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Diarrheal syndrome in SARS CoV2 infection

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Abstract

English:

SARS-CoV-2 is a new virus belonging to the Betacoronaviruses genus, from the Coronavirus family. The main clinical symptoms encountered in COVID 19 are fever, cough and shortness of breath and they have been affecting more than 80% of patients. Compared to the patients that are infected with MERS Co-V or SARS-Co-V, where diarrheal syndrome was present in approximately 25% of cases, in SARS-Co-V 2 infection, diarrhea syndrome is present in less than 10% of cases.
Clinical case: A 59-year-old patient, smoker, known to have a history of cardiovascular disease and type II Diabetes, presented to the emergency unit with fever, productive mucopurulent cough and multiple diarrhea stools. Pulmonary radiography was performed and showed multiple oval opacities with a tendency to confluence disseminated basally bilateral. A RT-PCR SARS-Co-V-2 test was performed with a positive result. The patient was admitted to the hospital and received specialized treatment during which the previous symptoms gradually recovered, including diarrhea syndrome. After 4 days of treatment, the diarrhea of the stools reappeared, and it was decided to investigate for Clostridium Difficile. The test proved to be positive. Treatment was established according to the protocol with favorable clinical and biological evolution.
Conclusions: The newly diagnosed diarrhea syndrome in a hospitalized patient should constantly raise the suspicion of a Clostridium Difficile infection, which may worsen the prognosis of patients infected with SARS-CoV-2.

Keywords

Diarrheal syndrome • SARS-CoV-2 infection • Clostridium Difficile • gastrointestinal damage in COVID19

Sindromul diareic în infecția cu SARS CoV 2

Rezumat

Romanian:

SARS CoV 2 s-a dovedit a fi un nou virus ce aparține genului Betacoronavirusuri, din familia Coronavirusurilor. Principalele simptome clinice întâlnite în COVID 19 sunt febra, tusea și dificultățile respiratorii fiind prezente la un procent de peste 80% dintre pacienți. Comparativ cu pacienții infectați cu MERS CoV sau SARS CoV unde sindromul diareic a fost prezent la aproximativ 25% din cazuri în infecția cu SARS CoV 2 sindromul diareic este prezent în mai puțin de 10% din cazuri.
Pacientă în vârstă de 59 de ani, fumătoare, cunoscută cu antecedente cardiovasculare și Diabet Zaharat tip II, se prezintă în Unitatea de primire urgențe acuzând febră, tuse productivă mucopurulentă și multiple scaune diareice. Se efectuează radiografie pulmonară care evidențiază multiple opacități ovalare cu tendință la confluare diseminate bazal bilateral și se efectuează RT PCR SARS CoV 2 cu rezultat pozitiv. Pacienta primește tratament de specialitate timp în care simptomatologia anterioară se remite treptat, inclusiv sindromul diareic. După 4 zile de tratament se constată reapariția scaunelor diareice și se decide determinarea genelor pentru Clostridium Difficile care se dovedesc a fi pozitive. Se instituie tratament conform protocolului cu evoluție clinică și paraclinică favorabilă.
Concluzii: Sindromul diareic nou aparut în cazul unui pacient internat trebuie să ridice constant suspiciunea unei infecții cu Clostridium Difficile, aceasta putând agrava prognosticul pacienților infectați cu SARS CoV 2.

Cuvinte-cheie

sindrom diareic • infectia SARS CoV2 • Clostridium Difficile • afectarea gastrointestinala in COVID 19

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Introduction

In late 2019, a new coronavirus called SARS-CoV-2 was identified as the cause of appearance of a group of Pneumonia cases in Wuhan, a city in Hubei Province, China. COVID-19 primarily manifests as a lung infection with symptoms ranging from a mild upper respiratory infection to severe Pneumonia, Acute respiratory distress syndrome and death. COVID-19 disproportionately affects patients with pre-existing comorbidities and/or older adults. All medical professionals, including gastroenterologists, are rapidly tasked to adjust their practice with the purpose of reducing the spread of COVID-19 while providing care to their patients. [1]

The gastrointestinal tract may be susceptible to SARS-CoV-2 infection due to angiotensin 2 conversion enzyme (ACE2) receptors, widely found in the gut. ACE2 is a receptor for the SARS-CoV-2 virus, and digestive symptoms associated with SARS-CoV-2 infection can be caused by a direct viral attack on tissues and organs, which is due to the immune response. [2-4]

Clinical case

59-year-old patient presented to the emergency room with fever (38.5 degrees C), intermittent productive cough, fatigue and multiple watery diarrhea stools (3 episodes/ day, for 4 days). The symptoms started about 5 days before hospitalization, and progressively worsened. Personal pathological antecedents showed: Type II Diabetes in treatment with oral antidiabetics, grade III Hypertension, Hashimoto's thyroiditis with substitution treatment. Due to the recommendation of the primary care physician, the patient was treated at home for 5 days with 500 mg/ day Levofloxacin combined with 500 mg / day of Azithromycin, without any improvement of symptoms. In the epidemiological context, the patient denied contact with people that were diagnosed with COVID 19.

Clinical examination showed the patient presenting with moderately influenced general condition, obesity grade I (BMI: 31.25 kg/ m^2), dehydrated skin, pale, no oedema, no palpable lymphadenopathy, normally conformed thorax, pulmonary auscultation: vesicular murmur present bilateral, crackling rales disseminated basal bilateral, rhythmic heart sounds, BP = 130/75 mmHg, AV = 85 bpm, regular, SpO2 = 89% atmospheric air, painless abdomen, no hepatomegaly or splenomegaly.

Laboratory tests showed positive SARS-CoV-2 RT-PCR, hepatic cytolysis (AST/ALT- 89/98 U/L), systemic inflammatory syndrome (ESR 79 mm/h, PCR 69 mg/L, fibrinogen 6.45 g/L), D-dimers 5.56 mcg/mL, Lactate dehydrogenase 590 U/L, reactive thrombocytosis (600,000 cells/microL), otherwise without further changes in the blood count.

The EKG showed sinus rate, 85 / minute, QRS axis at 15 degrees, without repolarization changes.

Chest X Ray performed at admission showed ill-defined ground-glass opacification, in the bilateral subpleural basal zones, hilar enlargement predominant on the right side, enlargement of the cardiac silhouette (cardiothoracic index higher than 0.55) (Figure 1).

Based on clinical and paraclinical data, the following diagnoses are supported: SARS-CoV-2 infection confirmed by RT-PCR, acute respiratory failure, bilateral viral pneumonia, acute diarrheal syndrome. During the hospitalization, the treatment was initiated according to the National Protocol for COVID 19, consisting of Hydroxychloroquine 4x200mg/first day, then 2x200mg/day for 6 days, Lopinavir/ Ritonavir 200/ 50mg x4/ day, for 4 days, antipyretics, antitussives, vitamin therapy, systemic corticosteroids and the treatment of diarrheal syndrome (Metronidazole 3x500mg/ day and Vancomycin 4x125 mg/ day) [5]. We initially considered the presence of multiple diarrheal stools as a symptomatology due to digestive impairment in COVID 19.

After 24 hours hospitalization, we take note of the absence of diarrhea and a slight improvement in symptoms. On the 4th day of treatment, the patient's condition deteriorates as there is an appearance of exertional dyspnea and the reappearance of watery diarrhea stools (5 episodes/ day). Suspicion of Clostridium Difficile (C. Difficile) infection is raised and testing is performed (Toxin A positive, Toxin B positive, GDH gene positive). The therapeutic regimen for COVID 19 (Remdesivir



Figure 1. Radiological aspect at admission: the ill-defined ground--glass opacification, in the bilateral subpleural basal zones.



Figure 2. Radiological aspect after 4 days: the bilateral alveolar consolidation of lower lobes.

200 mg/ first day, then 100 mg/day for other 5 days and Tocilizumab 8 mg/ kg, 3 doses, associated at high flow oxygen therapy 15 l/ min) was modified due to the aggravation of the radiological appearance consisted in bilateral alveolar consolidation of lower lobes (Figure 2) and the biological data with systemic inflammatory syndrome. The treatment against C. Difficile was also instituted (Metronidazole 3x500mg/ day and Vancomycin 125 mg x4/ day) according to the protocol [6]. The patient's condition improved (no more diarrhea for about 3 days) and was discharged at home after 14 days of hospitalization with cured status, with remission of systemic inflammatory syndrome and radiological, numerical and dimensional regression of described alveolar opacities.

Discussions

We present the case of a patient hospitalized for SARS-CoV-2 infection, acute respiratory failure and bilateral viral pneumonia, which was associated with acute diarrheal syndrome caused by C. Difficile.

The clinical presentation of several gastrointestinal diseases (Crohn's disease, ulcerative colitis) may mimic COVID-19 infection. Examples include diseases that manifest with diarrhea, nausea, vomiting, and/or anorexia. Thus, for patients with an existing diagnosis of chronic gastrointestinal disease, the clinician will need to assess whether the symptoms are related to the disease or COVID-19 [6,7].

Patients with COVID-19 usually have fever and respiratory symptoms; however, gastrointestinal symptoms have been reported frequently in patients diagnosed with COVID-19. In a study that included 318 adult patients who were hospitalized with COVID-19, 195 patients (61%) reported at least one digestive symptom and the most commonly reported symptoms were anorexia (35%), diarrhea (34%) and nausea (26%). Some patients with COVID-19 had isolated gastrointestinal symptoms that preceded the development of respiratory symptoms. For example, in a study of 1141 patients with COVID-19, 183 patients (16%) had gastrointestinal symptoms (eg, diarrhea, nausea, vomiting) in the absence of respiratory symptoms [3,7].

The clinical presentation of COVID-19 may include hepatic manifestations, such as acute hepatitis and abnormal liver biochemical tests.

The diagnosis of COVID-19 is suspected primarily in patients with fever and/ or respiratory tract symptoms (cough, dyspnea) associated with myalgias, diarrhea, anosmia and ageusia. For patients with gastrointestinal symptoms, COVID-19 testing is preferred in the following cases: hospitalized patients with sudden onset of gastrointestinal symptoms, outpatients with onset of gastrointestinal symptoms over 48 hours, patients with known gastrointestinal disease (Crohn's disease, ulcerative colitis) showing an episode of exacerbation (diarrhea, vomiting). [4,7]

C. difficile is a gram-positive anaerobic bacterium that forms spores, produces toxins and causes colitis associated with prolonged antibiotics therapy. It colonizes the human intestinal tract after the normal intestinal flora has been disturbed (frequently in combination with antibiotic therapy). C. difficile infection (CDI) is one of the most common healthcare-associated infections and a significant cause of morbidity and mortality, especially in elderly, hospitalized adult patients. [8]

However, in the case shown above, we cannot say with certainty whether the first episode of diarrhea was caused by SARS-CoV-2 infection or by C. difficile because the patient was under antibiotic treatment at home, then continued it in the hospital. Also, no samples were collected for C. difficile from the 1st day of hospitalization and there was an interval of 3-4 days without stools. In this context, even if diarrhea is one of the possible symptoms of SARS-CoV-2 infection, other etiologies such as C. difficile infection should not be ignored. Delayed diagnosis leads to unfavorable evolution with significant metabolic imbalances and impairment of clinical status.

Conclusions

The diagnosis of Clostridium difficile infection should be considered in patients with acute diarrhea (≥3 watery stools within 24 hours) without obvious alternative explanation, especially in the context of relevant risk factors (recent use

of antibiotics, hospitalization and old age). Patients with suspected Clostridium difficile infection must be preventively isolated pending diagnostic evaluation.
Outpatient antibiotic administration increases the risk of Clostridium Difficile infection, which is why cases requiring antibiotic therapy must be carefully selected in the current epidemiological context, given that bacterial superinfection in SARS-CoV-2 infection is rare and quite difficult to document.

Ethical approval

Inform consent was obtained from the patient in order to participate to the study and write the article.

Conflict of interest

The authors have no conflicts of interest.

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