The cascade of multiorgan dysfunction in COVID 19 patients. A case presentation

Dr. Sc. Migena QATO
Infectious Disease Department,
University Hospital Centre "Mother Theresa", Tirana

Prof. Dr. Najada COMO
Infectious Disease Department,
University Hospital Centre "Mother Theresa", Tirana

Dr. Sc. Esmeralda META
Infectious Disease Department,
University Hospital Centre "Mother Theresa", Tirana

Msc. Afrim YZEIRI
Infectious Disease Department,
University Hospital Centre "Mother Theresa", Tirana

Prof. Asoc. Dr. Albana GJYZELI
Nephrology Service,
University Hospital Centre "Mother Theresa", Tirana

Abstract

Introduction: *The SARS COV 2 epidemic has caused thousands of deaths due to different mechanisms of organ injury, starting from the respiratory and cardiovascular system and followed with significant involvement of kidneys, liver, pancreas and several metabolic dysfunctions which all caused a rapid progression of disease*

leading to death within the second week of hospitalization. ***Method:*** *We present the case of a 67-year-old woman who died within 24 hours of admission due to a rapid deterioration of her clinical condition with several successive complications. Results: The patient developed a fulminant clinical course, starting with flu-like prodromal symptoms proceeding to altered mental status, metabolic acidosis, acute respiratory distress syndrome (ARDS) and renal failure within 3 days. The rapid involvement of several vital organs predicted a poor diagnosis since the first evaluation in admission which resulted to be irreversible.* ***Conclusion****: The predictors of poor prognosis and severity may help clinicians to apply therapeutic regimens in order to avoid disease progression to multiorgan damage and potentially death.*

Key word*: Covid 19, multi organ dysfunction, cascade, case report*

Introduction

The SARS COV2 infection manifested a rapid spread throughout the world, quickly reaching the proportions of a pandemic. Although in its beginnings, this disease managed to demonstrate two characteristics almost immediately: the high contagiousness but also the various complications which were fatal in a significant percentage of infected patients. Even today, in addition to the low number of cases with COVID 19, the complications associated with it are present and still potentially lethal. Apart from the fact that COVID-19 is conventionally accepted and conceptualized as a respiratory disease, clinical reports suggest that severe cases reflect an overlap of the phenomena of vascular dysfunction, thrombosis and cascade and cytokine storm. The most common complications include pneumonia, Respiratory failure, acute respiratory distress syndrome (ARDS), sepsis and septic shock, cardiomyopathies, acute renal failure, pulmonary thromboembolism.

Method

A 67-year-old female presented to the Emergency Room of Infectious Disease Hospital with dyspnea, fever and altered mental status. In her medical information form was evidenced that the symptoms had started 3 days ago and had rapidly and progressively worsened. In admission the vital signs evidenced temperature 97.9 F^{o}, blood pressure 135/98 mmHg, respiratory rate 35 per minute, heart rate 89 beats per minute and oxygen saturation 90% on oxygen therapy. The nasopharyngeal swab for COVID-19 polymerase chain reaction (PCR) testing was collected. Immediately after hospitalization, the patient was placed in the Intensive Care Unit

with worsening hypoxia, saturating up to 85% on fifteen liters with facial mask; the mental status was further altered, bradycardia with a heart rate of 46 beats per minute, and hypotension not responsive to fluid boluses requiring thus vasopressor therapy and emergent intubation. The initial blood work revealed presence of hemolytic anemia (RBC 2.700.000 Hgb 7.8 Reticulocite 9% , Indirect bilirubine 5.7 mg/dl) acute kidney failure (creatinine 6.71) acute pancreatitis (amylasemia 1785 U/L) and other metabolic derangements showing elevated potassium 6.1 mmol/L, glucose 375 mg/dl, C-reactive protein 23,6 mg/dl, alkaline phosphatase 121 U/L, lactate dehydrogenase 1640 U/L aspartate aminotransferase 157 U/L, alanine aminotransferase 202 U/L, white blood cells 27.1 K/UL, lactic acid 6.2 mmol/L, D-Dimer 8.74 mg/L and severe acidosis with bicarbonate of 11 mmol/L, anion gap 18, arterial blood gas pH 7.21, partial pressure of carbon dioxide (PaCO2) 48, partial pressure of oxygen (PaO2) 61 on fifteen liters via facial mask . Computer tomography (CT) of the head was negative for acute process. Meantime the chest showed bilateral ground glass infiltrates and the abdomen computer tomography showed diffuse enlargement of the pancreas with irregular contour of the margins of the pancreas.

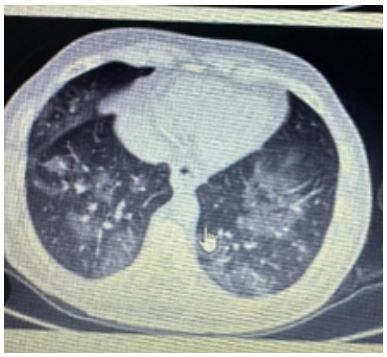

FIGURE 1

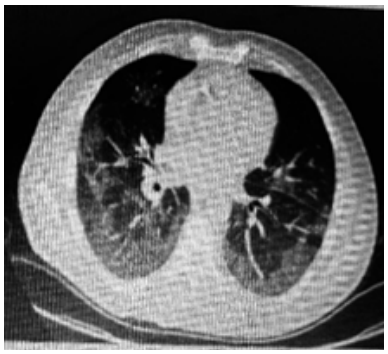

FIGURE 2

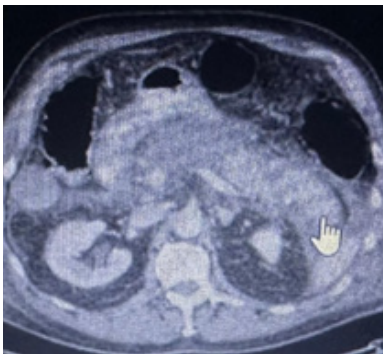

FIGURE 3

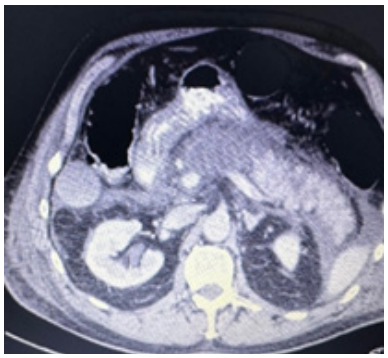

FIGURE 4

The follow-up biological examinations evidenced significant hyperkalemia 6.6 mmol/L, further aggravation of renal function with creatinine value of 7.19 mg/dl followed by metabolic acidosis with a lactic acid of 11.4 mmol/L and a hemogas analysis showing: pH 7.02, $PaCO_2$ 62, PaO_2 34 , bicarbonate 10 mmol/L).

After 27 hours of hospitalization the patient manifests extreme bradycardia, followed almost immediately by a cardiac arrest. The patient was assisted immediately by applying CPR (Cardio Pulmonary Resuscitation) but the return of vital signs was not achieved and exitus letalis was confirmed by Intensive Care medical staff.

Discussion

Looking back to one of the most important pandemic ,epidemiologically speaking, the COVID-19 pandemic, several retrospective studies worldwide tend to identify and highlight different predictive risk factors associated with disease severity and mortality .[1,2,3] The time frame of clinical and laboratory deterioration varies depending on the specific clinical and anamnestic features of the patient; on average major part of patients manifested complications like sepsis during the first 10 days of hospitalization and died during then third week of hospitalization .[5,6,7,8] The group of patients which manifested a poor prognosis and rapid deterioration were first presented to Primary Health Care services with symptoms that varies from mild to moderate ,such as productive cough, fever and dyspnea followed by a rapid worsening of the clinical course with severe ARDS ,followed by multiple organ dysfunction. The underlying process that could be explain these complications is the cytokine storm. The most relevant complications associated to this process are cardiac complications, acute renal failure (ARF) and metabolic decompesation.[4] Our patient manifested a rapid onset of septic shock, hemolytic anemia ,acute pancreatitis and acute renal failure. Consecutive hemogas analyses showed severe metabolic acidosis and ARDS which led to a fatal outcome in less than 72 hours of symptomatology and less than 30 hours of hospitalisation. Beside the cytokine storm associated to COVID 19, the extensive microvascular thrombosis also is now well described in patients with COVID-19 and may explain the severe multi- organ dysfunction .[9,10,11,12,13,]

One of these disfunctions is AIHA which is a relatively rare condition with an estimated incidence of 13/100,000 persons per year. Nevertheless, there is a progressive increase in the number of cases with hemolytic anemia, mainly correlated with the development of auto-Antibodies in the setting of COVID-19 . Given the known risk of thrombosis in patients with cold agglutinin hemolytic anemia, Maslov et al. (2020) speculated that this might contribute to thrombosis and the unfavorable outcomes in COVID-19 patients. [14] Appart from the COVID

19 pathogenesis, the hemolysis of RBCs can also be associated to morphologic and functional impairment due to virus infection. In case of co-morbidities such as hemoglobinopathies or other forms of inherited anemias ,this impairment can lead to poor prognosis.

Acute Renal Failure (ARF) is evidenced as one of the common complications of SARS COV2 infection and associated with in-hospital mortality. It can be present in almost 20% of patients with severe clinical conditions and manifested within the first week of hospitalization. It is important to highlight, in the first place, the coexistence between the acute renal precipitation and the septic shock which a major part of patients develop. The renal dysfunction thus may be related to sepsis pathogenesis, starting from hypoperfusion, acute tubular necrosis (ATN), microvascular thrombosis, or direct injury. Acute renal failure pathogenesis, in terms of COVID 19 infection involves the presence of angiotensin-converting enzyme (ACE) 2 receptors, and the high affinity that SARS-Cov-2 has towards these receptors. Some patients may also have an upregulation of these receptors, which explains the earlier or later onset of renal dysfunction[15,16,17]

Acute pancreatitis is another important complication due to SARS COV2 infection, despite its low incidence. The pancreatic dysfunction can be related to a direct cytopathic effect of SARS-CoV-2 virus on pancreatic cells (ACE 2 receptors are present in both exocrine glands and islets of pancreas) or can be mediated by a systemic immunological response to SARS-CoV-2 infection. [18,19,20]

The perfectly calculated regimen of critically ill patients with precipitation of multiorgan failure remains a challenge. Meanwhile, it is of vital importance that supportive and standard ICU protocols are followed, including fluid resuscitation combined with diuretics .Considering Acute Renal Failure as one of the most severe and potentially lethal complication, hemodialysis process has been a crucial part of intensive therapy. In several cases the continuous renal replacement therapy (CRRT) was shown to improve prognosis.

Recommendations

Multi organ disfunction in specific cases with SARS COV 2 infection is clearly related to several mechanisms which are already recognized, and respective therapeutic regimen and strategies have been formulated.

Identifying predictors of severity and mortality may help clinicians to apply therapeutic regimens in order to avoid disease progression to multiorgan damage, and ultimately death. One of those strategies may be early hemodialysis. Our patient obviously had strong indication to go under hemodialysis, but given the fulminant multiorgan failure, she was not able to tolerate the process. As a consequence, the fatal outcome was inevitable.

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