Diarrhea as an Early and Predominant Manifestation of Coronavirus Disease 2019 (COVID-19): A Case Report

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ABSTRAK

Coronavirus disease 2019 (COVID-19) merupakan salah satu penyakit infeksi baru yang dengan sangat cepat menyebar hingga WHO menyatakannya sebagai penyakit pandemik yang mendunia. Gejala klinis utama pada pasien COVID-19 adalah batuk dan demam, namun diare dapat menjadi salah satu gejala awal. Laporan kasus ini menerangkan seorang pasien yang datang dengan keluhan diare tanpa demam yang terkonfirmasi positif COVID-19 dalam perawatan. Adanya gejala awal yang tidak spesifik menuntut tenaga kesehatan untuk lebih waspada dalam menegakkan diagnosis COVID-19.

Kata kunci: COVID-19, SARS-Cov-2, diare, manifestasi awal, Indonesia.

ABSTRACT

Coronavirus disease 2019 (COVID-19) is a new infectious disease that spreads very rapidly and therefore, WHO has declared it as a global pandemic disease. The main clinical symptoms found in COVID-19 patients are cough and fever; however, in some cases, diarrhea can be one of the early symptoms. The present case report describes a patient who came with a complaint of diarrhea without fever and she was later confirmed to be positive for COVID-19 during hospitalization. The presence of unspecified initial symptoms calls for greater vigilance from health workers in establishing diagnosis patients with COVID-19.

Keywords: COVID-19, SARS-Cov-2, diarrhea, early manifestations, Indonesia.

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is a novel infectious disease emerging at the end of 2019. It is caused by Severe Acure Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), which first appears in Wuhan, China and spreads extremely fast worldwide; therefore, WHO declares it as a global pandemic disease. In such period of time, it spreads rapidly including in Indonesia. The first detected case in Indonesia was found in early March 2020. By the early of May 2020, there are over 3 million confirmed cases with more than 250 thousands of deaths worldwide.[1]

In Indonesia, based on data provided by the COVID 19 Mitigation Task Force, there are 12,776 confirmed cases by the early May with 930 deaths of all areas in the country.[2] The most

common early manifestations of the disease are fever and cough; however, some uncommon manifestation may also be found, which calls for extreme caution from medical health workers. One of the uncommon manifestations is gastrointestinal manifestation in the form of diarrhea.

In tropical country, where diarrhea is a common complaint found in the community; however, during the time of pandemic, COVID 19 should become one of differential diagnosis in patients with early symptom of diarrhea. Furthermore, it should be followed by a thorough directed history taking and necessary laboratory workup in order to establish or to exclude the diagnosis. In our case report, we are going to present a case of patient with early and predominant manifestation of diarrhea without fever that was later diagnosed with COVID 19. Another case reports and epidemiological data have shown that symptoms of diarrhea can be found in the course of COVID-19 disease. Case reports from the first COVID-19 patient in the United States, showed that COVID-19 patients had diarrhea symptoms. However, this patient admitted with respiratory problems accompanied by fever, whereas diarrhea appeared on the second day of treatment at the hospital.[3] Other case reports in Qatar and China showed similar cases. Diarrhea and abdominal pain are found as presenting symptoms, but later, high fever and worsening respiratory symptoms develop.[4,5] What makes this report interesting is that patients present with the main symptoms of diarrhea without fever. Even throughout the course of the disease fever was not found. In these patients the signs and symptoms of the respiratory tract throughout the course of the disease are also mild, including the X-ray picture that is not typical.

By studying the case, we expect that it may increase greater awareness and knowledge on manifestations of COVID19 disease

CASE ILLUSTRATION

There was a 72-year-old woman with a complaint of diarrhea for 3 days prior to her hospitalization. The patient also had a complaint of minimal infrequent cough and she felt aches and pain all over her body. History of fever was denied by the patient. She came for treatment after knowing that her sister had been tested positive with COVID-19 and her husband had the same symptoms with her sister's. Afterwards, the patient received treatment in an isolation ward. Her initial blood pressure was 144/70 mmHg with pulse rate of 73 beats/minute, respiratory rate of 20 times/minute and her body temperature was 36.5 ^{o}C.
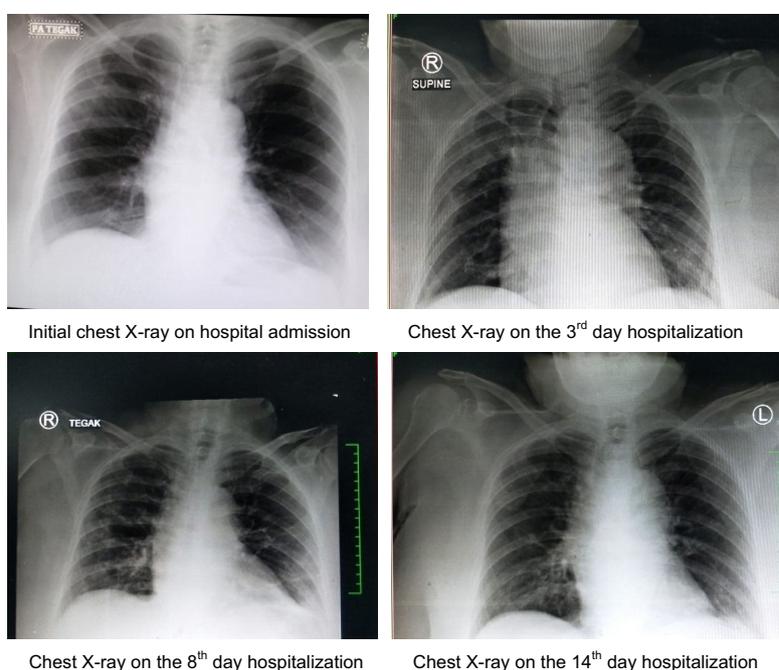
The early laboratory workup showed hemoglobin level (15.7 g/dL), hematocrit (46%), leukocytes (4200/uL), platelet counts (171000/ul) and lymphocytes (30%). Biochemical blood examination revealed AST (37 U/l), ALT (27 U/l), ureum (25 mg/dL), creatinine (1.3 mg/dL) levels and random blood glucose level (RBG) of 137 g/dL. In the early phase of hospitalization, her C-Reactive Protein (CRP) level was 1.5 mg/dL; while her procalcitonin level was 0.11 ng/mL and D-dimer level was 600 ng/mL. On the first day of hospitalization, the patient complained of reduced appetite; however, she denied having fever and short of breath, but she had cough once in a while. Her initial chest X-ray result revealed minimal infiltrate on her left lung. On the third day, the complaint of liquid stool had disappeared, but she still had loss of appetite. The laboratory workup on the third day of hospitalization showed that her CRP level increased to 2.2 mg/dL. The chest X-ray examination was repeated and there was infiltrate at the base of her left lung. On the 6th day, the patient complained about diarrhea again as many as 4 to 6 times of bowel movement daily with liquid stool. She also had a complaint of infrequent cough.

On the 6th day, the laboratory workup was repeated showing the following results of hemoglobin level (11.8 g/dL), hematocrit (37%), leukocyte (4600/uL), platelet count (122000/ul), netrophils (72%) and lymphocytes (18%). The biochemical blood examination revealed increased AST level into 80 U/l and ALT level of 50 U/l; moreover, her CRP level also increased into 4.8 mg/dL.

On the 8th day of hospitalization, she had more frequent cough without dyspnea, but there was no fever. Her vital sign was still

Tabel 1. Laboratory examination

Laboratory exm	Day 1	Day 3	Day 6	Day 8	Day 11
Hb (g/dl)	15.7		11.8	13.2	13.7
Leukocytes count (/uL)	4200		4600	5900	3700
Platelet count (/ul)	171.000		122.000	123.000	146.000
Lymphocytes (%)			18	10	18
AST (U/l)	37		80		
ALT(U/l)	27		50		
Ur (mg/dl)	25				
Cr (mg/dl)	1.3				
CRP (mg/dl)	1.5	2.2	4.8	11.1	5.7
Procalcitonin (ng/ml)	0.11				
DDIMER (ng/ml)	600			1900	

Initial chest X-ray on hospital admission

Chest X-ray on the 3rd day hospitalization

Chest X-ray on the 8th day hospitalization

Chest X-ray on the 14th day hospitalization

Figure 1. Initial chest X-ray on the day hospitalization.

normal. The patient still complained of diarrhea with liquid stool. Another laboratory workup was performed with the following results, i.e. hemoglobin level (13.2 g/dL), hematocrit (39%), leukocytes (5900/uL), platelet count (123000/ul) and neutrophils (77%) and lymphocytes (10%) . The CRP level increased into 11.1 mg/dL and D-dimer level was 1900 ng/mL. At the time, chest X-ray examination was repeated revealing an aggravated infiltrate at the base of both lungs (bilateral basal lung infiltrate).

On the 10th and 11th day of hospitalization,

the clinical condition was improved. The patient had no cough, no short of breath and no diarrhea as well as no fever. Another laboratory workup was carried out with the results of hemoglobin level (13.7 g/dL), hematocrit (42%), leukocytes (3700/uL), platelet count (146000/ul) and neutrophils (66%) and lymphocyte (18%). The CRP level was improved into 5.7 mg/dL. On the 14th day of hospitalization, another chest X-ray was performed and there was an improvement compared to previous chest X-ray result. During treatment, the test results of PCR pharyngeal swab

of the patient showed two times positive results.

DISCUSSION

The patient came to emergency unit with a complaint of diarrhea since 3 days prior to hospital admission. She had liquid stool diarrhea for 3 to 4 times a day. She denied any symptom of fever during admission, but she said that she had cough once in a while without any shortness of breath. Chen et al in their epidemiological study and clinical characteristics of COVID disease suggested that 83% of patients came with fever, 82% had complained cough and only 2% of patients who came with a complaint of diarrhea.[6] Huang et al in their study in Wuhan also suggested that diarrhea was found only in 3% of the patients.[7] Fang et al.[8] found that diarrhea may occur starting from the 1st to 8th day of symptom onset with a median of 3.3 days. The mean duration may reach 4.1 (SD 2.5) days.[9] The patient came with a history of husband and sister had been tested positive for COVID-19; therefore, she was tested and observed in an isolation ward.

COVID-19 is a disease that can affect many organs and various kinds of appearance. In a case report, COVID-19 can affect the central nervous system such as stroke[10] and meningitis[11] Viral exanthem with "Pin and Needles Sensation" was also reported in one case report.[12] In the cardiovascular system, COVID-19 can cause several disorders such as arrhythmia to myocarditis.[13] Because of this, Pathak, in his editor's note said that COVID-19 can join several diseases that are called "The Great Imitator". But not only the Great Imitator, COVID-19 can also be called the Great Invader, because it not only attacks the respiratory system but also many other organs.[14]

Gastrointestinal symptoms in COVID-19 patients may include abdominal pain, nausea, vomiting and diarrhea. Guan et al.[15] in their study demonstrated that nausea and vomiting was found in 5% of the patients. In deceased patients, the gastrointestinal symptoms were more likely to be nausea and vomiting compared to living patients (6.9% vs 4.9%).[15] Xi Jin et al.[16] also reported that gastrointestinal symptoms are more frequently found in patients who got infected from their family compared to those who got the disease from other places. Similar exposure might occur in our patient as she probably got infected from her husband and sister who had been diagnosed with COVID-19 earlier. The risk for disease transmission through household cluster is supported by the possibility of oral-fecal transmission of COVID-19.[18] In tropical country during the transition of weather, diarrhea can be caused by various microorganisms including bacteria, virus and parasite; therefore, it is necessary to perform adequate history taking, physical examination and laboratory work up in order to establish the diagnosis. Therefore, during the time of COVID-19 pandemic, the early symptom of diarrhea calls for great caution for health care worker, particularly in establishing diagnosis.

Currently, it has been known that in addition to respiratory droplet and direct contact, COVID 19 may also be transmitted via oral-fecal route. Some case reports have demonstrated the presence of SARS-CoV-2 in saliva and stool of patients with COVID-19. It has been known that SARS-CoV-2 infection requires a contact with ACE2 receptor located on the type II alveolar cells, intestinal epithelium and cholangiocytes.[18] It has been suggest that intestinal ACE2 receptors associated with metabolism of amino acid, expression of antimicobial peptides and intestinal microbial balance.[19] In patients with COVID-19, diarrhea may also be caused through several mechanisms including direct viral infection of digestive tract that may result in mucosal damage and diarrhea. The mechanism is supported by the presence of protein of nucleocapsid virus on intestinal epithelial cells.[9] Although not yet known with certainty, but viral infections can cause increased permeability of the gastrointestinal mucosa, causing malabsorption.[20] Secondly, it may be caused by antiviral drugs and thirdly it may occur due to dysbiosis of intestinal microbiota which is induced by antibiotic usage.[9] In our patient, it may be caused by direct viral infection as the patient had diarrhea as initial symptom of COVID-19.

On hospital admission, radiological examination was performed showing results

of minimal infiltrate in the bottom left lung. Wong et al.[10] in their study demonstrated that the sensitivity of chest X-ray at initial phase was only about 69%; therefore, there were many positive cases had initially normal or uncharacterized chest X-ray. The aggravation of chest X-ray reached its peak on the 10th to 12th day after the onset of symptoms. The characteristic chest X-ray features for COVID-19 were peripheral infiltrate at the basal area and the involvement of both lungs. Pleural effusion was rarely found and it was only approximately 3% of the patients.[10] In our patients, there was infiltrate and aggravated results of chest X-ray examinations during her history of illness, which later improved. The initial laboratory workup found the following results of leukopenia (4300/uL), thrombocytopenia (132,000/uL), normal lymphocyte (30%) and CRP of 1.5; however, during the clinical history of illness, there was increased CRP, which was in line with exacerbated clinical symptoms.
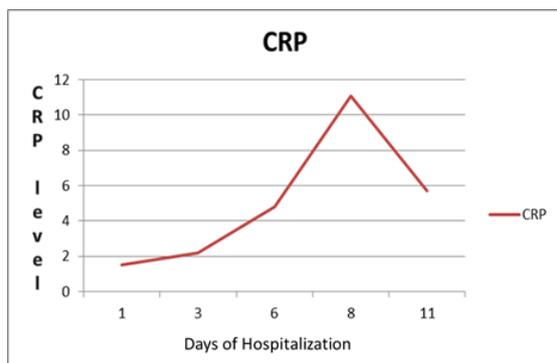
Figure 2. Graphic data on CRP level during hospitalization; CRP level, hospitalization day.

In the history of her present illness, the patient had another complaint of diarrhea on the 6th to 8th day of hospitalization and the complaint was followed by symptom of cough without any fever. Patients with COVID 19 in their history of illness may experience several phases starting from the prodromal phase, initial phase, pneumonia phase as well as inflammation and resolution. Pneumonia symptoms become more obvious in 4 to 7 days following the onset and inflammatory phase can be found in 8 to 12 days after the onset of disease.[21] Pneumonia and inflammatory phase are characterized by exacerbated clinical symptoms to Acute Lung Injury as well as increased level of acute phase protein such as CRP.[11,22] CRP is one of the laboratory tests that is recommended to be examined regularly in patients with COVID-19.[23] In our patient, there was increase CRP level, in which 1.5 mg/dL on the first day that increased to 2.2 mg/dL on the third day. Afterwards, it increased to 4.8 mg/dL on the 6th day and it reached the peak to 11.1 mg/dL on the eight day. Along with increased CRP level, the clinical respiratory symptoms became more obvious such as dry cough; however, it was not followed with fever. The symptoms were improved on the 10th to 11th day until the patient was discharged from hospital. The clinical improvement was observed through laboratory workup including improved chest X-ray results and improved CRP level to 5.7 mg/dL.

During hospital care, the patient received treatment of 500 mg chloroquine PO twice daily, 75 mg oseltamivir PO twice daily, 750 mg levofloxacin IV once daily, 400 mg vitamin C IV once daily, 5000 U of subcutaneous heparin twice daily as well as symptomatic treatment for cough and diarrhea. Chloroquine was given due to its ability in inhibiting viral entry and viral endocytosis as well as its capacity as an immunomodulator.[24] Chloroquine has gastrointestinal side effects such as nausea and vomiting, which probably had been experienced by our patient who had symptoms of nausea and loss of appetite. Guan et al suggested that increased D-dimer level was found in more than 40% of patients, which may be caused by microthrombus phenomenon.[25] Disrupted endothelial cell due to infection may result in the formation of thrombin causing hypercoagulability condition. Hypoxia may also occur in severe COVID-19 that may also induce thrombosis. (26) Tang et al in their study demonstrated that anticoagulant treatment may reduce mortality in patients with COVID-19.[26] Our patient had increased D-dimer from 600 ng/mL to 1900 ng/mL along with increased CRP and exacerbated clinical symptoms. Therefore, we decided to treat the patients with 5000 unit of heparin through subcutaneous injection twice daily. The patient was discharged from the hospital on the 14th

day of care without any complaint and she had improved laboratory and chest X-ray result. The patient then came for another follow-up visit in 1 week after her hospital discharge and she was in a good condition.

CONCLUSION

Coronavirus disease 2019 (COVID-19) is one of new infectious disease that emerges in December 2019. The clinical symptoms may be various, which requires great caution for health care worker in establishing diagnosis and providing treatment. Diarrhea, although it is rarely found, may become early and predominant manifestation of COVID-19; therefore, a thorough directed history taking and appropriate examination are necessary for diagnosis.

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