Original Article

Clinical characteristics of 60 discharged cases of 2019 novel coronavirus-infected pneumonia in Taizhou, China

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Background: The number of patients with pneumonia stemming from the 2019 novel coronavirus (COVID-19) infection has increased rapidly. However, the clinical characteristics of discharged patients remain little known. Here, we attempt to describe the clinical characteristics and treatment experiences of discharged cases from Taizhou, China.

Methods: A total of 60 patients with COVID-19-infected pneumonia who were discharged from Taizhou Enze Medical Center (Group), from January 31, 2020, to February 16, 2020, were included in the analysis. The discharge criteria were based on the New Coronavirus Pneumonia Prevention and Control Program (Fifth Edition, China).

Results: Of the 60 patients, the median age was 41 years, and 58.3% were male. Only 13.3% of patients were identified as having severe novel coronavirus pneumonia. All patients received combined antiviral treatment on admission, including β-interferon, lopinavir/tonavir, Abidol and oseltamivir. All patients with severe conditions received gamma globulin and hormone therapy. No patients had endotracheal intubation or died. The median duration from symptom onset to hospitalization was 3 (range, 0–15) days. The median duration of COVID-19 shedding was 14 (range, 5–26) days, and the median duration of hospital stay was 15 (range, 7–23) days.

Conclusions: Early therapy and comprehensive therapy are key to the outcome for patients with COVID-19-infected pneumonia, especially for those with severe pneumonia.

Trial registration number: ChiCTR2000029866.

Keywords: 2019 novel coronavirus (COVID-19); 2019 novel coronavirus-infection pneumonia (COVID-19-infection pneumonia; early treatment; antiviral

Submitted Mar 10, 2020. Accepted for publication Mar 30, 2020.
doi: 10.21037/atm.2020.04.20
View this article at: http://dx.doi.org/10.21037/atm.2020.04.20

Introduction

The 2019 novel coronavirus-infected pneumonia (NCIP) is a viral infectious disease that began in Wuhan, China and is now a global concern (1,2). Scientists have revealed a novel β-coronavirus from patients with NCIP, which is currently named COVID-19 (3). COVID-19 is a single-stranded RNA β-coronavirus with high infectivity (3). Similar to those of severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), the COVID-19 genome encodes nonstructural proteins, structural proteins, and accessory proteins (3,4). A familial cluster of NCIP has indicated person-to-person transmission (5), and COVID-19-infected patients are highly person-to-person infectious (6,7). COVID-19 is prevalent around the world today. Preventing COVID-19 from spreading is extremely difficult. Some severe cases have rapidly progressed to acute respiratory syndrome (ARDS) or even died (8). How to prevent and treat is the focus.

Effective antiviral therapy is very important for patients with COVID-19. Unfortunately, for patients with COVID-19, there are currently no specific antiviral drugs available, and supportive care is the main strategy (9). Therefore, effective antiviral drugs against COVID-19 are urgently needed during the COVID-19 outbreak. Corticosteroid treatment in patients with COVID-19 is controversial, which is a double-edged sword. The best of time and dosage of corticosteroid treat in NICP is relied on doctors' clinical experience. Thence, we conducted a retrospective, single-center analysis to reveal the clinical characteristics and treatment experience of 60 discharged patients to provide a clinical therapy reference for patients with NCIP.

Methods

Study design and patients

This study is a retrospective, observational, single-center study. The research was registered in the Chinese Clinical Trial Registry (ChiCTR2000029866). Ethics approval was granted by Hospital Ethics Committee of Enze Hospital of Taizhou Enze Medical Center (Group). Patients from Enze Hospital, Taizhou Enze Medical Center (Group), from January 31, 2020, to February 16, 2020, were included in the analysis. Written informed consent was obtained from all participants before inclusion.

Data collection

All data were extracted from electronic medical records, and included epidemiological characteristics (such as recent exposure history), clinical symptoms and signs, and laboratory findings. All patients were from Enze Hospital, Taizhou Enze Medical Center (Group), which includes the of Taizhou Public Health Center. Laboratory-confirmed cases with COVID-19-related pneumonia who improved and were discharged were consecutively included.

Diagnostic criteria

(I) Laboratory reverse transcription polymerase chain reaction (RT-PCR) was used to confirm COVID-19 infection, while (II) chest imaging was used to confirm lung involvement.

Discharge criteria

The criteria for patient discharge was as follows: (I) temperature returning to normal for at least 3 days; (II) significant improvement in respiratory symptoms; (III) inflammatory lung imaging showing significant absorption; (IV) two consecutive negative results of respiratory pathogen nucleic acid detection (sampling time interval of at least 1 day) (10).

Diagnostic criteria for severe patients

Patients were considered severe if they met any of the following criteria: respiratory distress [respiratory rate (RR) >30 breaths/min at rest], mean oxygen saturation ≤93%; arterial oxygen pressure/oxygen concentration (PaO_2/FiO_2) ≤300 mmHg (10).

RT-PCR for COVID-19 RNA

Laboratory confirmation of COVID-19 was conducted in the Taizhou Municipal Center for Disease Control and Prevention and Health Clinic for Enze Precision Medicine. The RT-PCR assay was conducted in accordance with the protocol established by the World Health Organization (11).

Firstly, RNA was extracted from 300 μL kinds of clinical samples using the SARS-CoV-2 RNA Kit (Zhijiang, Z-RR-0479-02-50). Then the targeting SARS-CoV-2 open reading frame1ab gene was amplification determined in an ABI 7500 machine as follows: 45 ℃ for 10 min, 95 ℃ for 3 min followed by 45 cycles consisting of 95 ℃ for 15 s, 58 ℃ for 30 s and finally a default melting curve step.

Detection of lymphokines

A flow cytometric bead array (CBA) was used as a rapid determination tool for Th1/Th2 cytokines, including IL-2, IL-4, IL-6, IL-10, TNF, and IFN-γ. The quantification of the 6 cytokines was evaluated by a FACSAria II Cell Sorter (BD, CA, USA) with a human Th1/Th2 subpopulation detection kit (CEGER, Zhejiang, China). The data acquired from the FACSAria II were analyzed with BD FCAP Array v.3.0.1 software. In total, 6 standard curves were obtained from 1 set of calibrators, and 6 results were obtained from each test sample. The maximum and minimum limits of the 6 detected cytokines were 1.0 and 5,000 pg/mL, respectively. Biochemical measurement was performed by a Siemens Advia 2400 (Siemens, BER, Germany).

Statistical methods

Data are expressed as the mean ± standard deviation (SD), mean ± standard error (SE), median with range, or percent with number of patients. Normality was evaluated by using the Shapiro-Wilk test (P value >0.05). Comparisons between groups of continuous variables that were normally distributed were carried out using Student's *t*-test or a corrected *t*-test. Comparisons of other scenarios were performed using the Mann-Whitney U test. Comparisons of categorical variables were performed using the χ^2 test or Fisher's exact test. P values <0.05 were considered significant. All statistical analyses were performed with SPSS 22.0.

Results

Among the 60 patients, 13.3% (n=8) had severe novel coronavirus pneumonia, 75% had visited Wuhan, and 25% had contact with people from Wuhan. The median age was 41 (range, 12–74) years, and 58.3% were male. The most common diseases in their personal medical histories included hypertension (8.3%) and diabetes (1.7%). Fever (71.7%) and cough (56.7%) were the most common symptoms. Diarrhea was uncommon (*Table 1*). The time from onset to hospitalization was 3 (range, 0–15) days, and diagnosis occurred 5.0 days after onset (range, 0–15). The time from onset to the beginning of antiviral therapy was 6.0 (range, 1.0–18.0) days (*Table 1*).

On admission, the white blood cell count did not increase in any of the patients, and the patients had obvious lymphopenia. The severe cases had more prominent laboratory abnormalities (e.g., potassium, phosphorus, $PaCO_2$, PaO_2/FiO_2) than the non-severe cases (*Table 2*). Significantly higher levels of several inflammatory factors, including IL-6, IL-10, and TFN-γ, were observed, although the levels of the inflammatory factors IL-2, IL-4, and TNF-α were not increased significantly. When the respiratory pathogen nucleic acid test was negative, the levels of the inflammatory factors decreased (*Figure 1*).

All patients were given antiviral treatment: β-interferon + lopinavir/tonavir, β-interferon + lopinavir/tonavir + Abidol, and β-interferon + lopinavir/tonavir + oseltamivir therapy were initiated in 70%, 25%, and 5% of patients, respectively. In addition, all severe patients were treated with glucocorticoids and gamma globulin. The median duration of COVID-19 shedding was 14 days, and the median duration of hospital stay was 15 days (*Table 3*).

Discussion

Early isolation and early treatment are very important for patients with COVID-19-infected pneumonia (NCIP). In this research, the median duration from symptom onset to hospitalization was 3 days, and the median duration from symptom onset to diagnosis confirmation was 5 days, which was relatively short. Most of the patients included in our study had a history of exposure in Wuhan, and the local government of Taizhou implemented medical isolation and observation at an early stage. After the onset of initial symptoms, such as fever and coughing, routine blood examination and chest computed tomography (CT) were immediately performed. If suspected patients were found, nucleic acid tests were conducted immediately to enable early diagnosis and treatment.

At present, glucocorticoid treatment for NCIP is controversial (9). High-dose glucocorticoid therapy is not recommended in SARS (12), and current evidence suggests that high-dose corticosteroid treatment does not improve the prognosis of patients with ARDS (13). Moreover, corticosteroid treatment is not routinely recommended for SARS-CoV-2 pneumonia (14,15). However, we observed

Table 1 Baseline characteristics of 60 patients with COVID-19 on admission

Characteristic	All patients (N=60)	Non-severe (N=52)	Severe (N=8)	P[a]
Age, median [range], y	41 [12–74]	40 [12–69]	58 [37–74]	0.003
Male sex, no./total no. (%)	35/60 (58.3)	30/52 (57.5)	5/8 (62.5)	1
Smoking history, no./total no. (%)	7/60 (50.0)	6/52 (11.5)	1/8 (12.5)	1
Exposure history, no./total no. (%)				
Recently visited Wuhan	45/60 (75.0)	37/52 (71.2)	8/8 (100.0)	0.079
Had contact with people from Wuhan	15/60 (25.0)	15/52 (28.8)	0	NA
Comorbidities				
Hypertension, no./total no. (%)	5/60 (8.3)	4/52 (7.7)	1/8 (12.5)	0.524
Diabetes, no./total no. (%)	1/60 (1.7)	1/52 (1.9)	0	NA
Coronary heart disease, no./total no. (%)				
Chronic obstructive pulmonary disease, no./total no. (%)	1/60 (1.7)	1/52 (1.9)	0	NA
Chronic liver disease, no./total no. (%)	2/60 (3.3)	2/52 (3.8)	0	NA
Symptoms				
Fever, no./total no. (%)	43/60 (71.7)	36/52 (69.2)	7/8 (87.5)	0.420
Highest temperature, mean ± SD, ℃	38.3±0.8	38.1±0.7	38.8±0.8	0.290
Duration of fever, mean ± SD, d	6±3	5±4	6±3	0.714
Cough, no./total no. (%)	34/60 (56.7)	29/52 (55.8)	5/8 (62.5)	1
Sore throat, no./total no. (%)	5/60 (8.3)	5/52 (9.6)	0	NA
Headache, no./total no. (%)	3/60 (5.0)	2/52 (3.8)	1/8 (12.5)	0.349
Diarrhea, no./total no. (%)	6/60 (10.0)	4/52 (7.7)	2/8 (25.0)	0.178
Chest tightness, no./total no. (%)	8/60 (13.3)	6/52 (11.5)	2/8 (25.0)	0.288
Fatigue, no./total no. (%)	16/60 (26.7)	12/52 (23.1)	4/8 (50.0)	0.192
Vomiting, no./total no. (%)	2/60 (3.3)	1/52 (1.9)	1/8 (12.5)	0.251
Course of disease				
Onset to hospitalization, median [range], d	3 [0–15]	3 [0–13]	5 [1–15]	0.312
Onset to diagnosis time, median [range], d	5 [0–15]	5 [0–14]	7 [2–15]	0.283
Onset to antiviral therapy, median [range], d	6 [1–18]	5 [1–18]	7 [1–15]	0.852

[a], Fisher's exact test, Student's *t*-test, and Mann-Whitney U test. COVID-19, 2019 novel coronavirus.

elevated levels of inflammatory markers, such as IL-6 and TFN-γ, in our patients (*Figure 1*). Cytokine storms and immunopathology are major causes of ARDS in patients with COVID-19-infected pneumonia (16). The latest pathological findings, including pulmonary and peripheral blood results, suggest that timely and appropriate use of corticosteroids should be considered for severe patients to prevent ARDS development (17). In our center, when a patient's PaO_2/FiO_2 is less than 300 mmHg, radiological manifestations of lung injury are aggravated, or dyspnea occurs, hormone and gamma globulin therapy are performed (*Figure 2*). The period of hormone therapy is approximately 1 week, and that of gamma globulin therapy is approximately 3 to 5 days. Notably, none of the severe patients progressed to critical illness or died. Our team found that it is important to detect severe cases in

Table 2 Laboratory items of 60 patients with COVID-19

Laboratory items	All patients (N=60)	Non-severe (N=52)	Severe (N=8)	P[a]
Routine blood parameters				
White cell count, $\times10^9$/L	5.7±2.9	5.4±1.8	7.4±6.6	0.424
Hemoglobin, g/L	140.1±16.7	139.5±15.9	144.0±21.8	0.478
Hematocrit, ratio	0.41±0.05	0.41±0.04	0.43±0.06	0.389
Platelet count, $\times10^9$/L	205.4±66.0	207.0±61.0	195.3±97.1	0.664
Absolute lymphocyte value, $\times10^9$/L	1.4±0.5	1.5±0.5	0.84±0.30	0.001
Absolute neutrophil value, $\times10^9$/L	3.8±2.8	3.5±1.5	6.2±6.6	0.289*
Blood biochemistry				
Aspartate aminotransferase, U/L	25.6±11.8	23.2±6.6	41.5±22.7	0.056*
Alanine aminotransferase, U/L	23.4±23.2	21.3±11.9	51.8±50.8	0.135*
Serum creatinine, μmol/L	78.6±18.5	79.1±19.6	75.1±9.3	0.578
Creatine kinase, U/L	76.2±56.9	72.6±58.8	99.4±38.0	0.219
Sodium, mmol/L	138.5±2.2	138.5±2.2	138.7±1.8	0.889
Potassium, mmol/L	3.8±0.4	3.7±0.4	4.1±0.4	0.014
Phosphorus, mmol/L	1.0±0.2	1.0±0.2	1.2±0.1	0.018
Calcium, mmol/L	2.2±0.2	2.2±0.2	2.2±0.2	0.278
Hemagglutination series				
International normalized ratio	1.1±0.1	1.1±0.1	1.0±0.1	0.574
Prothrombin time, s	11.7±2.3	11.7±2.4	11.9±1.2	0.772
Activated partial thromboplastin time, s	30.2±2.6	30.1±2.6	31.0±2.9	0.38
Thrombin time, s	16.7±1.1	16.6±1.1	17.4±1.2	0.065
D-dimer, mg/L	0.34±0.35	0.33±0.36	0.48±0.25	0.327
Blood gas analysis				
pH	7.5±1.3	7.6±1.4	7.4±0.1	0.73
$PaCO_2$, mmHg	42.9±4.1	43.2±4.2	40.9±2.3	0.039
PaO_2, mmHg	98.9±28.5	102.5±28.2	74.9±16.4	0.009
Lactate, mmol/L	1.7±0.6	1.7±0.6	1.6±0.6	0.775
PaO_2/FiO_2, mmHg	376±87	396±74	245±29	0

*, Mann-Whitney U test; [a], student's *t*-test and corrected *t*-test. COVID-19, 2019 novel coronavirus. All data are expressed as mean ± SD.

order to provide hormone and gamma globulin therapy in a timely manner. We look forward to the results of the glucocorticoid randomized controlled trial (RCT) (clinical trial registration number: ChiCTR2000029386).

In this study, all the patients were given antiviral treatment, which was usually a combination of 2 antiviral drugs, including β-interferon, lopinavir/tonavir, Abidol, and oseltamivir. The median duration of COVID-19 shedding

was 14 days. The effects of these antiviral drugs are still unclear, and further RCT studies are needed. All the patients required observation and isolation after discharge, and nucleic acid detection of feces and sputum specimens was performed 2 weeks after discharge. Some studies have found that COVID-19-infected patients' feces could harbor the virus for a long time (18), and it is currently uncertain whether fecal-oral transmission exists (18). Thus, we continued to monitor the patients carefully after their release.

Comprehensive measures are crucial for treating NCIP. In our center, physicians from the Department of Intensive Care and the Department of Respiratory and Infectious Disease, combined with psychologists, physical therapists and Traditional Chinese Medicine (TCM) physicians, participated throughout the treatment of each patient with NCIP to ensure that the patients received comprehensive treatment.

In conclusion, we here described the clinical characteristics of discharged patients with NCIP and shared our management experience. Our results suggest that early therapy and comprehensive therapy are important in NCIP treatment, especially for critical patients with severe pneumonia.

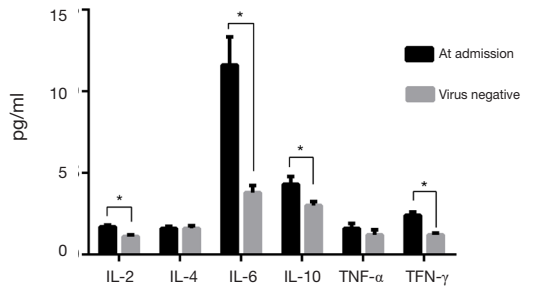

Figure 1 The levels of inflammatory factors, including IL-2, IL-4, IL-6, IL-10, TNF-α, and TFN-γ (All data are expressed as Mean ± SE), at the time of hospital admission and at the time of testing negative for the virus. Differences were considered to be statistically significant when P<0.05.

Acknowledgments

We would like to thank all the physicians and nurses in the Taizhou Public Health Center.

Funding: This work was supported by The Science and Technology Project of Taizhou (no. 1902ky02, 1902ky27) and The Natural Science Foundation of Zhejiang Province (no. Y20H150029).

Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.

Table 3 Treatments and clinical outcomes

Treatments	All patients (N=60)	Non-severe (N=52)	Severe (N=8)	P[a]
Intravenous antivirals				
β-interferon + lopinavir/tonavir, no./total no. [%]	42/60 [70]	39/52 [80]	3/8 [38]	0.045
β-interferon + lopinavir/tonavir + abidol, no./total no. [%]	15/60 [25]	10/52 [19]	5/8 [63]	0.019
β-interferon + lopinavir/tonavir + oseltamivir, no./total no. [%]	3/60 [5]	3/52 [6]	0	NA
Onset to antiviral therapy, median [range]	5 [1–18]	5 [1–18]	7 [1–15]	0.852
Glucocorticoid, no./total no. [%]	9/60 [15]	1/52 [2]	8/8 [100]	0
Gamma globulin, no./total no. [%]	9/60 [15]	0	8/8 [100]	NA
Intravenous antibiotics, no./total no. [%]	6/60 [10]	5/52 [10]	1/8 [1]	1.000
Clinical outcomes				
Days to negative virus detection, median [range], d	14 [5–26]	14 [5–26]	14 [12–19]	0.458
Onset to discharge, median [range], d	18 [9–32]	17 [9–32]	18 [14–23]	0.354
Hospital stay, median [range], d	15 [7–23]	15 [7–23]	14 [8–23]	0.571

[a], Fisher test and Mann-Whitney U test.

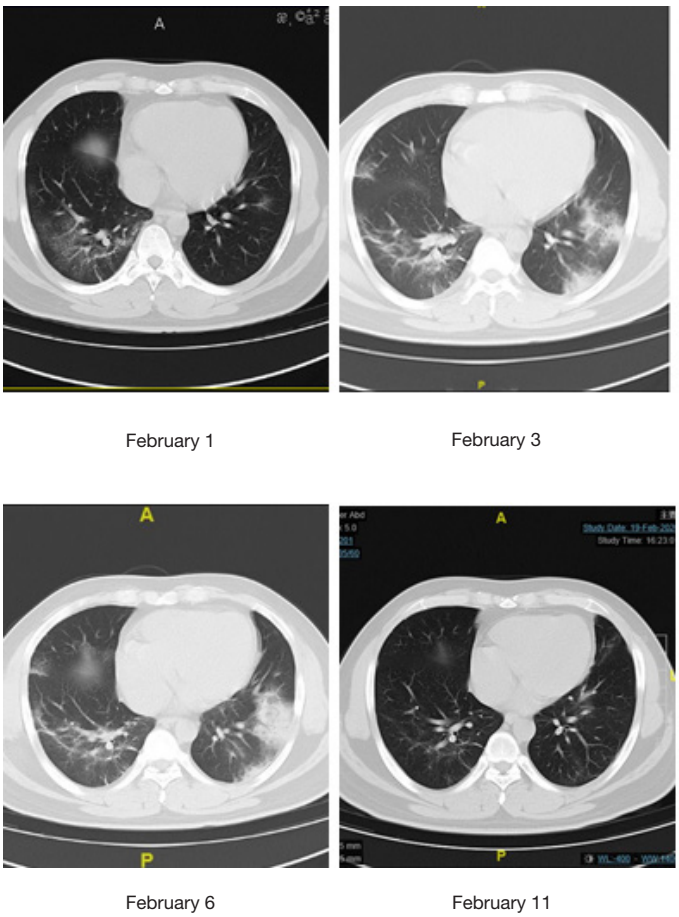

Figure 2 Chest computed tomography of a severe case who was admitted from February 1, 2020, to February 11, 2020. The patient was treated with glucocorticoids and gamma globules from February 3, to February 10.

org/10.21037/atm.2020.04.20). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. Ethics approval was granted by Hospital Ethics Committee of Enze Hospital of Taizhou Enze Medical Center (Group) (No. K20200204). Written informed consent was obtained from all participants before inclusion.

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Cite this article as: Jiang Y, He S, Zhang C, Wang X, Chen X, Jin Y, He Z, Cai M, Lin Z, Ying L, Mou J, Zhao H, Lin R, Zhang S, Wu X, Chen H, Lv D. Clinical characteristics of 60 discharged cases of 2019 novel coronavirus-infected pneumonia in Taizhou, China. Ann Transl Med 2020;8(8):547. doi: 10.21037/atm.2020.04.20

