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Acute acalculous cholecystitis caused by sars cov-2 infection: Another case report and literature review

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Keywords

Acute acalculous cholecystitis; SARS-CoV-2; COVID-19.

Abbreviations

ACE2: Angiotensin-converting enzyme 2; AAC: Acute acalculous cholecystitis; HT: Hypertension; DM: Diabetes mellitus; CRP: C-reactive protein; PE: Pulmonary thromboembolism; RT-PCR: Everse transcription-polymerase chain reaction; US: Ultrasound; Lap-c: Laparoscopic cholecystectomy; PTGBD: Percutaneous transhepatic gallbladder drainage; ND: Not described; HD: Heart disease; AR: Reumatoid arthrite; TM-PRSS2: Type II transmembrane serine proteases.

Introduction

Since the first diagnosed case of COVID-19 in December 2019, it nows patients infected with SARS-CoV-2 typically present with a variety of respiratory symptoms (ranging from asymptomatic disease to acute respiratory distress syndrome or respiratory failure), but in addition to pulmonary dysfunction, recent reports indicate that multiorgan diseases, such as gastrointestinal [11]. Several studies have reported that some patients with SARS-CoV-2 present with gastrointestinal symptoms, such as abdominal pain, diarrhea, and vomiting. Additionally, emerging data reported show that angiotensin-converting enzyme 2 (ACE2), which is known as the major receptor for SARS-CoV-2, is highly expressed in the gastrointestinal tract, biliary tract, pancreas, and liver [4,14,16]. Thus, gallbladder epithelial cells are very similar to bile duct cells, as they richly express receptors (ACE2), and could be a target for SARS-CoV-2 or body's dysregulated immunological response against the virus resulting in severe inflammation of the gallbladder, Acalculous cholecystitis (AAC) has been reported as an uncommon complication following severe COV- ID-19 pneumonia. We report another case and take the opportunity to review the literature in this regard.

Case Report

In February 2022, a 91-year-old man with moderate-severe pneumonia and pancytopenia was admitted to our COVID19 Unit, with multiple risk factors: hypertension (HT), Diabetes Mellitus (DM), past smoking, aortoiliac endoprothesis, pulmonary emphysema and right pneumonectomy for squamous cell carcinoma in 2014. All this, added a Rheumatoid Arthritis and pharmacological immunosuppression by Metrotrexate. Respiratory symptoms went back more than 7 days, so Remdesivir was not administered. After temporary suspension of methotrexate, oxygen support, respiratory physiotherapy, bronchodilator therapy and Dexamethasone, he presented a favorable clinical-biological evolution and could be discharged after 8 days of stay and 15 from the onset of symptoms with home oxygen therapy with a flow of 1.5 lpm, given evolution to fibrosing pneumonia (with indication of follow-up in external consultation). After remaining stable, 72 hours later he presented respiratory distress associated with continuous epigastric pain with irradiation to the right hypochondrium, feeling nauseous and vomiting. He goes to the emergency room, where fever (38ºC), elevated D-dimer, Serum level of C-reactive protein (CRP) and leukocyte count are confirmed with respect to the analytical control prior to discharge. The chest X-ray was similar to that at discharge (Figure 1). On physical examination, mild tachypnea with oxygen flow at 3 lpm, abolition of the vesicular murmur in the right hemithorax (pneumonectomy), fine crepitus in the left hemithorax and triggered pain on palpation in the epigastrium and right hypochondrium, without a clear Murphy's sign. He had no skin or scleral jaundice. Laboratory evaluation revealed a white blood cell (WBC) count of 11.840 /µL, hemoglobin of 11.6 g/dL, platelet count of 292 X 103/µL, LDH 499 U/L, CRP 9.9 mg/dl and hepatobiliary and pancreatic enzymes, and coagulation markers were within the normal range, but D-dímer increased 3751 ng/mL. Suspecting a nosocomial pulmonary infection or a pulmonary thromboembolism (PE), a chest CT scan was requested with enlarged cotes to the abdomen. Until the imaging study was performed, enteral rest, low molecular weight heparin at intermediate doses and antibiotic therapy with piperacillin -tazobactam were implemented. With these measures, he was apyretic and practically asymptomatic 48 hours after readmission and the blood cultures were negative. The CT scan no filling defects in the trunk of the pulmonary artery or in its main, lobar or segmental divisions suggestive of acute PE and showed right pneumonectomy chamber, left pulmonary emphysema, peripheral pulmonary consolidation and some focus of bronchocentric distribution in the left lower lobe compatible with lung disease due to SARS-COV2, very slight left pleural effusion and incidentally distended gallbladder (5 cm) with mild hyperechogenicity of perivesicular fat adjacent (Figure 2). Endovenous piperacillin-tazobactam was given for 7 days, with good clinical evolution and control abdominal ultrasound (US) after 11 days showed disappearance of vesicular damage (Figure 3).

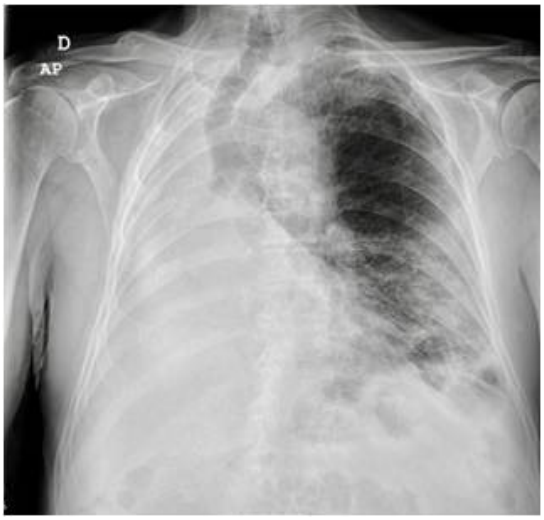

Figure 1: Chest x-ray: Right pneumonectomy. Left pulmonary infiltrates predominantly left basal, para and retrocardiac and blurriness of the diaphragmatic interface.

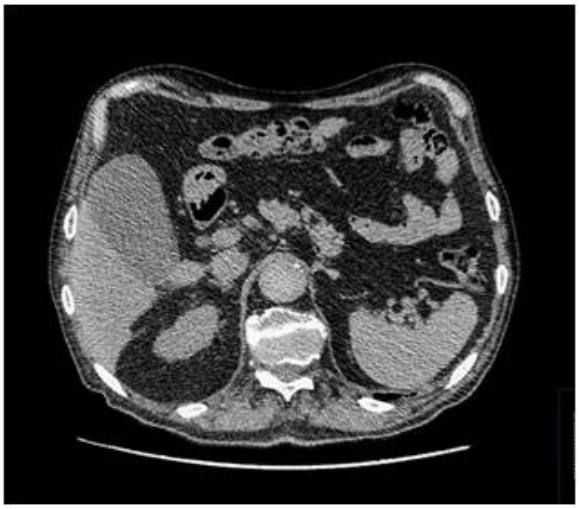

Figure 2: TC scan showing distended gallbladder (5 cm) with mild hyperechogenicity of perivesicular fat adjacent.

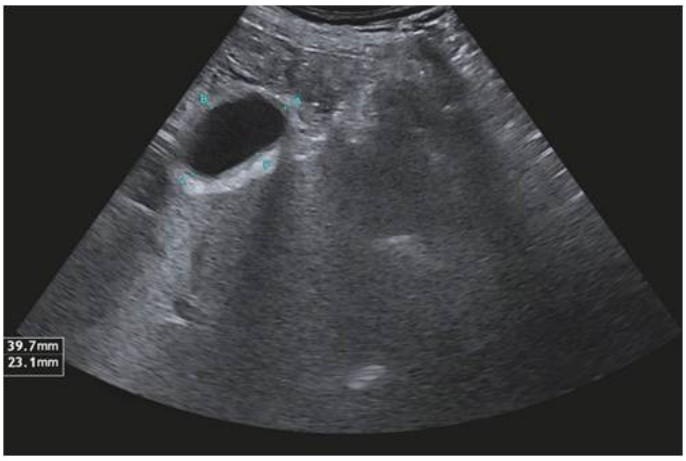

Figure 3: US showing normally distended gallbladder, without lithiasis or inflammatory changes. Bile duct in the visualized segments not dilated.

Discusion and Literature Review

We report a new case of acute acalculous cholecystitis (AAC) following pneumonia caused by SARS-CoV-2 infection, an extremely rare association in the medical literature. The exact pathogenesis of acute AAC in COVID-19 infection is not clear; however, it is proven that severe acute respiratory syndrome (SARS) coronaviruses have a tropism not only to the lungs but also to the liver. Intracellular entry of the virus occurs via an interaction with the angiotensin-converting enzyme 2 receptor (ACE2), which is present in several tissues, including lungs, liver, and biliary ducts [6,14]. Also, TMPRSS2 co-receptor is essential for viral entry, and it is widely found in gallbladder tissue [18]. In SARS-CoV-2 autopsies, liver tissue exhibited different patterns of hepatocyte injuries, and viral ribonucleic acid (RNA) was found inside hepatocytes [17]. Balaphas et al. confirmed by reverse transcription-polymerase chain reaction (RT-PCR) the presence of the virus in the gallbladder wall of a patient with cholecystectomy after an episode of AAC and COVID-19 infection [3]. Additionally, ACE2 is highly expressed in the vascular endothelium, and the attachment of

SARS-CoV-2 via ACE2 causes endothelitis, leading to thromboembolism in multiple organs, including the gallbladder [1].

On reviewing the literature using the PubMed database, we found 20 cases (including our case), reporting AAC related to the infection of SARS-CoV-2. There were 13 men and 7 women in the series, and the median patient age was 68 years (range: 40–96 years). At least five of the 20 patients had no comorbidities. Regarding the onset of AAC, whereas AAC developed during the treatment for pneumonia (median time lag, 14 days; range, 7-49 days) or was diagnosed at the same time in 15 out of 20 patients, there were 3 patients who had AAC followed by pneumonia and 2 patients were the ACC was the only manifestation (Table 1) [1,13,14].

As additional information, it should be noted that in a retrospective study carried out by Fenlon et al. in 2020, the imaging studies of 47 children and adolescents diagnosed with multisystemic involvement by SARS CoV2 were reviewed and 23% had thickening of the gallbladder Wall [15].

Table 1: Reported case of acute acalcoulose cholecystitis related to COVID19 (modification of a reproduced by Futagami et al [14].

Case	Study	Age/Sex	Comorbidity	Onset of AAC [a]	Time-lag[b]	Grade[c]	Initial treatment[d]	Second treatment	Outcome
1	Alhassan,et al.	40/F	None	Pneumonia -->AAC	14	I	Conservative		Discharge
2	Asti ,et al.	86/F	ND	Pneumonia -->AAC	ND	II	Lap-C		ND
3		72/M	ND	Pneumonia -->AA	ND	II	Lap-C		ND
4		40/M	ND	Pneumonia -->AAC	ND	II	Lap-C		ND
5	Balaphas,et al.	84/F	ND	AAC-->Pneumonia	4	II	Conservative	Lap-C	Multiple organ failure,Death
6		83/M	Renal failure	AAC-->Pneumonia	1	II	Conservative		ND
7	Bruni,et al.	59/M	ND	Pneumonia -->AAC	32	II	Cholecystectomy		Discharge
8	Cirillo,et al.	79/M	HT, DM	Pneumonia -->AAC	7	II	Cholecystectomy		Discharge
9	Hassani,et al.	65/M	HD,HT	0		I	Conservative		Discharge
10	Kabir,et al.	Uk/M	ND	Pneumonia -->AAC	9	II	Cholecystectomy		ND
11	Mattone,et al.	66/M	None	Pneumonia -->AAC	49	II	PTGBD	Lap-C	Discharge
12	Singh,et al.	66/M	HD	Synchronus		II	PTGBD		Hospitalization
13	Ying,et al.	68/F	None	Pneumonia -->AAC	9	ND	PTGBD		ND
14	Abaleka,et al.	76/F	HT,HD, asthma	Synchronus		II	Conservative		Discharge
15	Alam,et al.	84/F	None	Synchronus		II	Conservative		Pneumonia, Death
16	Rivera-Alonso, et al.	51/M	None	Synchronus		II	Conservative	Lap-C	Discharge
17	Futagami,et al.	42/M	Renal failure	Pneumonia -->AAC	18	II	PTGBD	Lap-C	Discharge
18	Berdugo,et al.	87/FM	ND	AAC		II	Conservative		Discharge
19		62/M	ND	AAC		II	Conservative		Discharge
20	Our study	91/M	DM,AR,HT Dyslipemia	Pneumonia -->AAC	18	I	Conservative		Discharge

Lap-c: laparoscopic cholecystectomy; PTGBD: Percutaneous transhepatic gallbladder drainage; AAC: acute acalculous cholecystitis; ND: Not described; HD; Heart disease; HT: Hypertension; AR: Reumatoid arthrite; DM: Diabetes Mellitus.
[a]Temporal relationship between AAC and COVID19 pneumonia.
[b]Time-lag between AAC and pneumonia.
[c]Severity grading for acute cholecystitis according to Tokyo guidelines 2018.
[d]Initial treatment within two days of onset.

The optimal management of AAC remains controversial, particularly when it is caused by SARS-CoV-2 infection [14], although it is important to point out that in 50% of the cases (ours included), the approach was conservative. The initial treatment for cases with moderate AAC (severity grading for acute cholecystitis according to Tokyo guidelines 2018), was emergency cholecystectomy in 6 patients and PT-GBD in 4 patients.

These results suggest that even with AAC caused by SARS-CoV-2, emergency cholecystectomy should be considered according to the Tokyo guidelines 2018 in cases with marked local inflammation [14]. On the other hand, considering that there were cases in which SARS-CoV-2- related pneumonia became evident after surgery, the treatment strategy for AAC with the elevation of inflammatory markers but without marked local inflammation such as gangrenous cholecystitis should be selected cautiously.Concretly, PTGBD could be a useful bridging treatment option before elective cholecystectomy in selecionated cases, such patients who required mechanical ventilation [14].

Conclusion

In conclusion, we have presented a new case of AAC related to SARS-CoV- 2 pneumonia and a literature review to gain insight into its clinical features. We cannot establish the true causative role of SARS-CoV-2 in the pathogenesis of acute cholecystitis in our patients. Although the presence of SARS-CoV-2 in the bile was not examined in our case, given that AAC typically develops in critically ill or immunosuppressed patients and that organ hypoperfusion is one of the underlying mechanisms according to the hypothesis suggested by H. Futagami et al. [14], we might consider SARS-CoV-2 infection was an important trigger for AAC in our case, with the added peculiarity that it is an almost centenarian patient who evolved favorably with a conservative approach. Finally, we conclude that further studies will be necessary to select the most appropriate treatment option in similar cases [8,14].

Declarations

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Consent: Written informed consent was obtained from the patient for publication of this case report and accompanying images.

Conflicts of interest: The authors declare no conflicts of interest.

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