Section 3

Clinical case

IRSTI 76.29.50: https://doi.org/10.26577/IAM.2020.v1.i2.09

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ACUTE VIRAL HEPATITIS CAUSED BY SARS-COV-2

Background Liver damage during SARS-CoV-2 is more often manifested as part of a cytokine storm and is a predictor of a more severe course of the disease. However, there is scant information on spontaneous liver damage during coronavirus infection.

Aims To report on the acute coronaviral hepatitis manifestations.

Methods In our study, we analyzed two clinical cases with SARS-CoV-2 debuted with acute hepatitis.

Results Patients who tested positive for coronavirus had symptoms of acute viral hepatitis, elevated transaminases titles and minimal lung involvement. Moreover, one of the patients developed diabetes for the first time. Steroid treatment resulted in improved liver function tests, clinical findings, but not diabetes.

Conclusion These cases indicate that acute hepatitis can be an independent manifestation of SARS-CoV-2 and that liver damage can be combined with damage to the pancreas, causing diabetes. Timely therapy with an adequate dose of glucocorticosteroids helped to stop the progression of the disease and avoid complications.

Key words: SARS-CoV-2, Acute Viral Hepatitis, Coronaviral Hepatitis

Introduction

Coronavirus-2 Severe Acute Respiratory Syndrome (SARS-CoV-2) caused by the RNA beta coronavirus spread in December 2019 from Wuhan, China and became a worldwide pandemic [1]. The main organ-specific manifestations are the lungs and the cardiovascular system, which lead to complications such as acute respiratory distress syndrome (ARDS) and thromboembolism [2]. It is known that due to the tropism of the coronavirus to the Angiotensin Converting Enzyme-2 receptor (ACE2) of the gastrointestinal tract (GIT), coronavirus can cause symptoms such as nausea and diarrhea appearing from, moreover it may be detected in gastrointestinal secret and stool and increase liver enzymes in 20-30% cases [3,4]. Using single-cell RNA sequencing, scientists have proven that ACE2 is present mainly in cholangiocytes and 20 times less in hepatocytes, and such a number of receptors cannot cause coronavirus-associated hepatitis [5]. Elevated transaminases occurs in patients during a cytokine storm, hypoxaemia caused by pneumonia and/or the toxic effect of drugs used for treatment [6,7]. In this report we showed that liver involvement can be an independent manifestation of SARS-CoV-2.

Case presentation

Previously healthy 40-year-old male doctor, on day 10 after contact with a SARS-CoV-2 infected patient was admitted to the hospital with a dry paroxysmal cough, fever up to 39 degrees, nausea, slight malaise in the right hypochondrium, general weakness. Two days after contact with a patient who tested positive for coronavirus by PCR, he developed the above symptoms. CT scan revealed: mild focal pneumonia of viral etiology. PCR for SARS-CoV-2 was positive, patient was negative for viral hepatitis B and C. There were no any signs of chronic liver disease, no peritoneal irritation, ascites or hepatic encephalopathy was observed on physical examination. In the lungs, hard breathing with fine bubbly hips on the left and weakening of breathing in the lower sections was detected. Abdominal percussion revealed dullness on the right. The general condition was severe due to liver damage. On admission blood test showed an increase in transaminases, bilirubin and glucose (table1). The lymphocyte count in this patient was the highest with an absolute number of 3.6 checked by FACS analysis.

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Table 1. Laboratory results

Timing	Before hospitalisation	During hospitalisation		At discharge	*Normal values*
ALT (U/I)	579	361	218	132.5	*(0–45 U/L)*
AST (U/I)	224	110	53.7	37.5	*(0-35 U/L)*
Total bilirubin (mg/dL)	9.9		6.9	8.2	*(5.1–9.0 mg/dL)*
Direct bilirubin (mg/ dL)	3.2				*(<0.3 mg/dL)*
Glucose (mmol/L)	6.3	6.37	6.76	7.4	*(3.89 – 5.83 mmol/L)*
Amylase (U/L)		32	55	54	*(30-110 U/L)*
CRP (mg/L)	15.3		4.9	3.1	*(<5 mg/L)*
Ferritin (ng/mL)	>1000				*(20-250 ng/mL)*
D-dimer (mg/L)	1.06	1.26	1.07	0.61	*(<500 mg/L)*
ESR (mm/h)	36				*(<10 mm/h)*
Leukocytes	11.5	12,3	13,18	13,44	*(4-9 x10^9/L)*
Lymphocytes	5.29	7,9	7,68	9,78	*(1.2-3.0 x10^9/L)*
Platelets	196	246	256	320	*(180-320 x10^9/L)*

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C reactive protein, ESR: Erythrocyte sedimentation rate.

Treatment

The patient was regularly tested to assess the condition of the liver and was treated with methylprednisolone 250 mg/day 1 day and ademetionine 500 mg/day 10 days, metformin 1500 mg/day daily.

Outcome and follow-up

During the hospital stay transaminases markedly improved (table 1) all clinical symptoms regressed, however, the patient had a persistent increase in blood glucose, fasting 9 mmol/L. In this case, a healthy person, after being infected with a coronavirus, developed type 2 diabetes. After discharge from the hospital, the patient took metformin protractedly.

Case presentation

A50-year-old man from another hospital 7 days after exposure to a SARS-CoV-2 infected person complained of severe dyspeptic symptoms: heaviness and pain in the epigastric region, bloating, absence of stool and gas, nausea, weakness, decreased appetite and sweating. The patient has a history of type 2 diabetes. Objectively, the liver is enlarged by 1 cm. His blood tests showed elevated amylase, transaminase and glucose levels (table 2). PCR for SARS-CoV-2 was positive. There were minimal changes in the lungs with signs of chronic bronchitis. An abdominal ultrasound revealed pancreatitis. During palpation, the abdomen was sensitive in the upper part, intestinal motility was sluggish.

Table 2. Laboratory results

Timing	Before hospitalisation	During hospitalisation		At discharge	*Normal values*
Amylase (U/I)	3455	3451	3600	35	*(30-110 U/L)*
ALT (U/I)	554		184	60.2	*(0–45 U/L)*
AST (U/I)	368.9		34	39	*(0-35 U/L)*
Total bilirubin (mg/ dL)	67.6			31.55	*(5.1–9.0 mg/dL)*
Glucose (mmol/l)	7.66	9.2	4.5	5.04	*(3.89 - 5.83 mmol/l)*
CRP (mg/L)	215.55	35.34	4.9	3.1	*(<5 mg/L)*
Ferritin (ng/mL)	1147.5			740.1	*(20-250 ng/mL)*
D-dimer (mg/L)	0.80			0.29	*(<500 mg/L)*
ESR (mm/h)	20			45	*(<10 mm/h)*
Leukocytes	12,3			15,3	*(4-9 x10^9/L)*
Lymphocytes	1,1			1,21	*(1.2-3.0 x10^9/L)*
Platelets	318			216	*(180-320 x10^9/L)*

AST: Aspartate aminotransferase, ALT: Alanine aminotransferase, CRP: C reactive protein, ESR: Erythrocyte sedimentation rate.

Treatmen

The patient was treated with octreotide 0.1μg 3 days together with ademetionine 800mg/day first, since a differential diagnosis was carried out between pancreatic necrosis and pancreatitis. Thereafter methylprednisolone 250mg/day 3 days was assigned for the treatment of hepatitis.

Outcome and follow-up

After the therapy the blood tests normalized progressively (table 2). The patient was discharged from the hospital without symptoms of dyspepsia. His liver function tests dropped significantly, although not all tests returned to normal. Blood sugar was regulated by the administration of metformin.

Discussion

The affinity of the virus for the ACE2 receptors that are located on special enterocytes and ileum explains the involvement of the gastrointestinal tract in the pathological process in patients with coronavirus [3,4]. While being negative for SARS-CoV-2 RNA in oral test, it was positive in anal and rectal swabs [5]. It has been reported that the digestive system and liver are affected in patients with COVID-19 who have more severe disease [8,9]. At the autopsy of the patients, it turned out that SARS-CoV2 was found in 41% of liver tissue [10]. Liver biopsies of patients showed hepatocellular necrosis, mitosis, cellular infiltration, fatty degeneration, microvesicular steatosis and mild inflammation in the lobular and portal area was observed. SARS-CoV2 can directly affect the liver or, most often, indirectly, through the activation of the innate immune system, in particular, an increase in the level of C-reactive protein, lymphocytes, neutrophils, cytokines and IL-6, the so-called "cytokine storm"[11]. According to our data, we showed acute hepatitis SARS-CoV2 with liver damage occurred from the very beginning, and minimal lung damage. Against the background of the treatment, the analyzes returned to normal very quickly. Subsequently, one of the patients for the first time after infection with SARS-CoV2 developed type II diabetes, for which he continues to receive antihyperglycemic therapy. We found only one publication that described a case of coronavirus hepatitis with minimal lung damage and a rapid positive trend in therapy [12]. It is very important in such cases to exclude direct and mediated covid-associated liver damage with increased ALT and AST during cytokine storm and in patients with ARDS. It is also necessary to exclude the reactivation of chronic viral hepatitis. In our case patients with coronavirus infection developed diabetes mellitus, possibly due to the direct action of the virus on the pancreas, or there was another mechanism. These patients had a different clinical course, apparently not related to the virus strain, since they became infected in patients with a typical coronavirus disease. The course of the disease was moderate, possibly associated with a higher level of lymphocytes in their blood than others. More new cases will be identified.

Conclusion

1. Acute coronavirus hepatitis has been associated with minimal lung damage.
2. Patients did not have lymphopenia.
3. After steroid therapy for at least 250 mg/day was a quick positive dynamics.

Treatment

The patient was treated with octreotide 0.1mAcute coronavirus hepatitis has been associated with minimal lung damage.

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