

COVID-19 with Acute Cholecystitis: A Case Report

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ABSTRACT

Novel Coronavirus 2019 (COVID-19) also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an enveloped, non-segmented positive-sense RNA virus that belonging to the beta-coronaviridae family. Patients were said to had various symptoms of fever, cough, anosmia, and chest stuffiness in addition to other non-specific clinical manifestations, including diarrhea, vomiting, anorexia, abdominal pain, and so on. Although this gastrointestinal symptoms were present in COVID-19 case, there was not enough evidence about the involvement of gallbladder and biliary tract in literature to date. We report a rare case of Acute Cholecystitis on a COVID-19 patient in Jakarta, Indonesia. A case of 54-year-old female with COVID-19 confirmed by RT-PCR Test who had constant pain in the right upper quadrant of her abdomen during her arrival at the hospital that was finally diagnosed as Acute Cholecystitis. The Laboratory Findings revealed normal level of White Blood Cells (6.73 K/aeL). The Multidisciplinary team decided to treat COVID-19 infection with antiviral (Favipiravir, according to Indonesian COVID-19 Guideline) for 2 weeks until her RT-PCR was found to be negative then perform a laparoscopic cholecystectomy as the first treatment. During the administration of Favipiravir, there was a reduction of pain in the right upper quadrant abdomen and an overall clinical improvement.

The precise mechanism of acute cholecystitis in COVID-19 patients was still unclear. However, acute cholecystitis could be a possible complication of COVID-19 although there was not enough evidence whether the gallbladder might be vulnerable to COVID-19. In this case, the normal level of white blood cells could be a hint that acute cholecystitis was not caused by bacterial colonization and could be potentially triggered by COVID-19. Laparoscopic cholecystectomy was chosen as the first management after RT-PCR COVID-19 was negative with 2-weeks of antiviral treatment. Although the lack of evidence and guidelines for acute cholecystitis management during The COVID-19 pandemic, laparoscopic cholecystectomy remains the chosen treatment for Acute Cholecystitis Management on COVID-19 Patients. More research is needed to understand the possible relationship between Acute Cholecystitis and COVID-19.

Keywords: 2019-nCoV, COVID-19, acute cholecystitis, case report

ABSTRAK

Novel Coronavirus Disease 2019 (COVID-19) adalah virus RNA untai positif berkapsul dan tidak tersegmentasi yang termasuk dalam famili beta-coronaviridae. Meskipun gejala gastrointestinal juga sering ditemui pada kasus COVID-19, belum ada cukup bukti tentang keterlibatan kandung dan saluran empedu. Kami melaporkan kasus langka Kolesistitis Akut pada pasien COVID-19 di Jakarta, Indonesia. Seorang wanita 54 tahun dengan COVID-19 terkonfirmasi oleh tes RT-PCR dengan keluhan utama rasa sakit yang konstan di perut daerah kuadran kanan atas. Pasien akhirnya didiagnosis sebagai Kolesistitis Akut. Tes laboratorium menunjukkan Sel Darah Putih normal (6,73 K/aeL). Tim Multidisiplin memutuskan untuk mengobati infeksi COVID-19 dengan Favipiravir selama 2 minggu sampai RT-PCR-nya negatif kemudian melakukan kolesistektomi laparoskopik sebagai terapi lini pertama. Selama pemberian Favipiravir, ditemukan perbaikan rasa sakit di perut kuadran kanan atas dan juga perbaikan klinis secara keseluruhan.

Mekanisme kolesistitis akut pada pasien COVID-19 masih belum jelas. Kolesistitis akut dapat menjadi komplikasi COVID-19 meskipun belum ada cukup bukti bahwa kantong empedu rentan terhadap COVID-19. Kadar sel darah putih yang normal bisa menjadi petunjuk bahwa kolesistitis akut pada kasus ini tidak disebabkan oleh kolonisasi bakteri. Namun, kolesistektomi laparoskopik tetap menjadi terapi pilihan untuk penatalaksanaan kolesistitis akut pada pasien COVID-19. Diperlukan lebih banyak penelitian lanjutan untuk memahami kemungkinan hubungan antara kolesistitis akut dengan COVID-19.

Keywords: 2019-nCoV, COVID-19, kolesistitis akut, laporan kasus

INTRODUCTION

Novel Coronavirus 2019 (COVID-19) also known as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an enveloped, non-segmented positive-sense RNA virus that belonging to the beta-coronaviridae family.¹ It was originated in Wuhan, China and right now has been a Global Burden that described as a communicable disease pandemic.² Patients were said to had various symptoms of fever, cough, anosmia, and chest stuffiness in addition to other non-specific clinical manifestations, including diarrhea, vomiting, anorexia, abdominal pain, and so on.^{3,4} SARS-CoV-2 enters the host cells through ACE2, which make this receptor is highly important to understand because many studies have shown that SARS-CoV-2 receptor ACE2 (angiotensin-converting enzyme 2) is expressed in many organs such as kidney, lung, heart, and gastrointestinal organs.^{5,6}

Meanwhile, Acute cholecystitis is inflammation of the gallbladder that happened due to occlusion of the cystic duct or impaired clearance of the gallbladder. Stones or biliary sludge are common cause of this impaired emptying.⁷ There has been a lot of discussion on COVID-19 relations with kidney, lungs, and gastrointestinal tract, but there hasn't been much information about the interaction of other organs such as liver and gallbladder.

According to current research, β -coronaviruses from lineage B, which are highly pathogenic to humans, can

triggered liver and induced acute hepatitis.⁸ However, There was not enough evidence about the involvement of gallbladder and biliary tract in literature to date.⁴ Only some study has mentioned the existence of ACE2 Receptor in Biliary tract that might have a possible relationship with acute cholecystitis on a COVID-19 patient.⁹ We report a rare case of Acute Cholecystitis on a COVID-19 patient in Jakarta Islamic Hospital, Jakarta, Indonesia.

CASE ILLUSTRATION

On April 2021, A 54-year-old female with no drug and inheritable genetic disease history, was admitted to Emergency Room of Jakarta Islamic Hospital with pain in the right upper quadrant of her abdomen that radiated to the back side, positive murphy's sign with no visible jaundice. Her body temperature was elevated to 38.1°C. Before developing pain in the abdomen, she had constant fever for 4-days, chest stuffiness, nausea and vomiting. She had a good history of physical health and no underlying disease before. She lived in Jakarta which was known to have a high numbers of confirmed COVID-19 cases in Indonesia.

The clinical parameter were: 90x/min. heart rate, 130/90 mmHg blood arterial pressure, 38.1°C body temperature, and 98% O₂ Saturation. Respiratory rate was 18x/min. breaths with no coarse/wheezing breath sounds from both lungs on auscultation. The laboratory findings revealed normal level of white blood cell 6.73

K/aL (Normal range 3.60-11.00) and high neutrophil lymphocyte ratio (NLT) level 3.95 (Normal range < 3.13). Chest X-ray showed mild infiltrate in both hilum of the lung and rapid SARS-CoV-2 antigen detection assay of pharyngeal swabs was negative for COVID-19 upon hospitalization. We suspected acute cholecystitis

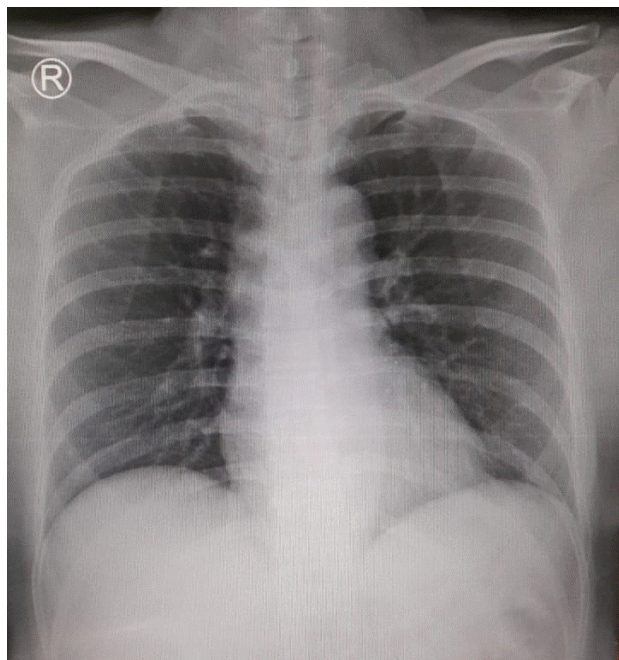


Figure 1. Chest X-ray in 54-year old Female with COVID-19 Pneumonia and acute cholecystitis. Chest X-ray shows mild infiltrate in both hilum of the lung

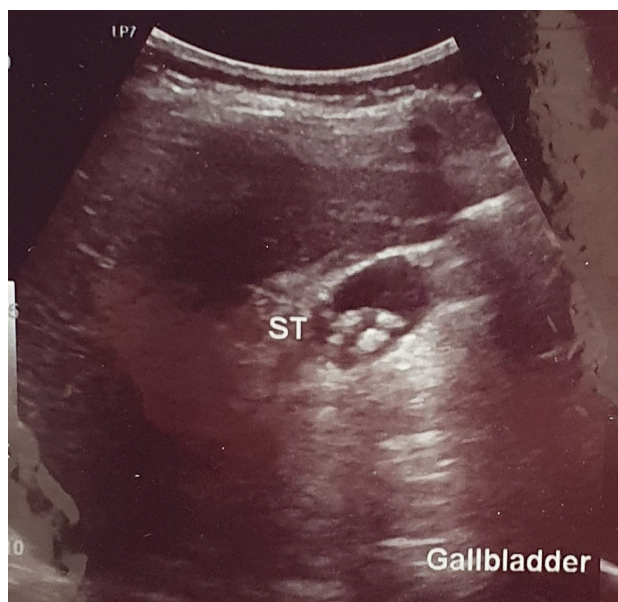


Figure 2. Abdominal Ultrasound In 54-year old Female with COVID-19 Pneumonia and Acute Cholecystitis. Abdominal ultrasound shows a gallbladder distention, thickening of the gallbladder wall, biliary sludge, and multiple stone in the gallbladder

or cholangitis and performed an abdominal ultrasound, which later discovered a gallbladder distention, thickening of the gallbladder wall, biliary sludge, and multiple stone in the gallbladder. She was finally diagnosed with confirmed acute cholecystitis.

We decided to performed a laparoscopic cholecystectomy as the first treatment with multidisciplinary team including general surgery unit and intensive care unit. As the standard operational procedure, we are obligated to do real-time fluorescence polymerase chain reaction (RT-PCR) assay of pharyngeal swabs and this time we found that her RT-PCR was positive.

Consequently patient was also diagnosed with confirmed case of mild COVID-19 pneumonia. She was immediately administered with Nasal cannula at 2 LPM for oxygen support and was treated according to Indonesian COVID-19 Guideline with Favipiravir 2x1600 mg for 1 day, Favipiravir 2x600 mg for the next 5 days with azithromycin 1x500 mg for 5 day. Vitamin C non-acidic 500 mg/8 hours, Vitamin D 400 IU-1000/day, Paracetamol 3x500 mg/day for 2 weeks. There was an overall clinical improvement after administration of drugs. Her pain in the right upper quadrant abdomen was reduced and her body temperature was going back to normal.

Finally, After 2 weeks of COVID-19 drugs administration, her RT-PCR was found to be negative then we performed a laparoscopic cholecystectomy as the first treatment. The gallbladder was found to be gangrenous and then dissected. We did not collect the green gallbladder bile to further analyze the involvement of COVID-19 in this case. The operative time was 90 minutes. The postoperative course was uneventful and it was well-tolerated by the patient, so she was subsequently discharged from the hospital on day-28 and referred to the clinic for follow-up.

DISCUSSION

The SARS-CoV-2 virus primarily damages the respiratory system, although it also affects other organ systems. Common symptoms of lower respiratory tract infection such as fever, dry cough, and chest stuffiness were reported in the initial case series from Wuhan, China. However, others symptoms were also discovered as more research were conducted, including headache, dizziness, generalized weakness, anosmia, vomiting, and diarrhea.¹⁰ In the present case, patient, who was admitted with 4-days fever, chest

stuffiness, nausea and vomiting, displayed a typical symptoms of COVID-19. Because ACE2 is highly expressed on the apical side of lung epithelial cells in the alveolar space, virus can easily enter and destroy them causing lung injury and manifested as dry cough with chest stuffiness. Innate immunity in the airway, such as, epithelial cells, alveolar macrophages, and dendritic cells, plays in an important part to fight against viruses till adaptive immunity is involved. This event causes an inflammatory pathway that send signal to the central nervous system to respond with elevated body temperature.^{10,11} Although the patient did not have a clear history of contact with patient diagnosed with COVID-19, she lived in Jakarta that was known to have a high number of confirmed cases in Indonesia. It means that she can be infected easily while she was going outside. Her lymphocytes were decreased (19%; normal range: 25-40%), chest X-ray showed mild infiltrate in both hilum of the lung and while the rapid SARS-CoV-2 antigen detection assay of pharyngeal swabs was negative for COVID-19, her RT-PCR COVID-19 nucleic acid assay of pharyngeal swabs was positive; thus, she was definitely diagnosed with mild COVID-19 pneumonia.

From recent meta-analysis, we found that RT-PCR had higher sensitivity and specificity to diagnose COVID-19 rather than rapid SARS-CoV-2 antigen. False negative from rapid SARS-CoV-2 result could be caused by faulty technique in operating the assay, insufficient clinical specimens, inhibitors, and antigen degradation.^{12,13}

Favipiravir, Azithromycin, Vitamin C, and Vitamin D was choose as the first treatment for Mild COVID-19 Pneumonia according to Indonesian COVID-19 Guideline. Favipiravir/Avigan has been developed for the treatment of avian influenza. It works selectively targeting viral RNA replication and induces destructive mutagenesis in RNA viruses. Azithromycin has been proven as adjunctive therapy to blunt the cytokine storm before it progresses to an exaggerated level and also it has immunomodulatory and anti-inflammatory effects potential in the treatment of some viral respiratory tract infections.¹⁴ Vitamin C and Vitamin D was administered because it has a robust evidence to optimize the modulation of the body's immune response and reducing the risk of infections.¹⁵ This research was supported by patient's clinical improvement after first administration of the drugs.

In our unique case, the patient developed constant pain in the right upper quadrant of the abdomen with positive murphy's sign after had constant fever for 4-days, chest stuffiness, nausea and vomiting. Because

of the obvious clinical presentation that this patient was most likely to be diagnosed as acute cholecystitis, We decided to subsequently confirmed it by ordering an abdominal ultrasound and discovered a gallbladder distention, thickening of the gallbladder wall, biliary sludge, and multiple stone in the gallbladder.

However there is not an available guideline for confirmed acute cholecystitis with COVID-19 in Indonesia, so we decided to wait until 2-weeks of drug administration and arranged pharyngeal swabs for RT-PCR. After the result was shown to be negative, Multidisciplinary team decided to perform an early laparoscopic cholecystectomy as the gold standard for the treatment of most gallbladder disease and for a shorter hospital stay to reduce the risk of nosocomial infection.¹⁶ Laparoscopic cholecystectomy was also preferred than open cholecystectomy because of the lack of evidence about an increased risk of SARS-CoV-2 infection during laparoscopy.¹⁷

The precise mechanism of acute cholecystitis in COVID-19 patients was still unclear. However, acute cholecystitis could be a possible complication of COVID-19 although there was not enough evidence whether the gallbladder might be vulnerable to COVID-19. From this unique case, we might found a possible relationship between acute cholecystitis and COVID-19 because after the drug administration, her pain in the right quadrant abdomen was reduced. There is a literature to report that gallbladder epithelial cells are very similar to bile duct cells, express ACE2 and could be a target of the SARS-CoV-2.⁹ To support the possible relation between COVID-19 and acute cholecystitis, blood test showed a normal level of white blood cells that could be a hint that acute cholecystitis was not caused by bacterial colonization and could be potentially triggered by COVID-19.¹⁸ We didn't order an RT-PCR nucleic acids for bile although the result may reinforce the hypothesis of COVID-19 can caused acute cholecystitis. Further studies are required to prove or disprove this hypothesis.

As a conclusion, we report a clinical course of a female with acute cholecystitis and confirmed COVID-19. Although the lack of evidence and guidelines for acute cholecystitis management during COVID-19 pandemic, laparoscopic cholecystectomy remains the chosen treatment for acute cholecystitis management on COVID-19 patients. More research is needed to understand the possible relationship between acute cholecystitis and COVID-19.

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