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Pancreatic Injury Patterns in Patients With Coronavirus Disease 19 Pneumonia

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In December 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) emerged in Wuhan, and it has rapidly spread throughout China.[1] Recent studies have focused mainly on the epidemiologic and clinical characteristics of patients with confirmed infection.[1–3] Little attention has been paid to the pancreatic injury caused by SARS-CoV-2 infection.

Methods

Fifty-two patients with coronavirus disease 2019 (COVID-19) pneumonia were admitted to Zhongnan Hospital of Wuhan University from January 20 to February 28, 2020. The disease was confirmed by detecting SARS-CoV-2 nucleic acid in throat swab samples by using the reverse-transcription polymerase chain reaction assay method. On admission, all patients had a comprehensive laboratory examination, including blood cytology, biochemistry, and inflammatory indicators. Pancreatic injury was defined as any abnormality in amylase (normal range, 0–90 U/L) or lipase (normal range, 0–70 U/L). Serious illness was defined if at least 1 of the following items was present: (1) breathing rate, $\geq$30/min; (2) pulse oximeter oxygen saturation, $\leq$93% at rest; or (3) ration of partial pressure of arterial oxygen to fraction of inspired oxygen, $\leq$300 mm Hg (1 mm Hg = 0.133 kPa). During the hospitalization, each patient had a swab virus test every other day. Negative conversion time of SARS-CoV-2 was defined as the interval between symptom onset and the first of 2 consecutive negative virus test results.

Categorical data are described as percentages and continuous data as mean with standard deviation (SD). Pearson correlation analysis was used to compare variables between the patients with COVID-19 with and without pancreatic injury. A 2-sided $P < .05$ was considered statistically significant.

Results

Among the 52 patients with COVID-19 pneumonia, the incidence was 33% for heart injury (abnormal lactate dehydrogenase or creatine kinase levels), 29% for liver injury (any abnormality in aspartate aminotransferase, alanine aminotransferase, γ-glutamyltransferase, or alkaline phosphatase levels), 17% for pancreatic injury, 8% for renal injury (abnormal creatinine level), and 2% for diarrhea. The 9 patients with pancreatic injury had an average age of 55 years, ranging from 25 to 71 years (Table 1). Five patients had underlying diseases such as hypertension, diabetes, and heart disease. The most common chief complaints were fever and respiratory symptoms. Four patients were categorized as having serious illness on admission. In laboratory tests, these patients had a decrease in lymphocytes and the lymphocyte subsets as well as an increase in hepatic and myocardial enzymes and inflammatory indicators. Seven patients received corticosteroid therapy, and 1 received mechanical ventilation. The median time of SARS-CoV-2 negative conversion was 22 days from symptom onset.

Compared with the patients without pancreatic injury, those with pancreatic injury had a higher incidence of loss of appetite and diarrhea; more severe illness on admission; lower levels of $CD3^+$ and $CD4^+$ T cells; and higher levels of aspartate aminotransferase, γ-glutamyltransferase, creatinine, lactate dehydrogenase, and erythrocyte sedimentation rate. The 2 groups showed no significant difference in corticosteroid treatment, mechanical ventilation, or virus negative conversion time.

Discussion

In this study, we found that the incidence of pancreatic injury was not very low in patients with COVID-19 pneumonia. In the previous pneumonia caused by SARS-CoV infection (2003), the virus was detected not only in the tissues of the lung, liver, kidney, and intestine but also of the pancreas, indicating the pancreas as a potential coronaviral target.[4] Moreover, the SARS-CoV receptor of angiotensin-converting enzyme 2 was highly expressed in pancreas islets, and SARS-CoV infection caused damage of the islets and subsequent acute diabetes.[5] In our study of 9 patients with COVID-19 with pancreatic injury, 6 patients were found to have abnormal blood glucose levels. These findings suggest that the pancreatic injury in COVID-19 might be caused

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Abbreviations used in this paper: COVID-19, coronavirus disease 2019; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2.

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Table 1. Characteristics of Patients With COVID-19 Pneumonia With Pancreatic Injury

Variable	Patients with COVID-19 with pancreatic injury										Patients with COVID-19 without pancreatic injury (N = 43)	*P* value
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Overall		
Age, *y*, mean ± SD	25	55	62	65	66	71	36	56	62	55 ± 15	52 ± 18	.633
Male, n (%)	Y	Y	Y	Y	Y	Y	N	N	N	6 (67)	18 (42)	.181
Comorbidities, n (%)												
Hypertension	N	Y	Y	N	Y	N	N	N	N	3 (33)	7 (16)	.246
Diabetes	Y	N	Y	N	Y	N	N	N	N	3 (33)	7 (16)	.246
Heart	N	N	N	N	N	N	N	N	Y	1 (11)	2 (5)	.460
Cerebrovascular	N	N	N	N	N	N	N	N	N	0 (0)	2 (5)	.519
Respiratory	N	N	N	N	N	N	N	N	N	0 (0)	1 (2)	.652
Chief complaints on admission, n (%)												
Fever	Y	Y	Y	Y	Y	Y	Y	Y	N	8 (89)	26 (60)	.107
Chest distress/breath shortness	Y	N	Y	Y	Y	N	N	N	N	4 (44)	7 (16)	.062
Cough	N	N	N	N	Y	Y	N	N	Y	3 (33)	10 (23)	.535
Fatigue	N	N	N	Y	N	N	N	N	N	1 (11)	9 (21)	.506
Anorexia	N	N	N	N	N	N	N	Y	N	1 (11)	0 (0)	.027
Diarrhea	N	N	N	Y	N	N	N	N	N	1 (11)	0 (0)	.027
Headache	N	N	N	N	N	N	N	N	N	0 (0)	1 (2)	.652
Severe illness on admission, n (%)	Y	N	Y	Y	Y	N	N	N	N	4 (44)	6 (14)	.035
Blood cytology												
Leukocytes ($3.5\sim9.5\times10^9$/L)	5.31	6.29	4.86	8.03	10.7	4.94	4.11	8.54	2.77	6.17 ± 2.48	5.21 ± 3.33	.421
Neutrophils ($1.8\sim6.3\times10^9$/L)	4.34	4.61	3.86	7.24	10.16	3.81	3.41	6.82	1.58	5.09 ± 2.56	3.76 ± 3.38	.276
Monocytes ($0.1\sim0.6\times10^9$/L)	0.34	0.79	0.28	0.38	0.25	0.37	0.10	0.76	0.26	0.39 ± 0.23	0.41 ± 0.17	.841
Platelets ($125\sim350\times10^9$/L)	219	248	112	279	179	74	209	220	134	186 ± 67	198 ± 87	.701
Lymphocytes ($1.1\sim3.2\times10^9$/L)	0.62	0.87	0.71	0.38	0.29	0.76	0.59	0.95	0.90	0.67 ± 0.23	0.94 ± 0.49	.119
$CD3^+$ T cell (805–4459/μL)	300	—	292	—	184	562	362	129	542	339 ± 165	948 ± 686	.027
$CD4^+$ T cell ($345\sim2350/\mu$L)	108	—	114	—	86	304	103	81	236	147 ± 87	503 ± 367	.016
$CD8^+$ T cell ($345\sim2350/\mu$L)	189	—	170	—	96	239	223	45	277	177 ± 82	397 ± 380	.138
CD4/CD8 ratio ($0.96\sim2.05$)	0.57	—	0.67	—	0.90	1.27	0.46	1.78	0.85	0.93 ± 0.46	1.68 ± 1.07	.078
$CD19^+$ B cell ($240\sim1317/\mu$L)	154	—	79	—	146	38	88	49	51	86 ± 47	147 ± 85	.078
$CD16^+CD56^+$ NK cell ($210\sim1514/\mu$L)	322	—	609	—	136	142	240	8	12	210 ± 209	210 ± 148	.994

Table 1. Continued

Variable	Patients with COVID-19 with pancreatic injury										Patients with COVID-19 without pancreatic injury (N = 43)	*P* value
	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8	Patient 9	Overall		
Blood biochemistry, mean ± SD												
ALT (9∼50 U/L)	175	54	47	48	55	13	13	11	23	49 ± 51	30 ± 32	.167
AST (15∼40 U/L)	90	69	82	55	71	29	19	16	33	52 ± 28	29 ± 15	.001
ALB (40∼55 g/L)	43.9	37	38.9	36.6	34.4	36.1	43	29.4	32.5	36.9 ± 4.6	36.7 ± 5.0	.943
GLB (20∼30 g/L)	32.1	35.3	37.6	36.3	28.8	29.0	29.7	27.3	28.7	31.6 ± 3.8	30.0 ± 6.9	.499
GGT (8∼57 U/L)	154	63	75	123	51	54	13	13	20	63 ± 49	31 ± 19	.003
ALP (30∼120 U/L)	74	84	76	106	85	52	63	87	65	77 ± 16	74 ± 30	.794
Creatinine (64∼104 μmol/L)	89.3	130.9	158.7	106.4	73.7	68.9	59.0	109.2	57.8	94.9 ± 34.5	61.6 ± 17.6	.000
Glucose (3.9∼6.1 mmol/L)	15.26	6.90	9.49	8.42	13.78	5.44	8.85	4.91	5.63	8.74 ± 3.66	11.11 ± 24.81	.779
LDH (125∼243 U/L)	292	435	646	94	533	186	207	192	281	318 ± 182	219 ± 81	.019
Creatinine kinase (<171 U/L)	472	297	253	654	195	191	69	20	125	253 ± 201	120 ± 206	.093
D-dimer (0∼500 ng/mL)	233	261	410	382	633	395	147	—	251	339 ± 150	889 ± 1757	.385
Amylase (0∼90 U/L)	84	107	113	109	149	136	100	151	86	115 ± 25	52 ± 18	.001
Lipase (0∼70 U/L)	83	47	45	112	124	21	45	85	77	71 ± 34	31 ± 13	.001
Blood inflammatory indicators, mean ± SD												
CRP (0∼10 mg/L)	10.0	98.0	137.3	161.1	104.5	11.4	20.0	2.3	15.0	62.2 ± 62.6	35.5 ± 47.0	.162
ESR (0∼15 mm/h)	8	93	56	82	62	—	34	—	19	51 ± 32	25 ± 23	.016
IL-6 (0.1∼2.9 pg/mL)	18.89	—	21.44	—	19.90	54.68	2.54	7.06	35.03	22.79 ± 17.56	19.76 ± 24.07	.756
Hospitalized treatment, n (%)												
Corticosteroid	Y	N	Y	Y	Y	Y	Y	Y	N	7 (78)	18 (42)	.051
Mechanical ventilation	N	N	N	Y	N	N	N	N	N	1 (11)	3 (7)	.679
Virus negative conversion time, *d*, mean ± SD[a]	40	20	13	17	21	25	19	21	18	22 ± 8	17 ± 8	.090

ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; GGT, γ-glutamyltranspeptidase; GLB, globulin; IL, interleukin; LDH, lactate dehydrogenase; N, no; NK, natural killer; SD, standard error; Y, yes.
[a]The interval between symptom onset and the first of 2 consecutive negative virus test results.

directly by the cytopathic effect mediated by local SARS-CoV-2 replication. On the other hand, the pancreatic injury might be caused indirectly by systemic responses to respiratory failure or the harmful immune response induced by SARS-CoV-2 infection, which also led to damage in multiple organs. In this study, heart, liver, and renal injuries were detected simultaneously. In addition, most patients took antipyretics before admission, which could also cause drug-related pancreatic injury.

In conclusion, these results show potential mild pancreatic injury patterns in patients with COVID-19 pneumonia, and these may be related to direct viral involvement of the pancreas or from secondary enzyme abnormalities in the context of severe illness without substantial pancreatic injury. They do not show clinically severe pancreatitis as a common manifestation. Further research and larger series are warranted to evaluate whether a subset of patients have clinical pancreatitis as a presenting or concomitant disease entity.

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Conflicts of interest
The authors disclose no conflicts.

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