

A comparative study on the clinical features of COVID-19 pneumonia to other pneumonias

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Summary: 2019-nCoV infection caused similar onsets to other pneumonias. CT scan may be a reliable test for screening NCOVID-19 cases. Liver function damage is more frequent in NCOVID-19 than NON-NCOVID-19. LDH and α -HBDH may be considerable markers for evaluation of NCOVID-19.

Abstract

Background

A novel coronavirus (2019-nCoV) has raised world concern since it emerged in Wuhan Hubei China in December, 2019. The infection may result into severe pneumonia with clusters illness onsets. Its impacts on public health make it paramount to clarify the clinical features with other pneumonias.

Methods

Nineteen 2019-nCoV pneumonia (NCOVID-19) and fifteen other pneumonia patients (NON-NCOVID-19) in out of Hubei places were involved in this study. Both NCOVID-19 and NON-NCOVID-19 patients were confirmed to be infected in throat swabs or/and sputa with or without 2019-nCoV by real-time RT-PCR. We analyzed the demographic, epidemiological, clinical, and radiological features from those patients, and compared the difference between NCOVID-19 and NON-NCOVID-19.

Results

All patients had a history of exposure to confirmed case of 2019-nCoV or travel to Hubei before illness. The median duration, respectively, was 8 (IQR:6~11) and 5 (IQR:4~11) days from exposure to onset in NCOVID-19 and NON-NCOVID-19. The clinical symptoms were similar between NCOVID-19 and NON-NCOVID-19. The most common symptoms were fever and cough. Fifteen (78.95%) NCOVID-19 but 4 (26.67%) NON-NCOVID-19 patients had bilateral involvement while 17 (89.47%) NCOVID-19 but 1 (6.67%) NON-NCOVID-19 patients had multiple mottling and ground-glass opacity of chest CT images. Compared to NON-NCOVID-19, NCOVID-19 present remarkably more abnormal laboratory tests including AST, ALT, γ -GT, LDH and α -HBDH.

Conclusion

The 2019-nCoV infection caused similar onsets to other pneumonias. CT scan may be a reliable test for screening NCOVID-19 cases. Liver function damage is more frequent in NCOVID-19 than NON-NCOVID-19 patients. LDH and α -HBDH may be considerable markers for evaluation of NCOVID-19.

Key words: Novel coronavirus pneumonia; Infectious diseases; Clinical features;

Respiratory infection

Background

In the end of 2019, a novel coronavirus (2019-nCoV) emerged in Wuhan Hubei province, China [1]. Reports showed that the 2019-nCoV infection caused clusters onset similar to severe acute respiratory syndrome coronavirus (SARS) [1, 2]. Previous study has shown that coronaviruses can cause respiratory and intestinal infections in animals and humans [3]. Generally, coronaviruses were not considered to be highly pathogenic to humans until the outbreak of severe acute respiratory syndrome (SARS) in 2002 and 2003 in Guangdong, China[4, 5]. Another highly pathogenic coronavirus, Middle East respiratory syndrome (MERS) coronavirus emerged in Middle Eastern countries in 2012[6]. 2019-nCoV is one more highly pathogenic coronavirus to human in history.

The virus has raised world concern because of its high transmission capability as well as high mobility and mortality[2, 7-9]. As of 14th Feb 2020, more than 60000 cases with over 8000 severe patients infected with the virus have been reported, and more than 1500 patients died. In addition to China, the patients have been detected in 25 countries globally. Early reports showed that almost all of confirmed patients have evidence of pneumonia[7, 9]. However, pneumonias are very common during a time of year when respiratory illnesses caused by other pathogens infection are highly prevalent [10, 11]. So it is a very hard time for public health as well as doctors in this outbreak.

In this study, we investigated the clinical features of 19 confirmed 2019-nCoV pneumonia (NCOVID-19) cases and 15 2019-nCoV negative confirmed pneumonia patients (NCOVID-19) with a history of travel to Hubei or exposure before illness to NCOVID-19 confirmed patients to describe the potential differences of clinical features between the two diseases.

Materials and methods

Patients

For comparative study, we recruited 19 NCOVID-19 patients and 15 NON-NCOVID-19 patients from Jan 23 to Feb 5, 2020, at the Second Affiliated Hospital of Anhui Medical University and Suzhou Municipal Hospital in Anhui province, China. NCOVID-19 or NON-NCOVID-19 cases were confirmed to be infected with or without 2019-nCoV by real-time RT-PCR. NCOVID-19 was defined to be 2019-nCoV negative by PCR detection. For NON-NCOVID-19 confirmation, we collected a throat swab or sputum sampling every other day.

The patient was confirmed as NON-NCOVID-19 if three consecutive real-time PCR tests were negative during first 7 days of admission.

Real-time PCR detection for identification of pathogens

According to the surveillance scheme of pneumonia cases with 2019-nCoV infection and the guideline of laboratory detection for NCOVID-19[12], local Centres for Disease Control and Prevention collected throat swabs or/and sputa from suspected patients, then shipped them to designated authoritative laboratories to detect the pathogen. RNA was extracted from those collected samples. Specific real-time reverse transcription polymerase chain reaction (rRT-PCR) assays were performed to identify influenza A virus (H1N1, H3N2, H5N1, H7N9), influenza B virus, respiratory syncytial virus, parainfluenza virus, adenovirus, SARS coronavirus (SARS-CoV), and MERS coronavirus (MERS-CoV) using commercial kits or designed nCoV rRT-PCR kit by China CDC.

Data collection

We reviewed clinical charts, nursing records, laboratory findings, and chest x-rays for all NCOVID-19 and NCOVID-19 patients. The admission data of these patients were from Jan 23 to Feb 5, 2020. Epidemiological, clinical, laboratory, and radiological characteristics data were obtained with standardized data collection forms from electronic medical records. Investigators interviewed each patient and their relatives, where necessary, to determine exposure or close contact histories during the 2 weeks before the illness onset. To ascertain the epidemiological and symptom data, which were not available from electronic medical records, the researchers also directly communicated with patients or their families to ascertain epidemiological or symptom data. If data were missing from the records or clarification was needed, we obtained data by direct communicating with attending doctors and other healthcare providers. All data were checked by two physicians.

Statistical analysis

The quantitative blood laboratory tests were compared by Mann-Whitney U test. The categorical variables were expressed as number (%) and compared by Fisher's exact test. Differences were considered significant at $p < 0.05$ with a two-tailed test. All analysis was performed using InStat software (Vision 5.0, GraphPad prism).

Results

Demographic characteristics of cases

As shown in table 1, 19 NCOVID-19 patients and 15 NON-NCOVID-19 patients were included in this study. The mean age was 48 (IQR: 27~56) and 35 (IQR: 27~46) in NCOVID-19 and NON-NCOVID-19 patients, respectively. Eight (42.11%) were female in NCOVID-19 patients, and 9 (60%) in NON-NCOVID-19 patients. Serum IgM detection suggested that 2 (10.53%) of NCOVID-19 patients had Coxsackie virus or mycoplasma co-infection. In addition, 3 (18.75%) of NCOVID-19 patients had history of Chronic medical illness. The median duration from exposure to onset is 8 (IQR: 6~11) and 5 (IQR: 4~11) days in NCOVID-19 and NON-NCOVID-19 patients, respectively. In NON-NCOVID-19 patients, no viral RNA or DNA was detected for mentioned targets in methods section while Serological assays showed mycoplasma against IgM positive in two patients.

Illness onset features of patients

To decrease the possible affect on laboratory results, we selected those patients with similar duration between nCoV and non-CoV in this study. The median duration, respectively, was 5 (IQR: 3~9) and 4 (IQR:2~7) days from onset to admission in NCOVID-19 and NON-NCOVID-19 patients. It was no statistical difference between them. On admission, the most common symptoms at onset of illness were fever and cough in both NCOVID-19 (15 [78.95%] and 9 [47.37%] of 19) and NON-NCOVID-19 (14 [93.33%] and 12 [80%] of 15) patients. Less common symptoms of NCOVID-19 patients were sore throat (4 [21.05%] of 19; 4 [26.67%] of 15), headache (2 [10.53%] of 19), fatigue (2 [10.53%] of 19), Diarrhea (1 [5.26%] of 19) and Chest tightness (1 [5.26%] of 19) while NON-NCOVID-19 patients has less common symptoms of sore throat (4 [26.67%] of 15) and diarrhea (1 [6.67%] of 15). All patients have pneumonia evidence of chest CT images, but only 2 (10.53%) NCOVID-19 patients and 5 (30%) NON-NCOVID-19 patients presented abnormal auscultation of lung (table 2). In comparison, no significant differences were observed between NCOVID-19 and NON-NCOVID-19 patients on these onsets.

The features of CT images

On admission, of the 19 NCOVID-19 patients, 15 (78.95%) had bilateral involvement (table 2). Similar with previous reports[13], the typical feature is multiple lobular ground-glass opacity (Figure A-F) and subsegmental areas of consolidation (Figure G) in NCOVID-19 patients. In addition, sequential CT images from same patient suggested that the inflammation was rapid infiltration in lobes of NCOVID-19 patients (Figure A-C, D-E, F-G). In comparison, of 15 NON-NCOVID-19 patients, only 4 (26.7%) had bilateral involvement (table 2). The typical features of NON-NCOVID-19 were patchy shadow or density increasing shadow (Figure H), except for one (6.67%) had multiple patchy and mottling shadows with partial ground-glass opacity (Figure I).

Laboratory abnormalities of the patients

On admission, except one NCOVID-19 patient, WBC numberings of the investigated patients were in normal range whereas most lymphocytes were decreased in NCOVID-19 (12 [63.18%] of 19) and NON-NCOVID-19 (10 [66.67%] of 15) patients. Increased ratio of neutrophils was observed in 11 (61.11%) NCOVID-19 or 9 (64.29%) NON-NCOVID-19 patients. Compared to NON-NCOVID-19 patients, NCOVID-19 patients had higher levels of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), γ -glutamyl transpeptidase (γ -GT) and α -hydroxybutyric dehydrogenase (α -HBDH). In addition, a proportion of NCOVID-19 but NCOVID-19 patients had abnormally increased AST (5 [27.78%] of 18), ALT (5 [27.78%] of 18), γ -GT (8 [44.4%] of 18) and LDH(6 [31.58%] of 19). Abnormally increased α -HBDH was seen in 6 (75%) of 8 NCOVID-19 patients and 3 (20%) of 15 NON-NCOVID-19 patients (Table 3). One of NCOVID-19 patient with abnormal LDH also showed abnormal CK (365 U/L) while there was no significant difference between CK levels of NCOVID-19 and NCOVID-19 patients. In addition, most of both NCOVID-19 and NON-NCOVID-19 patients presented increased levels of CRP and IL-6 whereas no significant difference was observed between the two grouped patients. Creatinine levels of all patients were normal (data not shown).

Outcome and treatments

By the end of 14th Feb 2020, no patient need be admitted to Intensive Care Unit (ICU) and administered with mechanical ventilation in these investigated NCOVID-19 and NON-NCOVID-19 patients. Except for two NCOVID-19 patients had a transient decreasing of pulse oxygen saturation (SpO₂) (92-93%) on admission, SpO₂ of others kept at 95%-99%. All of NCOVID-19 patients were treated with antiviral drug lopinavir and ritonavir tablets and symptomatic supports while NON-NCOVID-19 patients were treated with antibiotics (moxifloxacin) and other symptomatic supports. Besides drug treatments, a large proportion of the ingredients were psychological counseling for these NCOVID-19 patients because of the panic and anxiety to the illness.

Discussion

The 2019-nCoV which caused severe illness has impacted multiple countries in the world, and sustained human-to-human transmission making it a world concerning and serious public health threat [14]. So far, it is unclear when it will be end actually. However, the caused symptoms of the virus are similar to those of influenza (e.g., fever, cough, or sore throat), and the outbreak is occurring during a time of year when respiratory illnesses from influenza, respiratory syncytial virus, and other respiratory viruses are highly prevalent. It is a very important for clinics to identify the infected patients.

We report here a comparative analysis on 19 pneumonia patients with laboratory-confirmed 2019-nCoV infection and 15 pneumonia patients without 2019-nCoV infection. All patients had the exposure history to confirmed 2019-nCoV patient or traveled back from Hubei before illness. The epidemiology data showed the two group patients presented onsets after mean one week around. Similar symptoms were presented by both group patients. Fever and cough were the most common symptoms. These symptoms are also common in other acute respiratory infections such as influenza, respiratory syncytial virus and other respiratory viruses, which may be associated with the difficult control of this epidemic.

Early Classification of patients is necessary to prevent and control these epidemics when emergency management have to be conducted in some outbreaks like SARS and 2019-nCoV[15, 16]. Previous suggested that CT scan was a useful tool to screen the suspected cases of 2019-nCoV infection [13]. In this study, our data also showed that CT images had

remarkably significant difference between NCOVID-19 and NON-NCOVID-19 patients. Most NCOVID-19 patients but NON-NCOVID-19 had bilateral pneumonia with the feature of a multiple mottling and ground-glass opacity in CT images. In addition, somewhat like severe influenza (e.g. H7N9, H1N1pdm 09) [17, 18], inflammation spread quickly in lungs of NCOVID-19 patients. CT scan may be a reliable test for screening NCOVID-19 or NON-NCOVID-19 patients, will compact quick classification of suspected cases or common patients.

In terms of laboratory tests, the absolute value of lymphocytes in most NCOVID-19 and NON-NCOVID-19 patients was reduced. This result suggests that 2019-nCoV infection has similar feature with many other respiratory virus infections, triggered strong innate inflammatory immune response, and caused depletion of lymphocytes after infection[19-22]. Inflammation is a time-depend process, usually starting locally, and is recognized centrally later via blood born mediators[23]. Previous studies suggested that excessive immune response played an important role on pathogenesis of severe influenza or SARS[24]. And IL-6 and CRP may link to the excessive immune response [25, 26]. In this study, our results also showed abnormally increased CRP and IL-6 in most of both NCOVID-19 and NON-NCOVID-19 patients. In our results, the ratio mean of neutrophils is slightly higher in NCOVID-19 than in NON-NCOVID-19 although no statistic difference between them. That might be related to no severe cases involved in this study because numbers of neutrophils was much higher in severe NCOVID-19 than relatively mild NCOVID-19 in Early report [2]. Previous studies have shown that excessive neutrophils contributed to acute lung damage, and are associated with severe disease and fatality in patients with influenza infection[27, 28]. Hence, possibly, excessive immune of host may be associated with the pathogenesis of NCOVID-19 besides virus-specific factors.

Previous reports showed that a proportion of NCOVID-19 patients had differing degrees of liver function abnormality[2, 7]. Our data showed that the levels of liver function associated markers (ALT, AST and γ -GT) were significantly higher in NCOVID-19 patients than in NON-NCOVID-19 patients, and a proportion of NCOVID-19 patients (AST, 26.67%; ALT 27.78%; γ -GT, 44.44%) but NON-NCOVID-19 patients presented abnormal levels of these markers, suggested that acute liver damage was more frequent in NCOVID-19 patients than NON-NCOVID-19 patients. This was also observed in SARS or severe influenza (e.g. H7N9) patients [17, 29]. In addition, LDH showed abnormal level in a proportion of NCOVID-19 patients (31.58%) but in NON-NCOVID-19 patients. And available data showed that most of

NCOVID-19 patients (75%) but NCOVID-19 patients (20%) had an abnormal α -HBDH. The results suggested that 2019-nCoV infected patient may result into multiple tissues or organs damage besides liver injury.

As for treatment, all NCOVID-19 patients were diagnosed and treated in out of Wuhan places in this study. And all NCOVID-19 patients in this study didn't have severe complication like ARDS or multiple organ failure which was reported in Wuhan patients or SARS patients during the admission[2, 7, 29, 30]. However, as for a novel disease, common people have more panic and anxiety on it than other diseases. Psychological counseling should be involved in treatment ingredients.

There are several limitations in this study. Firstly, the sample size was very small. And some laboratory tests weren't conducted in some patients because the NCOVID-19 patients were from two hospitals. Secondly, there was lack of severe infection, to compare findings with severe infection with mild infection. Thirdly, there was lack of pediatric population.

NOTES

Contributors

RGao designed the study and wrote the report. DZhao and FYao gathered data and participated in the clinical treatment. ZhLing, YJun, FGuo and HZhao participated in the clinical treatment. RGao, DZhao and LWang performed data analyses. YGao joined in Collating data. All authors contributed to the review and revision of the manuscript and have read and approved the final version.

Acknowledgments

The authors would like to thank the local center for disease control and prevention for the confirmation of NCOVID-19 or NCOVID-19 patients.

Disclosure

The contents of this article are solely the responsibility of the authors and do not necessarily represent the views of the Centers for Disease Control and Prevention in China or other organizations.

Funding

This work was supported by the National Mega-projects for Infectious Diseases (grant numbers 2017ZX10304402-001-019), National Natural Scientific Foundation of China (grant numbers 81971946), and the second batch of research projects on novel coronavirus pneumonia epidemic of Anhui Medical University (grant numbers YJGG202008).

Conflicts of interests

We declare that we have no conflicts of interest.

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Figure legend

Transverse chest CT images from a 43-year-old male NCOVID-19 patient showing no obvious pneumonia change on day 1 after illness (A), a mottling and ground-glass opacity in right lower lobe on day 3 after illness (B), and multiple mottling and ground-glass opacity in right upper and lower lobes on day 6 after illness (C). Transverse chest CT images from a 56-year-old female NCOVID-19 patient showing bilateral multiple lobular mottling and ground-glass opacity on day 2 after illness onset (D), and extensively bilateral lobular ground-glass opacity on day 4 after illness onset (E). Transverse chest CT images from a 52-year-old female NCOVID-19 patient showing extensively bilateral ground-glass opacity and subsegmental areas of consolidation on day 9 after illness onset (F), and bilaterally reduced ground-glass opacity and subsegmental areas of consolidation on day 15 after illness onset (G). Transverse chest CT images from a 66-year-old female NON-NCOVID-19 patient showing multiple patchy and mottling shadows (H), and partial ground-glass opacity (I) on day 6 after illness onset.

Table.1 Characteristics of COVID-19 and NON-COVID-19 patients

Variable	COVID-19 patients (n=19)	NON-COVID-19 patients (n=15)
Age (y), Median (Interquartile range)	48 (27~56)	35 (27~46)
Females, No. (%)	8 (42.11%)	9 (60.00%)
Bacterial/viral co-infection NO.(%)	2 (10.53)	2 (13.33)
Coxsackie virus	1 (5.26)	0 (0)
Mycoplasma	1 (5.26)	2 (13.33)
Chronic medical illness, NO.(%)	3 (15.79%)	3 (20.00%)
Hypertension	2 (10.53)	1 (6.67)
Ventricular septal defect	0 (0)	1 (6.67)
HBV infection	1 (5.26)	0 (0)

Schizophrenia	0 (0)	1 (6.67)
Duration from exposure to onset (d), Median (Interquartile range)	8 (6~11)	5 (4~11)

Table 2. Clinical characteristics of COVID-19 and NON-COVID-19 patients

Variable	NCP patients (n=19)	NON-COVID-19 patients (n=15)	p value
Duration from onset to admission (d), Median (Interquartile range)	5 (3~9)	4 (2~7)	0.07
Clinical onset, No. (%)			
Fever	15 (78.95)	14 (93.33)	0.36
Cough	9 (47.37)	12 (80.00)	0.08
Sore throat	4 (21.05)	4 (26.67)	1.00
Headache	2 (10.53)	0 (0)	0.49
Fatigue	2 (10.53)	0 (0)	0.49
Diarrhea	1 (5.26)	1 (6.67)	1.00
Chest tightness	1 (5.26)	0 (0)	1.00
Abnormal auscultation of lung, No. (%)	2 (10.53)	5 (30.00)	0.20
Chest CT findings No. (%)			
Unilateral pneumonia	4(21.0 5)	11(23.33)	0.00 5

Bilateral pneumonia	15 (78.95)	4 (26.67)	0.00 5
Multiple mottling and ground-glass opacity	17(89. 47)	1(6.67)	< 0.00 01

Table 3. Laboratory results of COVID-19 and NON-COVID-19 patients

Variable (normal range)	COVID-19 patients (n=19)	NON-COVID-19 patients (n=15)	p value
WBC ($4-10 \times 10^9/L$)	4.92 (1.26-7.63)	6.18(3.37-12.38)	0.30
<4	7/19(36.84%)	4/15(26.67%)	0.72
>10	0 (0%)	2/15(13.33%)	0.19
Lymphocytes (1.1- $3.2 \times 10^9/L$)	0.97 (0.30-2.03)	1.11 (0.62-1.95)	0.66
<1.1	12/19 (63.18%)	10/15 (66.67%)	0.83
Ratio of neutrophils (45-75 %)	74.02 (55.30-93)	67.11 (29.7-82.5)	0.35
>75	11/18 (61.11%)	9/14 (64.29%)	0.85
AST* (15-40 U/L)	34.9 (17.6-103.8)	21.3(13-35)	0.005
>40	5/18(27.78%)	0/14 (0%)	0.03
ALT* (9-50 U/L)	36.37 (11.8-85.0)	21.38 (13-35)	0.03
>50	5/18 (27.78%)	0/14 (0%)	0.03
γ -GT(7-45 U/L)	42.17 (17.0-166.8)	23.14 (12-43)	0.04
>45	8/18 (44.44%)	0/14 (0%)	0.004
LDH (120-250 U/L)	256.94 (150-750)	160 (103-227)	0.008
>250	6/19 (31.58%)	0/15 (0%)	0.02
α -HBDH (72-182 U/L)	223.38 (124-373)	169.53 (124-220)	0.048
>182	6/8(75%)	3/15 (20%)	0.01
CK (50-310 U/L)	92.69 (25-365)	81.87 (36-166)	0.93
>310	1/18 (5.56%)	0/15 (0%)	1.00
CRP* (0-4 mg/L)	26.47 (10-127.1)	21.47 (0.4-142.2)	0.64
>4	18/19 (94.73%)	12/15 (80.00%)	0.3
IL-6 (0-7 pg/mL)	19.34 (8.7-45.3)	15.06 (4.4-33.9)	0.65
>7	6/7	8/11	1.00

AST=Aspartate aminotransferase; ALT=Alanine aminotransferase; LDH=Lactate dehydrogenase; γ -GT= γ -glutamyl transpeptidase; α -HBDH = α -hydroxybutyric dehydrogenase; CK= Creatine kinase; CRP= C-Reaction protein.

Figure 1

