoxins, although the mechanism responsible for this toxicity has not been completely elucidated. Steroid myopathy is often characterized by muscular atrophy, which is believed to be due to suppressed protein synthesis and growth, enhanced proteolysis, and apoptosis induction.[17, 18]

There are scarce reports in the literature associating rhabdomyolysis to levofloxacin and to others anti infectious.[18, 19, 20] While role of CYP3A4 inhibitors such as: macrolides (azithromycin), and azoles (fluconazole), in drugs-related myopathy is well established with statins.[17, 18]

Our findings highlight the need to consider checking CK levels in hospitalised patients with SARS COV 2 infection. Additionally, COVID 19 must remain in the differential for unexplained myopathy. Furthermore, the progressing to rhabdomyolysis is uncommon but is associated with life-threatening complications such as hyperkalemia, myocardial injury and acute renal failure.

Conflict of interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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