Translated by A.P. Strelkova

Research Article

https://doi.org/10.23934/2223-9022-2024-13-1-72-78

Liver Abscesses in Patients Who Have Had a New Coronavirus Infection

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AIM OF STUDY To analyze clinical, laboratory, instrumental and microbiological data in patients with diagnosed liver abscesses who had previously had a new coronavirus infection.

MATERIAL AND METHODS An analysis of the work carried out with 13 patients who received treatment at the surgical clinic of the Botkin Hospital in the emergency surgical department No. 76 from September 2021 to October 2022 for liver abscesses and previous COVID-19 is presented.

RESULTS All presented patients were comprehensively examined. Surgical intervention was performed — transcutaneous drainage of liver abscesses under ultrasound guidance. Positive changes were revealed in the course of complex therapy, including antibacterial (based on the results of a microbiological study with determination of the sensitivity of the flora to antibacterial drugs), anti-inflammatory, and daily sanitation of the abscess cavity. All patients were discharged for outpatient follow-up treatment in stable, satisfactory condition. Nine patients (69.2%) were discharged with drain under the supervision of clinic doctors. In 5 patients (30.8%) with regression of the abscess cavity, drainage from the abscess cavity was removed before discharge.

CONCLUSION Patients with previous COVID-19 may develop liver abscesses. It is important to conduct thorough diagnostic measures in patients who present with fever and (or) abdominal pain after a coronavirus infection. Further prospective studies are needed, including morphological assessment of liver changes (upon autopsy in case of death).

Keywords: coronavirus infection, liver abscess, percutaneous drain

For citation Bagatelia ZA, Bedin VV, Chechenin GM, Eminov MZ, Kolotilshchikov AA, Gorbanev SV, et al. Liver Abscesses in Patients Who Have Had a New Coronavirus Infection. *Russian Sklifosovsky Journal of Emergency Medical Care.* 2024;13(1):72–78. https://doi.org/10.23934/2223-9022-2024-13-1-72-78 (In Russ.)

Conflict of interest Authors declare lack of the conflicts of interests

Acknowledgments, sponsorship The study has no sponsorship

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ACE2 – angiotensin-converting enzyme 2
ALT – alanine aminotransferase
ARDS – acute respiratory distress syndrome
AST – aspartate aminotransferase
CRP – *C*-reactive protein
CT – computed tomography
MRI – magnetic resonance imaging

INTRODUCTION

Coronavirus infection (*COVID*-19) is an acute respiratory infectious disease caused by acute respiratory syndrome coronavirus (*Severe Acute Respiratory Syndrome Coronavirus - SARS-CoV* 2) and has become a public health problem worldwide [1]. *SARS-CoV* 2 belongs to the *Coronaviridae family* and is a single-stranded RNA virus. The main target of this virus is the angiotensin-converting enzyme 2 (ACE2) receptor. Thus, *COVID-19* primarily affects the respiratory system [2].

In addition, ACE2 receptors are also present in the liver, gastrointestinal tract, heart, kidneys, pancreas, muscles and nervous system. According to recent research works, *COVID*-19 is regarded as a systemic infectious and inflammatory disease [3, 4].

Several studies have been conducted on liver disease in patients who have had *SARS-CoV* 2 infection. Studies have shown that the coronavirus can bind to ACE2 receptors on cholangiocytes and lead to their dysfunction, which causes a systemic inflammatory response and liver damage [5]. In addition, immune-mediated inflammation in severe forms *of COVID*-19 is accompanied by increased levels of *C* -reactive protein (*CRP)*, *D*-dimer, interleukin-6 and ferritin, which contributes to liver damage [6].

Epidemiological studies have shown that half of the patients had liver dysfunction, in particular increased levels of alanine aminotransferase (ALT) or aspartate aminotransferase (AST), and 1% of patients had severe liver damage, including liver abscess [7].

MATERIAL AND METHODS

The work is based on an analysis of the medical records of 13 patients treated at the surgical clinic of the Botkin Hospital in the emergency surgical department No. 76 from September 2021 to October 2022 for liver abscesses. The main characteristics of the patients are presented in Table 1.

Table 1
Main clinical characteristics of patients

Indicators		
Age (*M±SD)*, years	61.2±9.3 (38–74)	
Gender, *n* (%)	Men 8 (61.54%)	Women 5 (38.46%)
Body mass index (*M±SD)*, kg/m^2	27.8±2.9 (21.9–32.4)	
Antibodies to *SARS-CoV* -2 (*M±SD)*	Ig *M*	Ig *G*
	0.93±1.03 (4.01–0.19)	163.17±130.7 (358.17–7.96)

The criterion for inclusion in the study was a history of a new coronavirus infection without previous vaccination. All patients underwent a systematic, comprehensive preoperative examination and postoperative monitoring. A full range of laboratory tests was performed, ultrasound of the abdominal cavity, computed tomography (CT) of the abdominal cavity with intravenous contrast, magnetic resonance imaging (MRI) of the abdominal cavity with intravenous contrast, cytological and microbiological studies.

RESULTS

Thirteen patients were hospitalized at the surgical clinic of the Botkin Hospital with complaints of abdominal pain and hyperthermia. During the screening examination, according to abdominal ultrasound, large fluid formations in the liver were visualized (from 1 to 3), ranging in size from 20×18×14 mm to 185×150×135 mm. Intra- and extrahepatic biliary hypertension was not detected in any patient. Also, all patients showed changes in the laboratory picture, namely leukocytosis, increased transaminases and *CRP*; hyperbilirubinemia, increased alkaline phosphatase and γ-glutamyl transpeptidase were not observed in any case.

All hospitalized patients had a history of a new coronavirus infection 4–6 months before the current hospitalization, without previous vaccination. Eight patients (61.5%) had bilateral polysegmental pneumonia during the period of *COVID-19* disease. In the remaining 5 patients (38.5%) no evidence of pneumonia was obtained. Therefore, these patients were required to undergo a blood test for antibodies to *SARS-CoV*-2 (Ig *M* and Ig *G)*. All patients showed a significant increase in Ig *G* antibody titer.

Upon further examination, according to abdominal CT data with intravenous contrast, in these patients, multi-chamber hypodense formations in the liver parenchyma were determined, with uneven, indistinct contours, actively accumulating contrast agent along the periphery (Fig. 1). There were no disturbances in hepatic blood flow, and no areas of hypoprefusion of the liver parenchyma were visualized.

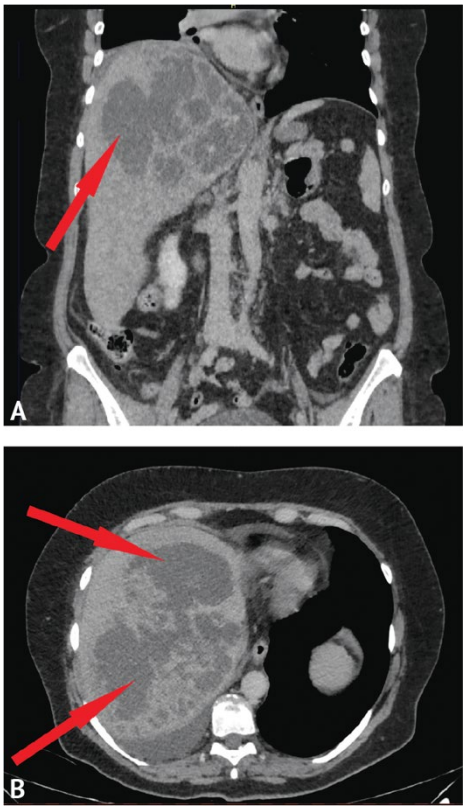

Fig. 1. Multislice computed tomography. Liver abscess. A - coronal section; B - axial section. Multichamber hypodense formations in the liver parenchyma with uneven, unclear contours (indicated by an arrow)

These patients also underwent MRI of the abdominal cavity with intravenous contrast, in which the above formations were described as cystic, with signs of limited diffusion and sedimentation, and weakly accumulating the contrast agent in the walls (Fig. 2).

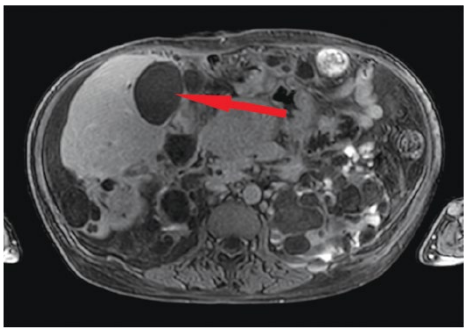

Fig. 2. Magnetic resonance imaging. Liver abscess. Axial section (abscess indicated by arrow)

Additionally, we performed a blood test for antibodies to parasitic liver diseases and tumor markers. In all cases the result was negative.

After a comprehensive additional examination, all patients underwent surgical intervention involving percutaneous drainage of fluid accumulations in the liver under ultrasound control. In all cases, thick, creamy pus was obtained.

The contents of the abscess cavity were subjected to cytological and microbiological studies. Cytological examination revealed large numbers of half-disintegrated neutrophilic leukocytes and macrophages in all patients. During microbiological analysis, *Klebsiella pneumonia* culture in various titers was revealed in all patients and *Escherichia coli* was additionally detected (in 3 cases, 21.3%). The sensitivity of the resulting microflora to antibacterial drugs was determined. Two types of antibiograms were obtained, which are presented in Table 2.

Table 2

Antibioticograms

n =10 (79.9%)	*n* =3 (23.1%)
Aztreonam: S	Amoxicillin/clavulanic acid: *S* (*MIC*: ⩽2/2)
Doripenem: *S*	Ampicillin: *R* (*MIC*: 16)
Imipenem: *S*	Ampicillin/sulbactam: *S* (*MIC*: 2/8)
Meropenem (other): *S* (*MIC:* ⩽0.25)	Piperacillin/tazobactam: *S* (*MIC:* ⩽4/4)
Ertapenem: *S* (*MIC:* ⩽0.12)	Gentamicin: *S* (*MIC:* ⩽2)
Amoxicillin: *R*	Amikacin: *S* (*MIC:* ⩽8)
Ampicillin: *R* (*MIC:* >16)	Imipenem: *S* (*MIC:* ⩽0.25)
Amoxicillin/clavulanic acid (other): *S* (*MIC:* ⩽2)	Ertapenem: *S* (*MIC:* ⩽0.25)
Gentamicin: *S* (*MIC:* ⩽1)	Meropenem: *S* (*MIC:* ⩽0.125)
Tobramycin: *S*	Levofloxacin: *S* (*MIC:* ⩽0.5)
Amikacin: *S* (*MIC:* ⩽2)	Ciprofloxacin: *S* (*MIC:* ⩽0.125)
Trimethoprim/sulfamethoxazole: *S* (*MIC:* ⩽20)	Trimethoprim/sulfamethoxazole: *S* (*MIC:* ⩽2.38)
Fosfomycin: *R* (*MIC:* 64)	Cefazolin: *I* (*MIC:* ⩽4)
Cefepime: *S* (*MIC:* ⩽0.12)	Cefepime: *S* (*MIC:* ⩽1)
Cefixime: *S*	Ceftazidime: *S* (*MIC:* ⩽1)
Cefoxitin: *S*	Ceftriaxone: *S* (*MIC:* ⩽1)
Cefotetan: *S*	Ceftolozane/tazobactam: *S* (*MIC:* ⩽1/4)
Ceftazidime: *S* (*MIC:* ⩽0.12)	Cefuroxime: *I* (*MIC:* ⩽4)
Ceftriaxone: *S*	
Ceftazidime/avibactam: *S*	
Ceftolozane/tazobactam: *S*	
Cefotaxime (other): *S* (*MIC:* ⩽0.25)	
Ciprofloxacin: *S* (*MIC:* ⩽0.25)	

Notes: *I* — intermediate resistance; *R* - resistant; *MIC* — minimum inhibitory concentration; *S* — sensitive

All patients received complex treatment, including appropriate antibacterial therapy based on culture results, anti-inflammatory therapy, and daily washing of abscess cavities with antiseptic solutions. During the treatment, there was an improvement in the general condition, regression of fever, a significant decrease in the discharge of discharge through the drainage, and in some cases, its complete absence.

During control laboratory tests, normalization of all parameters was noted, including leukocytes, transaminases and CRP. The dynamics of laboratory parameters are reflected in table 3.

During control instrumental studies (including fistulography), there was a significant reduction in abscess cavities, and in 5 cases a complete regression of the cavity to the size of a drainage tube (Fig. 3). There was no communication with the bile ducts in any case.

All patients were discharged for outpatient follow-up treatment in stable, satisfactory condition. Eight patients (61.5%) were discharged with drainage under the supervision of doctors at the clinic. Subsequently, the drains were removed on an outpatient basis 1–3 weeks after control studies were performed. In 5 patients (38.5%), where regression of the abscess cavity was noted, drainage from the abscess cavity was removed before discharge. No deaths were reported.

Table 3

Dynamics of laboratory parameters

Indicators	Before	After
Leukocytes (*M±SD*), ×10 ^{9} /l	16.1±4.19 (24.1–8.4)	7.7±1.3 (13.6–5.6)
ALT (*M±SD*), U/l	93.1±56.8 (363–17.3)	19.9±7.4 (30.1–5)
AST (*M±SD*), U/l	90.3±65.2 (282–21)	25.4±8.6 (41–14)
CRP (*M±SD*), mg/l	248.6±41.6 (333.8–177.8)	103.8±40.7 (175.2–3)

Notes: ALT — alanine aminotransferase; AST — aspartate aminotransferase; CRP — C-reactive protein

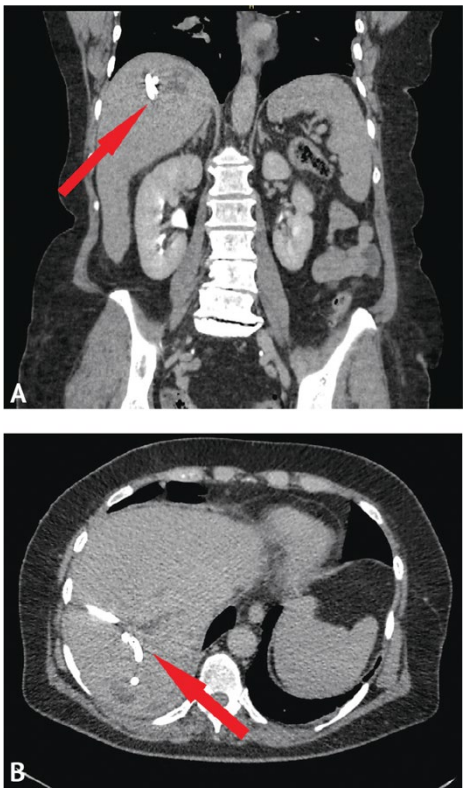

Fig. 3. Multislice computed tomography. Liver abscess after ultrasound drainage. A - coronal section; B - axial section. A drainage tube is visualized; the abscess cavity has shrunk (indicated by an arrow)

DISCUSSION

When analyzing domestic and foreign literature, little data was obtained on liver abscesses in patients who suffered a new coronavirus infection, which is reflected in isolated publications of clinical cases. Our work presents an analysis of the case histories of 13 patients.

Signs and symptoms of gastrointestinal diseases are common in patients who have had *COVID*-19. A study conducted by *J. Weng et al.* [8], shows that 52 patients (44%) out of 117 had gastrointestinal complications after suffering a new coronavirus infection, including lack of appetite, nausea, diarrhea, bloating, belching, vomiting, abdominal pain and bloody stools.

Among all the medical histories of patients analyzed by us, the prevailing complaints were abdominal pain syndrome and hyperthermia.

F. A. Ferri et al. [9] in 2020 presented a clinical case of a patient with a purulent liver abscess who had recovered from *COVID*-19. Liver abscess is an extremely rare disease with an annual incidence of 2.3 cases per 100,000 population. The authors believe that all medical workers, in particular surgeons, should be aware not only of the typical respiratory symptoms *of COVID*-19, but also of the possible extrapulmonary manifestations of this disease.

At the end of 2021, *A.K. Liemarto et al.* [10] published a description of a clinical case of liver abscess with necrosis in a patient who had *SARS-CoV*-2. The team of authors argues that the pathophysiological causes of liver damage after COVID-19 are direct cytotoxicity *of SARS-CoV*-2, immune-mediated damage due to systemic inflammatory response syndrome (*SIRS)*, hypoxemia and vascular changes due to coagulopathy, endothelialitis or congestion due to right ventricular failure and drug-induced liver damage.

Patients with severe *COVID*-19 may develop hypoxic-ischemic liver injury (*HILI)*. A study *by Zhong et al.* [11] showed that liver ischemia-reperfusion injury can activate Kupffer cells, neutrophils and platelets, causing cellular destructive responses that lead to inflammation and liver damage. Impaired microcirculation due to damage to liver endothelial sinusoidal cells will also aggravate liver ischemia and oxygen deficiency.

Hypoxia and inflammation are common in patients with severe *COVID*-19, which play an important role in regulating hepatocellular *ACE* 2 expression. This explains the reason for the extrapulmonary dissemination *of SARS-CoV* 2 in patients with acute respiratory distress syndrome (ARDS) and hypoxia. Hypercoagulability in patients with *COVID*-19 also promotes liver injury with pulmonary thrombotic complications, which aggravates acute right ventricular failure caused by high pulmonary vascular resistance in ARDS and leads to liver stasis [12].

Most likely, the combination of the above factors and pathophysiological processes led to the formation of liver abscesses in the patients we presented. However, despite the small number of scientific works and insufficient understanding of all the morphological changes occurring in patients after *COVID*-19, in our clinic there was not a single death in patients with diagnosed liver abscesses. It is worth noting that in all the patients presented, minimally invasive treatment methods were used, which made it possible to avoid traumatic surgery. All 13 patients were discharged in stable condition.

CONCLUSION

1. Patients with previous *COVID*-19 may develop liver abscesses, and most likely this is due to direct damage to cholangiocytes through direct binding of the coronavirus to angiotensin-converting enzyme receptors.

2. Also an important factor is the change in immune status against the background of a systemic infectious and inflammatory disease in these patients.

3. Patients with severe *COVID*-19 may develop hypoxic-ischemic liver damage. It is important to conduct thorough diagnostic measures in patients who present with fever and (or) abdominal pain after a coronavirus infection. Further prospective studies are needed, including morphological assessment of liver changes (upon autopsy in case of death).

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Received on 02/14/2023
Review completed on 09/20/2023
Accepted on 12/26/2023