Histopathology and Ultrastructural Findings of Fatal COVID-19 Infections in Kurdistan Province, Iran: A Case Series

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Abstract

Background: Coronaviruses, including severe acute respiratory syndrome coronavirus (SARS-CoV) and is the cause of an ongoing pandemic, with increasing deaths worldwide. Here in we present the results of the histopathological study of the main organs of 25 patients who died due to confirmed COVID-19.

Methods: In this case series, patients base on needle necropsy of multiple organs of dead patients with a positive antemortem SARS-CoV-2 (COVID-19) real time PCR. Needle necropsy of corpses of 25 patients enrolling the study were performed until 3 hours after death in the negative-pressure isolation morgue who hospitalized at Kurdistan University of medical sciences Tohid and Kowsar hospitals with proved COVID-19 infection and were died due to severe disease manifestations.

Results: The mean age of the participants in this study was 74.68 ± 9.41 (52–91) years old. The participants included 19 men (76%) and 6 women (24%). In myocardial necropsy, twelve patients were reported to be lymphocytic myocarditis, three of them were reported to have pericarditis as well, and in one case focal visual fibrosis was reported. Histopathological examinations of liver revealed that among twenty-two samples, five cases had acute hepatitis that four of them were mild in type. Steatohepatitis was reported in six cases and two of them were macrovesicular in type. Macrovesicular Steatosis was reported along with steatohepatitis and stage 4 fibrosis through trichrome staining. Muscles necropsy revealed viral myositis for three patients.

Conclusions: Our study shows extra-pulmonary multi organ involvement through COVID-19 disease. 77% of patients representing acute or chronic hepatitis and 48% of them revealed lymphocytic myocarditis accompanied with pericarditis in 12% of cases and 12% of patient's show myositis. It looks diffuse inflammatory disease which attacks to some organs like myocardium, liver and muscles. Broad extra pulmonary pathology and laboratory findings are occurred that all suggestive of multi organ involvement directly or through systemic viremia and immune system response.

Background

The high mortality rate of coronavirus (COVID-19) made it at the forefront of the scientific and health news during the last 17 months (1). So, immediate management of COVID-19 in terms of recognizing its epidemiological and pathological dimensions is essential due to its impact on various aspects of human lives worldwide (2). Though, multiple histopathological studies have been conducted in the field of post mortem autopsy but it still seems that the number of these studies is limited compared to the extent of disease and more assessments are demanded (3-7).

Needle necropsy is one of the method to evaluation of pathogenesis in main organs of dead patients due to Covid-19 with high level of infectivity by considering the principles of personal protection. Needle necropsy can be a useful way to determine underlying pathology in sudden death of communicable disease such COVID-19 and to save lives (5, 6). Although in early steps of the epidemic autopsies were more focused on pulmonary parenchyma, however gradually by identifying the involvement of various organ involvement in Covid-19 viremia, histopathological studies also shifted to multi organ sampling (1, 5). Here in we present the results of the histopathological study of the main organs of 25 patients who died due to confirmed COVID-19.

Methods

Patient's selection and necropsy procedures

This case series study designed base on needle necropsy of multiple organs of dead patients with a positive antemortem SARS-CoV-2 real time Polymerase chain reaction (PCR) from April 2020 to August 2020. The patients were included in the study who hospitalized at Kurdistan University of medical sciences Tohid and Kowsar hospitals with proved COVID-19 infection and were died due to severe disease manifestations. Both hospitals used the CDC-designed 2019 CoV real-time RT-PCR assay for virus detection. Needle necropsy of corpses of 25 patients enrolling the study were performed until 3 hours after death in the negative-pressure isolation morgue of the both hospitals. Full observance of health protocols and personal safety protection in accordance with the guidelines of the World Health Organization (WHO) were considered. Five formalin-filled containers were submitted per necropsy sampling of multi organs consisting heart, liver, muscles, breasts and scrotum. Next they transmitted to pathology laboratory in short time by observing all principles of the relevant standards. The license of the University Ethics Committee was obtained before the study began (IR.MUK.REC.1399.024).

Histologic examination

Necropsy materials of multi organs were put in containers filled by 10% neutral buffered formalin and labeled by patient's name, hospital and admission ward and then for standard processing, paraffin embedding, microtome sectioning and finally hematoxylin and eosin staining. For liver and heart samples trichrome and iron stains were done additionally.

Personal Safety Considerations

Complete precautions were taken during performing the necropsy in accordance with WHO guidelines to prevent infection during sampling including wearing a special gowns, gloves, eyeglasses, face mask and all necessary shielding.

Data Analysis

Descriptive statistical methods were used to present the collected data. All statistical analyses were performed using Stata16.0 software (StataCorp, College Station, TX).

Results

Patient characteristics

The mean age of the participants in this study was 74.68 ± 9.41 (52–91) years old. The participants included 19 men (76%) and 6 women (24%). Regarding underlying diseases, 18 patients were recognized. One of the patients had one kidney and seven of them had no comorbidities. The mean time of hospitalization was 7 days for patients, and the mean time of hospitalization in Intensive Care Unit (ICU) was 4.4 days and hospitalization in wards was 3.7 days. A patient was hospitalized for 54 days, and he was deleted from the average calculation (Table 1).

Fever, fatigue and pulmonary distress were the most common primary symptoms. Intubation was conducted for 19 patients (76%) during the time of hospitalization. Other patients were intubated during cardiopulmonary resuscitation (CPR). Most of the intubation cases were performed in the first 24 hours of admission. Two patients were intubated and expired six hours after being admitted to the emergency ward. All patients were treated using venous anticoagulants or subcutaneous injection except for four ones (Table 1).

Patients' medical records were retrospectively reviewed. The requested laboratory tests showed that lactic acid dehydrogenase (LDH) had been measured in 17 cases, which were reported for five patients over 1000, including cases 3, 10, 15, 17 and 2 with LDH levels of 1649, 1274, 1037, 1011, and 7158, respectively. The highest level of LDH (7158) belonged to patient number 2, which had eighty-four year old. LDH was 500 to 1000 in eight cases (patients No. 6, 7, 8, 9, 13, 14, 16, and 20), and was normal (< 500) in four cases. Serum creatinine level was reported in the range of 1-3 for all patients except for three cases. An eighty-six-year-old woman with CKD and HTN (Patient No. 14) and fifty-two-year-old woman (Patient No. 8) with Hypertension (HTN) in their history were reported to have $Cr=7$. A sixty-seven-year-old man (Patient No. 12) with chronic active hepatitis was reported to have $Cr=5$. Blood urea nitrogen (BUN) was reported in the range from 74 to 218 for sixteen patients. Creatine phosphokinase (CPK) was reported in the range from 61 to 4984 for twelve cases. The highest level of CPK belonged to cases number 5, 6, and 10. The reported CPK levels were reported 4984, 2261, and 1032, respectively. The CPK level was reported 829 and 779 for cases number 17 and 12. Erythrocyte sedimentation rate (ESR) was in the range from 16 to >100 for eleven cases. The highest level belonged to patient number 19 (>100). D-dimer was checked for eight patients. It was reported 2188 for patient number 3 who was 80 years old male with previous medical history of cerebrovascular accident (CVA) and 200 for three cases (cases number 2, 15, 20) that were 84-year-old male, 91-year-old male and 71-year-old female with single kidney respectively. The checked D-dimer was reported 115 for patient number 8. Patient number 2, had the highest LDH level (7158). CRP and ESR were reported 68 and 16. The patient had $Hb=13$ and $Hct=60.1$ at admission, and the before mentioned factors were reported 20 and 58.4 before death. At the time of admission, Plt was 203 and White blood cells (WBC) was reported 14.3 and at the time of death they were registered as $Plt=185$ and $WBC=14$. Hemoglobin level was checked at the time of admission for nineteen patients. $Hb<6$ was reported in four cases (number 8, 14, 17, and 23). For patient number 20, $Hb=8$ was reported at the time of admission. The range of Hb was 10-15 for the other ten patients (Table 3).

Hemoglobin (HB) level for patient's number 13, 9, 6, and 2 were 17.10, 17.70, 20, and 21.6 respectively. The lowest hemoglobin level checked before death belonged to the patient number 25 ($Hb=2.63$). Plt checked for patients ranged from 31 (in Patient No. 8) up to 324 (for Patient No. 19). White blood cells of the patients ranged from 5–15.50. For case number 6, $Hb=21.6$, $Hct=56.8$, $Plt=89$, and $WBC=5$ were reported at the time of admission. Hb was decreased to 16.4 with $Hct=48$ and $Plt=15$ before expiry. Ferritin was measured for nine patients and the results ranged from 8.5 to 2375. The ferritin level was reported above 2000 in three cases including case number 14 (2375), number 9 (2250), and number 3 (2310). It was reported 1650 for case number 10 and 500 for cases Patients No. 2, 8, 25. Calcium was checked for nine patients. The results ranged from 7.50 mg/dl in patient number 6 to 9.10 mg/dl in patient's number 2 and 7 (Table 1)

Magnesium (Mg) was checked in twelve patients. The results ranged 1.7 (for Patient No. 3) and 3 (for Patients No. 2 and 20). Serum glutamic oxaloacetic transaminase (SGOT) and serum glutamic pyruvic transaminase (SGPT) were measured for fifteen patients. SGOT ranged 18 (case number 20) to 180 (case number 12). SGPT ranged 10 (case number 18) to 3170 (case number 12). ALKP was checked in thirteen patients. The results ranged 119 (case number 9) to 373 (case number 11) (Table 2).

Eighteen patients had clinically significant comorbidities, the most common being hypertension, CVA, and diabetes disease (Table 3)

Histopathological analysis

In myocardial necropsy, twelve patients were reported to be lymphocytic myocarditis, three of them were reported to have pericarditis as well (Patients No. 13, 20, 21), and in one case focal visual fibrosis was reported (Patient No. 12) (Figure 1, Figure 2). Histopathological examinations of liver revealed that among twenty-two samples, five cases had acute hepatitis that four of them were mild in type. Steatohepatitis was reported in six cases and two of them were macrovesicular in type (Patients No. 21, 23) (Figure 3). Chronic active hepatitis was reported in four cases. Liver necropsy revealed that there was one case of cirrhosis (Patient No. 13) (Figure 4). Also there was a case of incomplete cirrhosis (Patient No. 11). Macrovesicular Steatosis was reported along with steatohepatitis and stage 4 fibrosis through trichrome staining for patient number 21. Mild periportal fibrosis (stage 1) was observed for patient number 23. Muscles necropsy revealed viral myositis for three patients (Patients No. 11, 12, 18). Testicular necropsy revealed one case of sertoli-cell only syndrome (germinal cell aplasia) and other testicular samples were unremarkable (Table 4).

Discussion

A vast range of pathologic findings have been reported about expired COVID-19 patients (8, 9). Several histopathologic evidences of severe extrapulmonary involvement leading to death in SARS-Cov-2 patients were investigated (1).

Endothelial injury risk increases along with micro thrombosis risk in COVID-19 patient (1, 10). Microvascular injuries in coronavirus infection were reported in initial reports proving endotheliitis as well as endothelial cells containing Corona viruses like particles in COVID-19 patients (11). However, regarding endothelial injuries, investigating endothelial cells containing corona virus is being done (12). A study, conducted using an electron microscope or immunohistochemistry, revealed the presence of corona viruses like particles in renal endothelial cells. However, similar findings were not reported in investigating endothelial cells of other organs. Moreover, histologic evidences for endotheliitis were not reported. In some studies, conducted using complete autopsy, evidences supporting micro thrombosis were not reported (1).

Cardiac injuries are prevalent in covid-19 patients although some studies did not reveal evidences supporting it (1). In a clinical study, 33% of ICU patients in Kirkland had cardiomyopathy with unclear reasons. After expiration, RNA of the virus was found in cardiac tissues of a patient. However, histopathologic evidences supporting myocarditis were not found (13).

In a study, 3 out of 14 patients had increased troponin; myocarditis histopathologic evidences were found for only one patient (1). In the present study, viral lymphocytic myocarditis histopathologic evidences were found in 12 patients, which is more than similar studies. It is important to mention that pericarditis in 3 patients and focal fibrosis in a patient were reported.

In the study 3 patients out of 14 had troponin increase and histopathologic evidences for myocarditis were found for only one patient (1). Viral RNA was extracted from PCR. However, immunohistochemistry and electron microscope results were negative. Regarding the fact that the patient had viremia, the low RNA extracted from cardiac tissues might be caused by viremia and the viruses in the bloodstream rather than direct injuries of the cardiac tissues.

The extension of extrapulmonary involvement in SARS-Cov-2 patients suffering from the non-severe type of COVID-19 is still unclear. Since SARS-Cov-2 was reported in stool and urine sample tests of non-severe type COVID-19 patients, there are evidences supporting presence of infection in extrapulmonary tissues (14, 15). These reports highlight concerns about high risk groups like patients suffering from chronic renal diseases, renal transplant and inflammatory bowel diseases patients. If such patients are exposed to higher risks of SARS-Cov-2 complications, accurate monitoring of these patients seems necessary.

Although extrapulmonary involvement in sub-clinical and mild type COVID-19 patients is lower, extrapulmonary active infection in patients without pulmonary infection has remained unclear.

One of the limitations of the present study is that sampling was not performed under the guide of ultrasound. Therefore, necropsy failed in some patients and sampling from liver tissues of three patients was not done correctly. So, those cases were excluded from the study.

Inflammatory myocarditis in 48% of patients, pericarditis in 3 patients (Patients No. 13, 20, 21), as well as inflammation in liver and muscles revealed the extent of inflammatory involvement in COVID-19 patients, which sometimes emerge with focal fibrosis.

Hepatitis has been observed as a super imposed disease to the underlying diseases in patients with chronic underlying liver diseases like cirrhosis. In the present study, 6 patients were suffering from hepatic steatosis.

Macrovesicular type was reported in 3 cases and stage 4 fibrosis was reported in one case. Five patients had acute hepatitis. This means that 11 patients (44% of the cases) experienced acute hepatitis. Four patients had chronic hepatitis. Active chronic hepatitis indicating stage 1, 2 fibrosis. Therefore, 60% of the patients had acute or chronic hepatitis according to histology findings. COVID-19 induced cirrhosis was reported in one patient (Patient No. 13) that was recognized with mild type acute hepatitis, negative trichrome staining and negative iron).

Overall, the main findings are 24% hepatic steatosis and 44% acute hepatitis. Regarding the number of patients with active chronic hepatitis, 60% of the patients had experienced different levels of hepatitis.

Fat droplets in hepatocytes along with vesicular steatosis were demonstrated in photomicrograph of small case series studies.

In Tian S et al. study, core needle biopsy of four patients' liver demonstrated that liver histopathologic changes were not exclusive, and the results might be associated to previous problems or perimortem injuries (13).

A study demonstrated moderate acute hepatitis along with acute cell rejection in patients receiving liver allograft (16, 17). Concerning the vast spectrum of the observed histopathology of liver in several studies, a significant question must be noticed. The question is whether the liver is directly affected by virus invasion or whether the damages are resulted from cytokine storm, or both.

The angiotensin converting enzyme receptors (ACE 2), commonly found on cholangiocytes in liver and rarely on hepatocytes, have been recognized as the main mode of entering cells. However, the number of the receptors increases on hepatocytes in physiologic stressful conditions (18). They are found on endothelial cells of portal liver coroners, either (11).

Autopsy of 40 COVID-19 patients revealed that two thirds of the cases had disordered liver function tests. In this study, fibrosis in two livers, abscess for one of the cases and different levels of inflammation, ischemia, and steatosis in others livers were reported

The most prevalent histologic findings were macrovesicular steatosis, moderate acute hepatitis and minimal-to-mild portal inflammation. In the above mentioned study, 75% of the patients were reported to have liver steatosis, which was macrovesicular in all cases. It is required to mention that the majority of the patients in that study had diabetes. This can justify the high percentage of patients with liver steatosis reported in the study.

Liver enzyme disorders like variations in SGOT, SGPT and ALKP were observed as shown in table 2. In another study, 50% of liver autopsy were reported to be steatotic (19).

It seems that regardless of underlying diseases like diabetes or drinking, COVID-19 infection causes steatosis in some patients. There are probably several contributing factors such as prescribing corticosteroids, hypoxia, malnutrition, and direct invasive impacts of the virus.

A study conducted in China showed the association between steatosis and the neutrophil to lymphocyte ratio (NLR ratio). The investigations showed that higher NLR is associated to more severe systemic inflammation. Thus, understanding the main mechanism of steatosis in Covid-19 requires further studies. findings of this study demonstrated that AST, ALT enzyme rising, revealed no statistically significant difference between patients with acute hepatitis and patients without lobular necroinflammation (20).

In the Stephen M et al. study (21), it was indicated that positive PCR test was significantly associated to acute hepatitis comparing to cases with negative PCR test results. The percentage of patients with acute hepatitis was 64% and 44% in positive PCR test group and negative PCR test group, respectively.

Bile duct injury was not observed in the present study like other related studies despite of the presence of ACE2 receptors (22) but cholestasis occurs commonly. Presence of lobular cholestasis without damaging biliary ducts is beneficial for hepatocellular injuries.

Endothelial injuries like lymphocytes endothelial inflammation and injury caused by COVID-19 have been reported in several studies (11, 22). In the present study vascular injury was not detected

A case series study conducted in Italy investigated vascular pathology (23). However, there were no evidences supporting vast vascular liver injuries in our study like Stephen M. et.al study (21).

Conclusions

Our study shows extra-pulmonary multi organ involvement through COVID-19 disease. 77% of patients representing acute or chronic hepatitis and 48% of them revealed lymphocytic myocarditis accompanied with pericarditis in 12% of cases and 12% of patient's show myositis. It looks diffuse inflammatory disease which attacks to some organs like myocardium, liver and muscles. Broad extra pulmonary pathology and laboratory findings are occurred that all suggestive of multi organ involvement directly or through systemic viremia and immune system response.

Declarations

Ethics approval and consent to participate

The Ethics Committee of Kurdistan University of Medical Sciences (IR.MUK. REC.1399.024) reviewed and approved this study. All patients provided written informed consents. The relevant guidelines and regulations performed all methods.

Consent for publication

Not applicable

Availability of data and materials

The datasets used and analyzed during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

BM, BN, and KN conceived and designed the study. BN, BM, KN and MAR analyzed and interpreted the data and drafted the manuscript. BM, BN, and KN were involved in the composition of the study tool, collect data, supervision of the research process, and critical revision and review of the manuscript. All the authors read and approved the final manuscript.

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Tables

Table 1. Patient characteristics, comorbidities and select initial laboratory findings

Age	Sex	Comorbidity	Hospitalization(Day)	Hospitalization in ICU ward	Hospitalization in ward	Intubation	Cr	LDH	Anticoagulation	BUN	ESR
77	Male	Diabetes/ CVA	1	1	0	Yes	3	353	positive	-	
84	Male	BPH	5	5		Yes	3	7158	positive	-	16
80	Male	CVA	12	6	6	Yes	1	1011	positive	-	
59	Male	-	1			Yes		-	negative	-	
72	Female	-	5	3	2	No	2	22	positive	-	
65	Male	-	5	4	1	Yes	1	988	positive	-	
85	Female	COPD	8	7	1	Yes	1	949	negative	45	13
52	Female	Hypertension	24	8	16	Yes	7	575	negative	74	
80	Male	-	8	0	8	No	1	630	positive	45	50
78	Male	Hypertension	13	4	9	Yes	1	1037	positive	29	50
85	Male	Cirrhosis	2	0	2	Yes	3	-	negative	72	
67	Male	CVA	11	8	3	Yes	5	336	positive	81	52
76	Male	-	7	2	5	Yes	1	746	negative	37	5
86	Female	Hypertension/ CKD	4	0	4	Yes	7	674	positive	67	40
91	Male	-	6	5	1	No	1	1274	positive	18	15
78	Male	MI	1	0	1	No	1	927	positive	17	
80	Male	Hypertension	4	0	4	Yes	2	1649	positive	3	30
70	Male	Hypertension	54	35	19	Yes	1		positive	7	38
79	Male	Diabetes/ Prostate Cancer	10	2	8	Yes	1	435	negative	3	1649
71	Female	Single kidney	28	28	-	Yes	2	564	negative	58	
68	Male	Diabetes	2	0	2	Yes	3	-	positive	60	
64	Male	RA/COPD/ Hypertension	1	1	0	No		-	positive	-	
70	Male	MI	1			Yes		-	negative	-	
66	Male	Hypertension	1	0	0	Yes	3	353	positive	-	
84	Female	-	8	7	1	No	3	7158	positive	27	16

Table 2. Summary of laboratory result

variable	Mean±SD (Min-Max)	Normal Range
r, N=20	2.29±1.89 (1-7)	Male: 0.8-1.3, Female: 0.6-1.2
UN, N=16	40.16±26.49 (3-81)	6 - 20 mg/dl
SR, N=11	178±488 (5-1649)	Male:5 - 12, Female: 6-20
DH, N=17	1136±1599 (22-7158)	235-470
PK, N=12	919±1429 (61-4984)	Male: 0-171, Female: 0-145
-dimer, N=8	365±741 (1-2188)	<200
erritin, N=9	1206±941 (8.5-2375)	Male: 21.8- 276, Female:4.63-204
a, N=13	8.41±0.46 (7.5-9.1)	8.6-10.3
lg, N=12	2.46±0.76 (1.7-7.5)	1.53-2.55
GOT, N=15	65.6±53.4 (14-180)	Male: <40, Female: <40
GPT, N=15	253.9±808.6 (10-3170)	Male: <45, Female: <34
LKP	225±88.1 (119-373)	Male: 0-270, Female: 0-240

Table 3. Frequency of patient's comorbidities

comorbidity	N=25	Percent
hypertension	7	28
II	2	8
VA	3	12
diabetes	3	12
cirrhosis	1	4
KD	1	4
single kidney	1	4
OPD	2	8
prostate Cancer	1	4
benign prostatic hyperplasia (BPH)	1	4
no Comorbidity	7	28

Table 4. Post-mortem findings by organ system by patient

ase	Heart	Liver	Muscle	Testis
	Unremarkable cardiac tissue	Unremarkable	Unremarkable	Unremarkable
	Skin tissue	Trichrome stain: Mild periportal fibrosis		
	Iron stain negative			
		Iron stain: negative		
	The smooth muscle (seems to have been sampled from the large artery)	Chronic acute hepatitis grade 1/6		
	Mild viral myocarditis	Trichrome stain: fibrosis stage 1/6	Mild lymphocytic (Viral) myositis	Unremarkable
		Iron stain: negative	myositis	
	Adipose tissue (Pericardium)	Skin tissue	Mild viral myositis	Sertolicell only syndrome (germinal cell aplasia)
	Unremarkable skin tissue	-	-	Skin tissue
	Iron stain: negative			
	Unremarkable iron stain: negative	Muscle tissue	Unremarkable	-
	Mild lymphosytis miocarditis	Macrovesicular steatostist	Unremarkable	Unremarkable
		Hepatitis(Steatohepatitis)		
	Miocarditis	Trichrom stain: negative		
	Iron stain: negative	Iron stain: negative		
	Unremarkable	Unremarkable	Unremarkable	-
	Iron stain: negative	Trichrome stain: negative		
		Iron stain: negative		
		Unremarkable liver tissue	Unremarkable	-
		Trichrome stain: normal		
		Iron stain: normal		
	Unremarkable	Unremarkable	Unremarkable	Unremarkable
	Iron stain: negative			
0	Connective tissue, fat, striated muscle, cartilage tissues (Non cardiac tissue)	Unremarkable	Unremarkable	Unremarkable
	Iron stain: negative	Trichrome stain: negative		
		Iron stain: negative		
1	Unremarkable	Cirrhosis (Incomplete)	Unremarkable	Unremarkable
	Mild lymphocytis myocarditis	Fibrosis stage:5	Unremarkable	
		Trichrome stain: incomplete cirrhosis		
	Iron stain: negative			
2	Mild lymphocytis	Chronic active hepatitis	Unremarkable	Connective tissue
	Myocarditis with focal interstitial fibrosis	Fibrosis stage: 2		
	Iron stain: negative	Iron stain: negative		
3	Mild	Chronic Cirrhosis	Unremarkable	Unremarkable
	Myocarditis	Hepatitis (mild form)		
	Pricarditis	Trichrome stain: negative		
	Iron stain: negative	Iron stain: negative		
4	Connective tissue, fat and skin tissue	Chronic active hepatitis (grade 1/6)	Unremarkable	-
		Trichrome stain: negative		
		Iron stain: negative		
5	Connective tissue, fat and skin tissue	Chronic active hepatitis (grade 1/6)	Unremarkable+ Skin tissue	Unremarkable
		Trichrome stain: fibrosis stage 2		
		Iron stain: normal		
6	Connective tissue, fat, cartilage tissues (Non cardiac tissue)	Mild acute hepatitis	Unremarkable	Unremarkable
		Trichrome stain: negative		
		Iron stain: normal		
7	Stomach tissue	Mild acute hepatitis	Unremarkable	Unremarkable
		Trichrome stain: negative		
		Iron stain: negative		
8	Mild lymphocytis	Acute hepatitis	Unremarkable	Unremarkable
	Miocarditis	Trichrome stain: negative		

	Iron stain: negative	Iron stain: negative		
9	Mild lymphocytis	Steato hepatitis		
	Miocarditis	Trichrome stain: fibrosis stage 1	Unremarkable	-
	Iron stain: negative	Iron stain: negative		
0	Miocarditis	Mild acute hepatitis		Unremarkable
	Pricarditis	Trichrome stain: negative		
	lymphocytis	Iron stain: negative		
	Viral miocarditis			
1	Mild miocarditis	Macrovesicular steatosis	Unremarkable	Unremarkable
	Precarditis	Hepatitis (Steato-hepatitis)		
	Iron stain: negative	Fibrosis stage 4 (Trichrome stain)		
		Iron stain: negative		
2	Mild lymphocytic	Steato-hepatitis	Unremarkable	Unremarkable
	Miocarditis	Trichrome stain: negative		
	Iron stain: negative	Iron stain: negative		
3	Unremarkable	Mcrovascular stratosis	Unremarkable	Unremarkable
	Iron stain: negative	Hepatitis (Steato-hepatitis)		
		Trichrome stain: mild periportal fibrosis(stage 1)		
		Iron stain: normal		
4	Fatty replacement	Steatohepatitis	Unremarkable	Unremarkable
	Mild lymphocytis	Trichrome stain: negative		
	Miocarditis			
	Iron stain: negative			
5	Mild miocarditis	Mild lobular	Mild viral myositis	-
		Portal hepatitis		

Figures

Figure 1

Mild lymphocytic myocarditis

Figure 2

Heart, fatty replacement

Figure 3

Steatohepatitis (Medium power)

Figure 4

Cirrhosis