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EMERGENCENCIES IN CORONAVIRUS DISEASE CAUSED BY COVID-19 VIRUS

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Abstract

In 2019, the new coronavirus was identified as the cause of a disease originating from the city of Wuhan in China, now known as SARS-CoV-2. The World Health Organization declared COVID-19 a pandemic in March 2020. Some people may have only a few symptoms or may not have any symptoms at all.

Some people may experience worsening symptoms, such as shortness of breath and pneumonia, about a week after the onset of symptoms, and some may experience systemic complications caused by COVID-19 infection. Many of these complications can be caused by a condition known as cytokine release syndrome or cytokine storm. Cytokines can significantly damage vital organ tissue, including the lungs, heart, and kidneys.

The pathology of coronavirus disease (COVID-19) is exacerbated by the progression of thrombosis, disseminated intravascular coagulation (DIC), and cytokine storm. Signs and symptoms of an emergency may include: difficulty breathing, rapid, shallow breathing, persistent chest pain or pressure, somnolence, confusion, collapse, pale, gray or blue skin, lips or nails - depending on skin tone. In hospitalized patients, constant monitoring and monitoring of parameters that may indicate a certain complication in the disease requiring prompt timely treatment, is necessary.

The following emergency conditions, complications in COVID-19 have been described in this paper: acute respiratory failure, ARDS, COVID-19 coagulopathy and DIC, septic shock, rhabdomyolysis, acute renal failure, acute hepatic failure, acute heart disease, myocarditis, MIS-C, emergency neurological diseases and spontaneous rectus sheath hematoma.

Keywords: emergencies in COVID-19, cytokine storm, COVID-19 coagulopathy, COVID-19 complications, multisystem inflammatory syndrome in children, MIS-C

Introduction

Coronaviruses are a family of viruses that can cause illnesses such as colds, severe acute respiratory syndrome (SARS), and Middle East Respiratory Syndrome (MERS). In 2019, the new coronavirus was identified as the cause of a disease originating from the city of Wuhan in China. The virus is now known as severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2).The disease it causes is called coronavirus disease 2019 (COVID-19). In March 2020, the World Health Organization (WHO) declared COVID-19 a pandemic.

Signs and symptoms of coronavirus disease COVID-19 may occur two to 14 days after exposure. This period after exposure and before the onset of symptoms is called the incubation period. Common signs and symptoms may include: fever, cough, fatigue. Early symptoms of COVID-19 may include loss of taste or smell. Other symptoms include: shortness of breath or difficulty breathing, muscle aches, fever, sore throat, runny nose, headache, chest pain, pink eye (conjunctivitis), nausea, vomiting, diarrhea, rash, etc. Children have similar symptoms to adults and usually have a mild illness.

The severity of COVID-19 symptoms can range from very mild to severe. Some people may have only a few symptoms, and some people may not have any symptoms at all. Some people may experience

worsening of symptoms, such as shortness of breath and pneumonia, about a week after the onset of symptoms, and some may experience systemic complications caused by Covid-19 infection. Many of these complications can be caused by a condition known as cytokine release syndrome or cytokine storm. This is when the infection activates the immune system to flood the bloodstream with inflammatory proteins called cytokines. They can significantly damage vital organ tissues, including the lungs, heart, and kidneys.

People who are older have a higher risk of serious illness from COVID-19, and the risk increases with age. People who have pre-existing medical conditions may also have a higher risk of serious illness.

Certain medical conditions that may increase the risk of serious COVID-19 disease include: serious heart disease, such as heart failure, coronary artery disease or cardiomyopathy, cancer, chronic obstructive pulmonary disease (COPD), asthma, type 1 or type 2 diabetes, overweight or obesity, high blood pressure, smoking, chronic kidney disease, sickle cell disease or thalassemia, weakened immune system from solid organ transplantation, pregnancy, chronic lung disease such as cystic fibrosis or pulmonary fibrosis, liver disease, dementia, Down syndrome, weakened immune system from bone marrow transplantation, HIV or some medications, brain and nervous system conditions, substance use disorders.

If there is a deterioration in the health condition, it is necessary to seek medical help immediately. Signs and symptoms of an emergency may include: trouble breathing (difficulty breathing, rapid, shallow breathing), persistent chest pain or pressure, somnolence, confusion, collapse, pale, gray or blue skin, lips or nails - depending on skin tone. Evaluation of vital signs will provide some initial information regarding a possible infection. A high fever may be present, but some patients develop only a low-grade fever when infected. Tachycardia can accompany a fever and may be present in the early stages of shock. Tachypnea can indicate the beginning of respiratory distress. In addition, a pulse oximeter can be used to catch a COVID-19 infection, as many patients have been found on initial assessment to be hypoxic[1].

The remainder of atypical physical exam on a COVID-19-infected patient may reveal increased work of breathing using accessory muscles, circumpolar cyanosis, and/or confusion from hypoxia. Lung sounds initially are unremarkable, but the patient can develop a mild expiratory wheeze. As the disease progresses, fine crackles can be heard, as in early pneumonia. Once a patient has developed acute respiratory distress syndrome (ARDS), rough breathing and diffuse rhonchi are heard. [2]

The physical exam will continue to evolve throughout the course of the illness. As an inpatient, repeat examinations will help to assess if the patient is progressing to a more critical state. Much of the physical exam, in the emergency department or during hospitalization, can be performed by merely observing the patient for outward signs of disease, i.e., increased work of breathing, retractions, tachypnea, and diaphoresis, in addition to the aforementioned evaluation of vital signs.

Complications of coronavirus disease are urgent life-threatening conditions requiring immediate treatment. Emergencies in COVID-19 infection are:

- Acute respiratory failure
- Acute Respiratory Distress Syndrome (ARDS)
- Covid-19 coagulopathy and disseminated intravascular coagulation
- Septic shock
- Rhabdomyolysis
- Acute renal failure
- Acute hepatic failure
- Acute heart disease, myocarditis
- Multisystem Inflammatory Syndrome in Children (MIS-C)
- Emergency neurological diseases (bleeding, cerebrovascular strokes)
- Bleeding in the abdominal wall (spontaneous rectus sheath hematoma), intra-abdominal, retroperitoneal bleeding in COVID-19 patients

Purpose

Presenting the emergencies in COVID-19 in this review article increases the skills of every professional to recognize them and emphasizes the importance of collaboration and communication among the interprofessional team in enhancing treatment and care coordination of COVID-19 patients.

Acute respiratory failure

Acute respiratory failure is a condition in which fluid accumulates in the alveoli of the lungs with the inability to release an adequate amount of oxygen into the blood due to impaired gas exchange between the capillaries and alveoli and consequently, tissue hypoxia occurs. The symptoms of acute respiratory failure depend on its underlying cause and the levels of carbon dioxide and oxygen in the blood. People with high levels of carbon dioxide have symptoms of rapid breathing and confusion. People with low oxygen levels have shortness of breath, blue skin, fingertips or lips.

People with acute lung failure and low oxygen levels present with these symptoms: restlessness, anxiety, drowsiness, loss of consciousness, rapid and shallow breathing, rapid heartbeat, arrhythmias, profuse sweating. The diagnosis is confirmed on the basis of medical history, physical examination, pulse oximetry, chest X-ray, gas analysis. In addition to antibiotic, antiviral, anti-inflammatory, anti-aggregation, and other supportive and symptomatic therapy given according to laboratory findings, physical examination according to WHO guidelines, oxygen support plays the main role in the treatment. Treatment consists of analgesic therapy that will help improve breathing.

Depending on the degree of hypoxia, oxygen therapy is administered with a face mask, nasal canila or, if necessary, the patient is placed on a mechanical ventilator with a mask or tube.

Some individuals who catch the new coronavirus have severe pneumonia in both lungs. COVID-19 pneumonia is a serious disease that can be fatal. When pneumonia is present, the air sacs in the lungs become inflamed, causing difficulties in breathing.

Scientists who have studied the lung images of many sick patients with COVID-19 have found that they are full of fluid, pus and cell debris. In those cases, patients' bodies are unable to carry oxygen to the bloodstream to maintain their systems properly [3,4].

Acute Respiratory Distress Syndrome (ARDS)

COVID-19 can cause lung complications such as pneumonia and, in the most severe cases, acute respiratory distress syndrome (ARDS). Sepsis, another possible complication of COVID-19, can also cause lasting harm to the lungs and other organs.[5]

ARDS is a severe condition of the lungs. It occurs when fluid fills the alveoli in the lungs. Th the formation of a hyaline membrane in the alveoli in the acute phase is followed by interstitial dilation and edema and by proliferation of fibroblasts in the organizing phase. Too much fluid in the alveoli can reduce the amount of oxygen or increase the amount of carbon dioxide in the bloodstream. ARDS leads to tissue hypoxia and can eventually cause organ failure. Lung fibrosis occurs as part of COVID- 19 ARDS. Fibrous lesions may form during the healing of chronic pulmonary inflammation or proliferative disease, with gradual replacement of cellular components by scar tissue. ARDS most commonly occurs in hospitalized people who are very ill.

Symptoms usually appear within one to three days of the initial illness in the form of extreme shortness of breath and hunger for air. ARDS is an emergency and potentially life-threatening condition. Common symptoms and signs of ARDS include: shortness of breath, muscle fatigue and general weakness, low blood pressure, rapid pulse, discoloration of the skin or nails, dry irritating cough, fever, headache, mental confusion. Diagnosis is based on medical history, physical examination, blood tests, X-ray, CT scan, pulse oximetry, gas analysis. ECG monitoring, blood pressure, ultrasound.

Treatment consists of oxygen support with mask (high-flow), nasal cannula or mechanical ventilation (prone ventilation - proven method), infusion therapy, drug therapy with analgesics, antibiotics and anticoagulants, corticosteroids, antiviral drugs + antiviral drugs + 1b or ramdesivir [4,6].

COVID-19 coagulopathy and disseminated intravascular coagulation

The pathology of coronavirus disease is exacerbated by the progression of thrombosis, disseminated intravascular coagulation (DIC), and cytokine storm. COVID-19 thrombosis involves macro- and microthrombosis, with the diagnosis of the latter depending on the markers of coagulation and fibrinolysis. Therefore, the treatment of COVID-19 is supplemented with the treatment of thrombosis. In severe COVID-19 infections, systemic levels of proinflammatory cytokines, such as tumor necrosis factor-α (TNF-α) and interleukin (IL) -1 and IL-6, are markedly elevated. IL-6 induces tissue factor expression of monocytes and macrophages, which in turn leads to thrombin generation.

A cytokine "storm" characterized by high levels of proinflammatory cytokines and chemokines can be detected in a subset of the most severely affected patients with COVID-19. Coronavirus infections are associated with a remarkable fibrinolytic profile. In patients with SARS-CoV-1 infection, the plasma concentration of tissue-type plasminogen activator (t-PA) was six-fold higher than normal.

Inflammation-induced endothelial cell disruption is likely to result in significant release of plasminogen activators that explains high d-dimer levels in the most severely affected patients with COVID-19. Also, the effects of plasmin on metalloproteinases may result in extracellular matrix modification, accelerating capillary leakage, and pulmonary edema.

There is a significant link between bronchoalveolar coagulation and fibrinolysis and the development of acute respiratory distress syndrome (ARDS), in which intrapulmonary fibrin deposition due to impaired bronchoalveolar fibrin circulation is a critical step.

The coagulation changes associated with COVID-19 infection lead to a hypercoagulable state that may at least cause an increased risk of thromboembolic complications. Immobilization and vascular damage are other factors that may increase the risk of thrombosis. It appears that there are two parallel clinical manifestations of COVID-19 coagulopathy: (1) 'classic' venous thromboembolism (probably provoked by cytokine-mediated activation in combination with other thrombosis risk factors) and (2) diffuse microthrombosis with endothelial damage (in the lungs) directly caused by the coronavirus [7]. Monitoring D-dimer level, prothrombin time, platelet count and fibrinogen content is important for determining indications for treatment and hospitalization in COVID-19 patients.

In case such parameters deteriorate, a more proactive "aggressive" intensive care should be applied. Low molecular weight heparin (LMWH) should be administered to all patients with diagnosed COVID-19 infection (including non-critical patients) requiring hospitalization, but having no contraindications to LMWH [8].

The combination of increased D-dimers, low platelet count, and (slightly) prolonged clotting time (such as PT) is reminiscent of the abnormalities most commonly seen in DIC. However, there are significant differences between COVID-19 coagulopathy and DIC most commonly seen in patients with severe infections and sepsis. Severe thrombocytopenia is usually seen in DIC associated with sepsis. Also, these patients usually have much lower levels of clotting factors and marked decreased plasma concentrations of coagulation inhibitors such as antithrombin and protein C.

The clinical manifestation of COVID-19 coagulopathy is prethrombotic in the absence of coagulopathy and true consumption, with a high rate of venous (and possibly arterial) thromboembolism and not very haemorrhagic complications. Based on all this, COVID-19 cannot be classified as a common manifestation of DIC and should be categorized as a specific form of intravascular coagulation syndrome that may require new diagnostic criteria.

Also, the (additional) therapeutic interventions to be tested for this coagulopathy should take this difference into account, moreover because there is currently no specific therapy for the most common forms of DIC.[9]

Septic shock

Most patients infected with SARS-Cov-2 in intensive care show an unregulated host response characterized by hyperinflammation, changes in coagulation, and impaired regulation of the immune response that further contribute to multiorgan failure, as occurs in sepsis. Patients with COVID-19 who

have a septic condition have a changed mental state, dyspnea, oliguria, tachycardia, weakened pulse and cold extremities, features that are also found in patients with septic shock.

These symptoms are probably caused by low blood pressure and hypercoagulation with direct and indirect action of SARS-Cov-2. In addition, thrombocytopenia and high lactates (serum lactate levels > 2 mmol / L) have also been reported in most of these patients, which are clinical manifestations of septic shock. Peripheral vasoconstriction and DIC are typical features of septic patients [10].

Rhabdomyolysis

Rhabdomyolysis is the breakdown of skeletal muscle myocytes and the release of intracellular contents. Because of this, rhabdomyolysis is characterized by elevated levels of CK, myoglobin, potassium, LDH, urate, and ALT. Rhabdomyolysis can be a potentially life-threatening condition due to complications caused by the release of excess amounts of these intracellular contents.

Rhabdomyolysis can cause renal injury when the release of myoglobin exceeds the protein-binding capacity and excess pigment is precipitated in the glomeruli. Hyperkalemia, acute renal failure, metabolic acidosis, disseminated intravascular coagulation, arrhythmias, and cardiac arrest are potential complications of rhabdomyolysis.

Immune mechanisms play an important role in muscle damage by cross-reactivity between the virus and myocytes. Direct invasion of myocytes as well as other viral diseases may be the other mechanism. Excessive immune response resulting in a cytokine storm can lead to muscle damage. Some viral myositis may be damaged by T-cell-led myocytes.

Rhabdomyolysis is treated by aggressively replenishing intravascular volume and resolving the causative agent. Infusion therapy should be titrated according to urinary output. Administration of mannitol and bicarbonate may be necessary for certain patients. Electrolyte and metabolic abnormalities need to be corrected. Several patients may need dialysis due to persistent acidosis or life-threatening potassium levels or oliguric renal failure.

Rhabdomyolysis may be the initial extrapulmonary manifestation of COVID-19, with very few cases described in the literature to date. It is crucial to increase CK levels in initial screening laboratories while assessing suspected COVID-19 infection with myalgias and generalized weakness, which helps prevent acute renal failure[11].

Acute renal failure / Acute kidney injury (AKI)

Hypovolemia and dehydration are common causes of AKI in patients with KOVID-19. Those who develop AKI during hospitalization exhibit worse prognostic factors in terms of pulmonary impairment, renal impairment, and analytical findings.

The etiology may be prerenal, acute tubular necrosis in the context of sepsis, glomerular, and tubular toxicity. Patients develop proteinuria and hematuria. How does the coronavirus damage the kidneys? The virus itself infects kidney cells. Kidney cells have receptors that allow the new coronavirus to attach to them, attack and make copies of themselves, potentially damaging those tissues. Similar receptors are found in the cells of the lungs and heart, where the new coronavirus has been shown to cause injury.

Another possibility is that kidney problems in patients with coronavirus are due to abnormally low levels of oxygen in the blood, the result of pneumonia, which is most commonly seen in severe cases of the disease. Other contributors to AKI might include rhabdomyolysis, macrophage activation syndrome, and the development of microemboli and microthrombi in the context of hypercoagulability and endotheliitis [12].

The immune response to the new coronavirus can be extreme in some people, leading to what is called a cytokine storm. When this happens, the immune system sends a surge of cytokines into the body. Cytokines are small proteins that help cells communicate while the immune system fights infection. But this sudden, large influx of cytokines can cause severe inflammation. In an attempt to kill the invading virus, this inflammatory reaction can destroy healthy tissue, including the kidneys. COVID-19 can cause

formation of small clots in the bloodstream, which can clog the smallest blood vessels in the kidney and impair its function [13].

Patients who develop AKI during their hospital stay have higher CRP, LDH and d-dimers, more severe lung damage, elevated degradation products, and often require renal replacement therapy in addition to prescribed therapy. Dialysis may be needed until the kidneys return to normal function. But sometimes, people get chronic kidney disease, which needs to be treated in the long run [14].

Acute hepatic failure

Gastrointestinal/hepatic effects such as diarrhea, nausea, vomiting, and elevated liver enzymes have also been reported. Previous studies and data on coronavirus infections from China, Singapore and other countries have shown that elevations in liver enzymes can be seen in 20-50% of cases. Severe diseases may be associated with deterioration of liver enzymes. Studies show that the most seriously ill patients have the highest risk of liver damage. Acute liver injury and liver failure are life-threatening complications [15].

Acute heart disease, myocarditis

Patients with COVID-19 have a significant incidence of acute heart failure, which is associated with a very high mortality rate. In addition, patients with a history of chronic heart failure are prone to develop acute decompensation after COVID-19 infection.

Because cytokine storm is also the major pathophysiological mechanism of fulminant myocarditis, COVID-19 heart damage should be considered, especially if there are symptoms of angina pectoris in the absence of respiratory symptoms.

Coronavirus-associated myocarditis in humans is known, and a number of cases of coronavirus-associated myocarditis (COVID-19) have been reported. The pathophysiology of COVID-19-associated myocarditis is thought to be a combination of direct viral injury and heart damage due to the host immune response.

Clinical findings include changes in the electrocardiogram and biomarkers of the heart and impaired cardiac function. The pathology is usually focused in the myocardium, but there is a risk of arrhythmia as well as progression to fulminant heart failure and cardiogenic shock. Coronary angiography, cardiac ultrasonography and ECG of the heart may be used to rule out severe coronary artery disease and to identify myocardial inflammatory patterns.

A large number of patients with COVID-19 have cardiovascular comorbidities, hence, myocardial infarction is more likely to occur in a COVID-19 patient. The clinical presentation of SARS-Cov-2 myocarditis varies between cases. Some patients may present with relatively mild symptoms, such as fatigue and dyspnea, while others report chest pain or chest tightness on exertion.

The condition in many patients can worsen, showing symptoms of tachycardia and acute heart failure with cardiogenic shock. In this severe form, patients may also present with signs of right heart failure, including increased jugular venous pressure, peripheral edema, and pain in the upper right quadrant of ventricular dysfunction and heart failure within 2 to 3 weeks of infection with the virus. The early signs of fulminant myocarditis usually resemble those of sepsis: the patient is often febrile with low pulse pressure, cold or variegated limbs, and sinus tachycardia.

Blood test results in patients with myocarditis often show elevated levels of lactate and other inflammatory markers, including CRP, erythrocyte sedimentation rate, and procalcitonin, which usually rise according to the clinical picture of infection. It is important to distinguish fulminant myocarditis from sepsis because fluid resuscitation, a common sepsis protocol, exacerbates fulminant myocarditis with fluid overload. Laboratory tests of essential cardiac enzymes (troponin and N-terminal pro-B type natriuretic peptide [NT-proBNP]) are performed on admission to the hospital. Cardiac troponin I (cTnI), cardiac troponin T (cTnT), NT-level proBNP and BNP are usually elevated in myocarditis due to acute myocardial injury and possible ventricular dilatation. Elevated levels of troponin and NT-proBNP have been reported in cases of COVID-19-associated myocarditis.

Although a negative troponin test cannot rule out myocarditis, especially for atypical forms such as giant cell myocarditis or those in the chronic phase, high-sensitivity serial negative cardiac troponin still aids in diagnosis in the acute phase. In patients with COVID-19, (NT-pro) BNP levels may also increase secondary to myocardial stress, a possible effect of serious respiratory disease [16,17].

Electrocardiogram (ECG) abnormalities commonly seen with pericarditis, such as elevated ST and PR depression, may be seen in myocarditis; however, these findings are not sensitive to disease detection and their absence is not exclusive. Other ECG abnormalities, including onset of branch block, QT prolongation, pseudoinfarction pattern, premature ventricular contractions, and bradyarrhythmia with advanced atrioventricular nodal block, may be seen in myocarditis.

While there is a paucity of literature detailing COVID-19-related arrhythmogenic complications, there are reports of ventricular tachycardia and ventricular fibrillation as late manifestations of COVID-19. An early case series from China reported a 16.7% incidence of arrhythmia, but the cause or type was not specified. The incidence of ACS increases in the setting of viral infection, probably due to inflammation-mediated plaque destabilization. The risk in the setting of COVID-19 infection is unknown, but other viruses are associated with a 3- to 10-fold increased risk [18,19].

One expert analysis published by the American College of Cardiology explains the drug treatment and use of the most commonly used drugs, their dosage and effect on pericarditis in COVID-19 patients (Table 1).

Table 1: Current Treatments for Pericarditis and COVID-19 Infection [19]

Drug	**Attack dose**	**Duration**	**LOE**	**Effect on COVID-19***
NSAIDs	**Aspirin** 750-1000 mg x 3/day **Ibuprofen** 600-800 mg x 3/day **Indomethacin** 25-50 mg x 3/day	1-2 weeks but until symptoms resolution and CRP normalization	A	Harmful (?)
Colchicine	0.5 mg x 2/day (0.5 mg7day if <70 kg)	3 months (acute) 6 months (recurrent)	A	Potential therapy
Corticosteroid	0.2 to 0.5 mg/kg/day of prednisone	Up to 1 month	B	Therapy for advanced cases
Azathioprine	Up to 2 mg/kg	> 6 months	B	Unknown
NHIG	400 to 500 mg/kg/day	5 days (can be repeated after 1 month)	B	Potential therapy
Anakinra	2 mg/kg/day up to 100mg/day	3-6 months then tapered	B	Potential therapy

NSAID = non-steroidal anti-inflammatory drugs; NHIG = normal human immunoglobulins; LOE = level of evidence for pericarditis: A for multiple RCTs or metanalyses, B for a single RCT or observational studies, C for experts consensus; CRP = C-reactive protein,*= current knowledge on the effect for COVID-19 infection, for corticosteroids and anakinra dosing for severe cases with COVID-19 is higher and intravenous: e.g., methylprednisolone 1 mg/kg/day IvGTT for 7 days; anakinra IV infusion 4 times daily for 15 days, 400 mg/day in total, divided into 4 doses given every 6 hours.

Multisystem Inflammatory Syndrome in Children (MIS-C)

Multisystem Inflammatory Syndrome in Children (MIS-C) is a serious condition associated with COVID-19 disease. Most children who become infected with the COVID-19 virus have only a mild illness. However, children who develop MIS-C develop severe inflammation and damage to the heart, lungs, blood vessels, kidneys, digestive system, brain, skin, or eyes.

This new and serious syndrome is also rare in adults, called multisystem inflammatory syndrome in adults (MIS-A) and occurs in adults who have previously been infected with the COVID-19 virus and many were unaware of it. MIS-A appears to occur several weeks after infection with COVID-19, although some people have an immediate infection. If MIS-A is suspected, a COVID-19 antibody test may help confirm current or past infection with the virus, which helps diagnose MIS-A.

Most children with MIS-C are 3 to 12 years old, with an average age of 8 years. But there are cases in older children and babies. Symptoms of MIS-C appear between two and six weeks (average four weeks) after infection with COVID-19. Most children with MIS-C have antibodies to the SARS-Cov-2 virus. The symptoms of the disease are similar to those of toxic shock syndrome or Kawasaki disease, which causes inflammation of the blood vessels in children. MIS-C is an inflammatory disease resulting from an overactive immune response.

High prevalence of mucocutaneous manifestations, in addition to gastrointestinal and cardiovascular complications, are found in MIS-C. Symptoms that indicate MIS-C are: fever lasting 24 hours or longer, vomiting, diarrhea, abdominal pain, macular and/or papular or polymorphic skin rash, unusual tiredness, tachycardia, tachypnea, red eyes, redness or swelling of the lips and tongue, redness or swelling of the arms or legs, headache or dizziness, enlarged lymph nodes. MIS-C warning signs that require urgent medical treatment are: severe abdominal pain, shortness of breath, persistent pain or chest tightness, pale, gray or blue skin, lips or fingernails, confusion, somnolence, inability to wake up or stay awake.

Treatment uses drugs such as intravenous immunoglobulins, steroids, and other anti-inflammatory drugs to reduce inflammation and protect the heart, kidneys, and other organs from permanent damage. Without early diagnosis and proper management and treatment, MIS-C can lead to serious problems with vital organs, such as the heart, lungs, or kidneys. In rare cases, MIS-C can result in permanent organ damage or death [20-22].

Emergency neurological diseases (bleeding, cerebrovascular strokes)

SARS-CoV-2 infection is associated with many neurological complications and the presence of neurological symptoms appears to be quite common, occurring in 84% of those with a more severe form of the disease. The majority of acute cerebrovascular diseases associated with COVID-19 infection are acute ischemic stroke, intracerebral hemorrhage, venous sinus thrombosis, posterior reversible encephalopathy (PRES), reversible cerebellar infarction syndrome, and cerebellar vasculitis.

Neurological complications of COVID-19 are divided into acute and chronic. Acute complications include: encephalopathy, myalgia, loss or disturbance of the sense of smell and taste, headache, cerebrovascular complications, epilepsy, meningoencephalitis, cranial and peripheral neuropathies, myoclonus, movement disorders, psychosis.

Parainfectious and postinfectious complications include: acute disseminated encephalomyelitis, acute necrotizing hemorrhagic encephalopathy, autoimmune (steroid-responsive) encephalopathy, myositis, critical illness without neuromyopathy, Gulenin's disease, Guillain-Barre syndrome.

COVID-19-associated cerebrovascular disease is more severe with poorer functional outcomes and higher mortality than non-COVID-19-associated cerebrovascular disease. Intracerebral hemorrhage is less common in patients with COVID-19 than in acute ischemic stroke.

Several reports in the spring of 2020 in the United States noted that bleeding occurred predominantly in hospitalized patients with anticoagulation, often prescribed for elevated d-dimer levels. Other risk factors associated with intracerebral hemorrhage include prolonged INR and partial thromboplastin time regardless of anticoagulation use, thrombocytopenia, older age, and mechanical ventilation. Several mechanisms may lead to ischemic stroke in patients with COVID-19.

One of the most widely accepted hypotheses is that SARS-CoV-2 causes endothelial cell damage, leading to activation of inflammatory and thrombotic pathways, microvascular and macrovascular injury, and eventually coagulopathy similar to that observed in sepsis, characterized by enlarged thromboplastin time, elevated d-dimer levels, and sometimes thrombocytopenia. Some studies have also noted a high prevalence of antiphospholipid antibodies in critically ill patients with COVID-19. SARS-CoV-2 can also cause a hyperinflammatory condition and a cytokine storm similar to that seen in hemophagocytic lymphohistiocytosis.

Other researchers have suggested a possible direct endothelial invasion and replication of the arterial wall, a process previously described in the varicella zoster virus. In addition, there is a congenital risk of stroke including destabilization of atherosclerotic plaque, activation of atrial fibrillation or increased thrombus formation in conditions of hypoxia.

For patients with acute ischemic stroke who do not meet the criteria for intervention with intravenous tissue plasminogen activator (tPA) or mechanical thrombectomy, the priorities generally shift to follow-up monitoring of clinical progression as well as treatment of potential preoperative measures. There is limited data on whether this specific patient population is at an increased risk of clinically significant hemorrhagic transformation compared to the general population, altering the risk-benefit ratio [23].

Bleeding in the abdominal wall (spontaneous rectus sheath hematoma), intra-abdominal, retroperitoneal bleeding in COVID-19 patients

If COVID-19 patients treated with anticoagulant therapy develop acute abdominal pain with pre-existing palpable tenderness, the possibility of abdominal flushing should be considered.

The upper epigastric artery lies deep in the muscle *m. rectus abdominis* and continues to perforate and supply the rectus sheath. Sudden and violent contraction of *m. rectus abdominis* can cause tearing of the epigastric arteries. Rectal sheath hematoma (RSH) is a rare complication seen in patients with acute abdominal pain with mass present in the abdominal wall that may result from several cases, mainly from the use of anticoagulants and/or anti-aggregating drugs for a variety of reasons. Endothelial dysfunction, thrombosis, and unregulated inflammation are the causes of vascular disease in patients with SARS-Cov-2. For this reason, low molecular weight heparin (LMWH) anticoagulant therapy has become part of the medical therapy in hospitalized patients with COVID-19.

This approach may increase the risk of spontaneous bleeding, especially in elderly patients with comorbidities, which underscores the importance of active monitoring of spontaneous bleeding, which requires the active involvement of medical staff in that emergency. On physical examination, patients with RSH will show a hard, tense abdominal wall along the rectal sheath with a palpable abdominal mass. Hypotension and tachycardia may also be seen in patients with hemodynamically unstable RSH.

Physical examination should distinguish between intra-abdominal bleeding and abdominal wall bleeding. Carnett's sign is one such test in which increased or unchanged sensitivity to abdominal muscle tension suggests probable pathology of the abdominal wall. CT findings are used to classify RSH into three types: mild, moderate, and severe. Type 1 is mild and does not require hospitalization, while type 3, typically associated with anticoagulation, is severe and requires transfusion, hospitalization and hemodynamic stabilization.

As with all cases of bleeding, monitoring the hematocrit level is essential to determine if a transfusion is needed. The hematocrit level in patients with RSH varies with severity, with normal values

in small RSH to large decreases in hematocrit level reported in cases of high RSH. Most cases of RSH are self-limiting and can be successfully treated without the need for invasive surgery. Recovery from RSH can take between 2 and 3 months and most patients recover without complications.

Mortality rates are estimated to be 4%, but rates as high as 25% have been reported in patients on anticoagulation therapy.

Angioembolization is the most desirable intervention when persistent bleeding is observed. Patients receiving oral anticoagulation must be monitored for coagulation factors, and treatment may include either discontinuation of anticoagulation therapy or anticoagulant reversal [24,25].

Conclusion

Coronavirus disease COVID-19 can occur individually in mild, moderate, and severe forms depending on the immune status of the patient, age, and comorbidities. The severity of COVID-19 symptoms can range from very mild to severe. Some people may have only a few symptoms, and some people may not have any symptoms at all.

Some people may experience worsening symptoms about a week after the onset of symptoms, and some may experience systemic complications caused by COVID-19 infection. Therefore, it is necessary to constantly monitor the medical condition of patients, monitor their vital parameters, repeat physical examination and laboratory tests and timely administer adequate therapy in accordance with WHO protocols.

Because the condition often worsens suddenly, it is necessary to educate patients to visit a doctor on time in order to receive adequate therapy not allowing the disease to get worse. In hospitalized patients, constant monitoring and monitoring of parameters that may indicate complications of the disease, is required. In children, but also in some adults, there may be an immune response to the disease and inflammation of the blood vessels throughout the body that show symptoms similar to those of toxic shock syndrome and Kawasaki disease.

Emergencies in COVID-19 are increasing. This paper has presented and described those that we encounter in our work so far. It is necessary they are to be recognized and treated in a timely manner.

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