

## Review of Unusual Presentations of COVID-19

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### Abstract

The world has faced the coronavirus disease 2019 (COVID-19) pandemic since the H1N1 influenza pandemic in 1918. The symptoms of this disease are spreading rapidly and affect almost all systems of the body. In addition to the common symptoms of the virus, numerous reports of rare symptoms of the virus have also been published. These atypical presentations can result in difficulty in diagnosing the disease. The aim of this work is to summarize “uncommon atypical presentations”, which have not received enough attention in descriptions of the disease presentation to date and the authors specifically discuss the important uncommon atypical presentations of COVID-19.

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### Introduction

The world has faced the coronavirus disease 2019 (COVID-19) pandemic since the Spanish flu, also known as the 1918 flu pandemic, was an unusually deadly pandemic influenza caused by the H1N1 influenza A virus. On January 30<sup>th</sup>, 2020, the WHO declared the Chinese outbreak of COVID-19 to be a public health emergency of international concern posing a high risk to countries with vulnerable health systems (1). The outbreak of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was considered to have originally started via a zoonotic transmission associated with the seafood market in Wuhan, China. Later, it was recognized that human to

human transmission played a major role in the subsequent outbreak (1). Health systems have been challenged since the introduction of the coronavirus to the world from Wuhan, China. As with other pandemics, the symptoms of the disease were first identified (2). And the disease was first diagnosed with respiratory symptoms such as cough and shortness of breath. And the doctors' focus on recognizing and diagnosing patients with the disease was focused on these symptoms (3). The majority of cases have spontaneously resolved. However, some have developed various fatal complications including organ failure, septic shock, pulmonary edema, severe pneumonia,

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and acute respiratory distress syndrome (ARDS). Gradually, numerous reports from around the world pointed to other symptoms of the disease. In a meta-analysis reported by Tian et al., 17.6% of patients with coronavirus had gastrointestinal symptoms, including anorexia (26.8%), diarrhea (12.5%), nausea and vomiting (10%), and abdominal pain (9%) (4). Recently, new symptoms have been added, including changes in the sense of smell and taste. As mentioned, with the passage of time and a better understanding of this disease, the range of symptoms of this virus has greatly increased. And you can boldly compare the range of symptoms of this virus with tuberculosis. Among the most common symptoms ever reported are numerous reports

from around the world about the unusual symptoms of the virus. Unusual symptoms that became more pronounced after the patient became late due to late diagnosis. In this study, we review the case reports of unusual symptoms of the virus.

### Methods

In this review, we searched for all articles published in various databases including PubMed, Scopus, Embase, Science Direct and Web of Science using MeSH-compliant keywords including COVID-19, unusual symptoms, case report, Coronavirus 2019, SARS-CoV-2 and 2019-nCoV from December 2019 to March 25 2020 and then reviewed them.

**Table 1.** Unusual presentation of COVID-19 that reported in 10 studies

Study	Gender	Age (yr)	Unusual presentation	Initial manifestation	Study	Outcome
Hemasian et al. (2020) Iran(5)	Male	65	Cerebral venous thrombosis	Loss of consciousness, upward gaze and tongue biting	Case report	Alive
Packwood Et al (2020) USA(6)	Male	58	Meningitis symptoms and shingles	Headache and then progressed to a meningitis like illness with co-existing shingles rash	Case report	Alive
Mingxiang Et al (2020) China (3)	Male	30	Encephalitis	fever, shortness of breath, and myalgia	Case report	Alive
Devika(7)	Male	34	Heart brake	High-grade fevers, dry cough and shortness of breath	Case report	Alive
Parminder Et al(2020) USA(8)	Male	43	Acute limb Ischemia	Dyspnea and acute pain in his right leg	Case report	Died
Aydin et al(2020) Turkey (9)	Male	24	Pneumothorax	Fever, cough, shortness of breath and increased pain in the left hemithorax fever,	Case report	Alive
Davoodi et al(2020) Iran(10)	Female	57	Deep Vein Thrombosis	Pain, redness, and leg swelling	Case report	Alive
Siddamreddy,et al(2020) USA(11)	Female	61	Acute ST elevation myocardial infarction	Left-sided chest pain	Case report	Alive
Sarma et al (2020) USA(12)	Female	28	Acute Transverse Myelitis	Low back pain, myalgias, and rhinorrhea	Case report	Alive
Klein et al(2020) USA(13)	Male	46	Tremors and gait disturbance	Fever, generalized myalgias, sore throat	Case report	Alive

## Results

In this search, 10 articles were found on the rare symptoms of coronavirus. All articles were reviewed. Data and results were analyzed. In three studies, thrombotic events caused rare symptoms, including: cerebral venous thrombosis, acute limb ischemia, and deep vein thrombosis. In four studies, the involvement of the neurological system caused symptoms, including: meningitis symptoms and shingles, encephalitis, acute transverse myelitis, tremors and gait disturbance. In two studies, involvement of the cardiovascular system caused symptoms including: heart attack, acute myocardial infarction and in one study, lung involvement caused symptoms including: pneumothorax. These symptoms included the involvement of the cardiovascular system, the nervous system, and the pulmonary system. The data are provided in table 1.

## Discussion

COVID-19 is a new emerging virus infection that has become a global public health problem with a number of possible clinical presentations. COVID-19, the illness caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), presents similarly to other viral respiratory illnesses with common symptoms including fever, cough, fatigue, myalgias, and diarrhea (14). Some patients develop respiratory distress requiring supplemental oxygen or ventilator support, while others have mild cases without complications (15). As the number of COVID-19 infections continues to rise, more patients are presenting to the emergency department with novel coronavirus-related symptoms and associated complications (16). Healthcare workers, especially emergency providers on the frontlines, treat these affected patients and bear witness to their different presentations and clinical courses (4). Some might have non-respiratory clinical presentations. Those clinical presentations are called atypical

presentations, in the same way atypical presentations were observed in earlier coronavirus infections such as SARS CoV and MERS CoV. The practitioner might not recognize these atypical presentations resulting in missed or delayed diagnoses. An exaggerated immune response also may underlie atypical presentations in COVID-19 patients. Many patients who experience unusual symptoms exhibit a profound activation of their immune system. This response can produce a cytokine storm that can damage many organs, including the lungs, heart and brain. In some cases, an overactive immune system has been shown to trigger autoimmune conditions in COVID-19 patients about two to three weeks after infection (17). Such neurological autoimmune conditions include: Bickerstaff encephalitis/Guillain-Barré syndrome, acute disseminated encephalomyelitis and rhabdomyolysis (12). Review of articles reported on the rare symptoms of the virus showed that most of the involvement of the neurological and cardiovascular systems occurred. Possible pathophysiology is related to the virological structure of the virus (11). Virologic studies of SARS-CoV-2 and Middle Eastern respiratory syndrome coronavirus (MERS-CoV) have shown their ability to enter the brain and spread to specific areas such as the thalamus and brainstem, although the route of entry has yet to be elucidated (12). Given this, it is likely that SARS-CoV-2 has similar neuro-invasive potential. The most commonly documented atypical symptoms include malaise, disorientation or exhaustion. Moreover, a significant proportion of patients also experience the loss of smell and taste. Cardiovascular complications include dysrhythmias, venous thromboembolic events and myocardial infarction. COVID-19 also may cause clotting in blood vessels in the brain, increasing risk of ischemic stroke. The mechanisms are multifactorial but may include a hypercoagulable state with micro- and

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macro-circulatory thrombosis (8). The virus can bind to endothelial cells, damage the vessels and lead to platelet aggregation. The coagulation function is deranged. Clots in the small vessels of all organs were described (5). Finally, as discussed, coronavirus can affect all organs of the body by various mechanisms. Furthermore, it can have different symptoms. Knowing that the virus is capable of infecting all organs of the body can help in early diagnosis of patients in pandemics.

### Conclusion

Increasing the knowledge of the unusual ways COVID-19 presents may help ensure that patients get timely and appropriate treatment. It also may help promote the investigation of screening protocols and biomarkers of disease progression. By raising the awareness of atypical symptoms, we may also encourage health care workers to approach patients with a higher index of suspicion for SARS-CoV-2 infection, especially when symptoms are present without explanation.

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