



Research Article

First Case of Pseudomembranous Colitis in a Sars-Cov-2 Patient with Chronic Cerebral Vasculopathy: A Rare Multiple Organ Involvement in the Covid-19 Era

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Background

In December 2019, an outbreak of pneumonia of unknown cause in Wuhan, Hubei province, China led to the identification of a new betacoronavirus, called Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) [1]. The SARS-CoV-2 pandemic has already infected more than 114 million people worldwide and resulted in 2.6 million deaths. Recent reports suggest that though originally described as a respiratory virus, SARS-CoV-2 has now been shown to have multiple organ involvement [2]. Colonic -pseudo-obstruction caused by pseudomembranous colitis has emerged as a risk factor for adverse outcomes. We report an Italian patient with Sars-Cov-2 and colonic distension caused by pseudomembranous colitis.

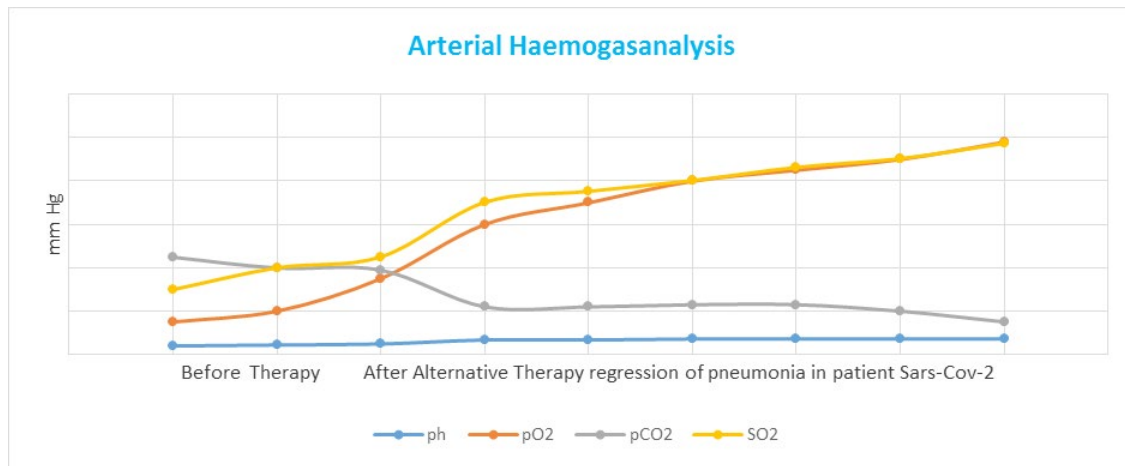
Case Description

Our Italian patient 96-year-old, woman, developed fever up to 38.5 degrees C, diarrhea, asthenia, myalgia, dyspnea and cough on 1 January 2021. In the Hospital she was admitted immediately after Computed Tomography (CT) imaging of her chest showed multiple and bilateral ground-glass opacities located in both subpleural and apico-basal spaces (especially on the right). Nasopharyngeal swab specimens were collected to detect severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) nucleic acid. The swab specimens were tested by real-time reverse transcriptase-polymerase chain reaction; a positive result was received 2 days later on 3 January 2021. Our patient was diagnosed with COVID-19 and not recommended treatment with Remdesivir for nephrotoxicity in elderly patient. She received 400 mg of moxifloxacin I.V daily for 3 days; O₂ Therapy; methylprednisolone three i.v. boluses of 200mg; Tocilizumab was given in a single

i.v. 400-mg dose; prophylactic enoxaparin was prescribed (she no presented thrombotic events).

The patient had a history of cognitive impairment, chronic cerebral vasculopathy and Urinary Tract Infection (UTI). On day five, our patient developed abdominal pain, fever and increasing diarrhea. Biochemistry test indicated leucocytes $9.58 \times 10^3/\mu\text{l}$ (reference $4-11 \times 10^3/\mu\text{l}$), D-dimer 3.3 $\mu\text{g}/\text{ml}$ (reference 0.1-0.5 $\mu\text{g}/\text{ml}$), C-reactive protein 329 mg/l (reference 0-5 mg/l), procalcitonin 6.72 ng/ml (reference 0-0.1 ng/ml), lactate dehydrogenase 316 u/l (reference 135-225 u/l) and lactic acid 3.6 mmol/l (reference 0.5-1 mmol/l). Clostridium Difficile screening was positive; Enzyme Immunoassay of Glutamate Dehydrogenase (GDH-EIA) and toxin A and B Enzyme Immunoassay (EIA) were positive. Treatment with intravenous metronidazole and intrarectal vancomycin was started. The response to treatment was refractory. The patient's haemodynamic status worsened and she suffered sepsis, respiratory and renal failure. An abdominal Computed Tomography (CT) showed distension of cecum and proximal colon and thickening with no signs of perforation.

Colonoscopy with serial biopsies of intestinal mucosa revealed a massively dilated and had a serosal tear, focal erosion of colonic mucosa with overlying acute inflammatory cells, fibrin deposits, mucus, and epithelial cells consistent with pseudomembranous colitis. Fortunately, After the maintenance of intensive medical treatment in hospital with clindamycin, cephalosporins and fluoroquinolones, our patient progressively improved to total recovery and hemicolectomy was not necessary. On January 30, 2021, our patient was negative and she has after Computed Tomography (CT) imaging of her chest a complete resolution of bilateral areas of altered density a ground glass after treatment Figure 1.



Note: This figure show Arterial Haemogasanalysis before Antiviral and Antimicrobial Agents for Sars-Cov-2 and Pseudomembranous Collitis and After Therapy with regression of pneumonia.

Figure 1: Arterial Haemogasanalysis.

Discussion

The Sars-Cov-2 pandemic has greatly affected gastroenterology and can to impact on the intestinal microbiota with an increase of opportunistic pathogens (dysbiosis). Firstly, severe dilatation of the colon in our elderly patient appear to be at increased risk for infection due to viral transmission next to an enhanced risk for mortality as compared to the general population, even in the face of an often apparently mild clinical presentation. Derangements in the innate and adaptive immune systems may be responsible for a reduced antiviral response, whereas chronic activation of the immune system and endothelial dysfunction provide a background for a more severe course. The presence of severe comorbidity in an elderly patient and a reduction of organ reserve may lead to a rapid deterioration of the clinical situation. Secondly, patients with Sars-Cov-2 are at increased risk of acute fulminant colitis, which is related to the severity of the clinical disease. The presence of pseudomembranous colitis, toxic megacolon (severe dilatation of the colon) and sepsis and/or multiple organ dysfunction syndrome is associated with an increased risk of mortality. Fulminant colitis in Sars-Cov-2 by *Clostridium Difficile* has a multifactorial origin, in which direct viral invasion causes a hyperinflammatory response, hypercoagulability, erosion and ulceration of the epithelium and markedly dilated crypts, presence of abundant clusters of goblet cells expelled to pseudomembranes and non-specific factors such as hypoxemia and necrosis may be involved [3,4].

Our patient with pseudomembranous colitis, responding to antimicrobial therapy with regression of hyperinflammation and dilatation of the colon pneumonia caused by Sars-Cov-2 and fortunately hemicolectomy was not necessary. Pseudomembranous

colitis with or without fulminant colitis and necrosis should therefore be considered a risk group, both in terms of infection risk and outcome. Moreover, a high degree of clinical suspicion is needed as the clinical presentation in Pseudomembranous colitis may be obscured because the febrile response may be blunted. However, in studies in which universal screening for Sars-Cov-2 was applied, a significant proportion of patients with chronic diarrhoea were asymptomatic positive. This allowed earlier adjustment and improved prognosis.

Conclusion

Currently we know very little of the multifaceted biologic characteristics of Sars-Cov-2. To our knowledge Sars-Cov-2 can to impact on the intestinal microbiota with an increase of opportunistic pathogens (dysbiosis) and *Clostridium Difficile*. Given that Sars-Cov-2 infection is a pro-thrombotic condition, possible ischemia secondary to COVID-19 infection related coagulopathy should also be a consideration a gastrointestinal involvment.

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