

[ORIGINAL ARTICLE]

Non-COVID-19 Patients with Life-threatening Diseases Who Visited a Fever Clinic: A Single-center, Observational Study in Tokyo, Japan

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Abstract:

Objective In fever clinics screening coronavirus disease (COVID-19), there could be patients with life-threatening diseases that physicians should not overlook. We exploratorily investigated the final diagnosis among non-COVID-19 hospitalized patients who visited the fever clinic.

Methods This was a retrospective, observational, and single-centered study conducted in the National Center for Global Health and Medicine (NCGM), Tokyo, Japan. We conducted a retrospective chart review of patients who visited the fever clinic in the NCGM from 11 March 2020 to 24 April 2020.

Patients Patients who met the following clinical criteria visited the fever clinic in the NCGM: (1) body temperature $>37.5^{\circ}\text{C}$, (2) any symptoms consistent with COVID-19 or (3) referral from local healthcare facilities. In the fever clinic, all patients who met the above criteria had severe acute respiratory syndrome coronavirus 2 polymerase chain reaction test with nasopharyngeal swab specimens. Patients with severe symptoms or an unstable condition were sent to an outpatient clinic for infectious diseases for further evaluation and treatment.

Results Among 1,470 patients who visited the fever clinic, 84 patients were hospitalized, and 45 of them were diagnosed as having COVID-19. Among the remaining 39 non-COVID-19 patients, there were nine patients with life-threatening diseases. The life-threatening diseases included acute heart failure, septic shock, pneumocystis pneumonia, peritonsillar abscess, and necrotizing fasciitis.

Conclusion Physicians should evaluate each patient carefully while considering other life-threatening conditions even in such a COVID-19 pandemic era.

Key words: COVID-19, coronavirus disease, fever clinic, differential diagnosis, life-threatening diseases

(Intern Med 59: 3131-3133, 2020)

(DOI: 10.2169/internalmedicine.5614-20)

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Received: June 15, 2020; Accepted: September 22, 2020; Advance Publication by J-STAGE: November 2, 2020

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Introduction

The outbreak of coronavirus disease (COVID-19) has become a global public health issue (1). Since March 2020, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread throughout Japan, and the number of patients with COVID-19 increased rapidly (2). To prevent nosocomial and community transmissions of SARS-CoV-2, the Japanese Government established fever clinics across the country, with the goal of swiftly identifying individuals with COVID-19.

Patients with COVID-19 were typically afflicted with cold symptoms, such as fever, fatigue, dry cough, myalgia, and dyspnea (3). These symptoms were non-specific and like those of many other frequently encountered infectious diseases. In the era of emerging disease outbreaks, there could be patients with life-threatening diseases that physicians should not overlook. For example, Fairley et al. reported that among 25 persons under investigation for Ebola virus disease (EVD), none were diagnosed with EVD, while 4 patients (16%) were diagnosed with life-threatening infections or conditions other than EVD at the EVD treatment center in the United States in 2014-2015 (4). In the fever clinics, there is a risk of misdiagnosing such life-threatening diseases because there are so many patients that physicians do not have enough time to examine each of them carefully. Besides, there is limited access to imaging studies such as a computed tomography scans to prevent the spreading of viruses.

In order not to overlook life-threatening diseases, it is important to know the epidemiology of diseases concealed under the suspicion of COVID-19. We exploratorily investigated the final diagnosis among non-COVID-19 hospitalized patients who visited the fever clinic.

Materials and Methods

Study design

This was a retrospective, observational, and single-centered study conducted in the National Center for Global Health and Medicine (NCGM), Tokyo, Japan. This clinical study was approved by the Institutional Review Board of the NCGM.

Patients

Patients who met the following clinical criteria were allowed to visit the fever clinic in the NCGM: (1) a body temperature $>37.5^{\circ}\text{C}$, (2) any symptoms consistent with COVID-19 (i.e. running nose, sore throat, cough, shortness of breath, and fatigue) or (3) referral from local healthcare facilities. In the fever clinic, all patients who met the above criteria had SARS-CoV-2 polymerase chain reaction (PCR) test with nasopharyngeal swab specimens. Patients with severe symptoms or an unstable condition were sent to an out-

Table. Final Diagnoses of the Hospitalized Patients Who Visited the Fever Clinic.

Case variable	Total n=84 (%)
COVID-19	45 (54)
Pneumonia*	12 (14)
Pharyngotonsillitis	4 (5)
Pulmonary tuberculosis	3 (4)
Acute heart failure	3 (4)
HIV-pneumocystis pneumonia	2 (2)
Malignant tumor	2 (2)
Bronchitis	2 (2)
Septic shock†	2 (2)
Others‡	9(11)

* Causative pathogens are human metapneumovirus (n=2), *Mycoplasma pneumoniae* (n=1). In the other cases, the causative pathogens could not be identified.

† Caused by urinary tract infection (*Morganella morganii*) and central venous access port-related bloodstream infection (*Streptococcus agalactiae*).

‡ Others include peritonsillar abscess, necrotizing fasciitis, drug eruption, gastroenteritis, cholangitis, gastrointestinal hemorrhage, bronchial asthma, and epilepsy.

HIV: human immunodeficiency virus

patient clinic for infectious diseases (ID) for further evaluation and treatment. Following that, the ID physicians made a diagnosis, and admitted some of them accordingly. The results of the SARS-CoV-2 PCR test was available the day after the patients visited. In other words, doctors in the outpatient clinic for ID did not know whether the patients had COVID-19 or not at the time they were referred.

We conducted a retrospective chart review of patients who visited the fever clinic in the NCGM from 11 March 2020 to 24 April 2020 when it was opened. We collected data regarding the SARS-CoV-2 PCR test results and the final diagnoses of hospitalized patients who visited the fever clinic. Further, we investigated patients with life-threatening diseases. We defined life-threatening diseases as cancer, heart disease, stroke, Human Immunodeficiency Virus/Acquired Immunodeficiency Syndrome (HIV/AIDS) (5), and other diseases that would have a high mortality rate without the intervention of any emergency measures.

Results

In total, 1,470 patients visited the fever clinic in the NCGM. Of these, 84 patients (5.7%) were hospitalized and 45 (3.1%) were diagnosed as COVID-19 positive, as detected through a PCR test. All the patients who had a positive result for the PCR test were hospitalized. Diagnoses of hospitalized patients whose SARS-CoV-2 PCR test results were negative are summarized in Table. The most common disease was pneumonia due to either bacterial or viral infection (n=12, 14%), followed by pharyngotonsillitis (n=4, 5%), pulmonary tuberculosis (n=3, 4%), and acute heart failure (n=3, 4%).

Of the nine patients with life-threatening diseases, three patients with acute heart failure needed non-invasive positive-pressure ventilation and diuretic therapy. Two patients with septic shock needed catecholamines for hemodynamic stabilization. Two patients with pneumocystis pneumonia were newly diagnosed to have HIV/AIDS at this occasion. One patient was diagnosed with a peritonsillar abscess and needed urgent drainage of the tonsils. A patient with necrotizing fasciitis of the right lower extremity required initial debridement immediately; although he had severe pain, redness and swelling in the right leg, he was suspected of being COVID-19 positive and was, thus, referred from a local hospital.

Discussion

We assessed the final diagnosis of the non-COVID-19 hospitalized patients who visited the fever clinic in the NCGM.

One of the most important findings of our study was that nine patients (0.6%) went to the fever clinic with life-threatening conditions during the COVID-19 outbreak. However, in the clinic, the physicians, with the goal of screening COVID-19 patients, were obliged to focus on ruling out COVID-19, and did not consider other differential diagnoses due to a limited amount of time and poor access to imaging studies. With a heuristic method that focuses on assessing whether a patient is COVID-19 positive or not, physicians should check vital signs and complaints, and examine each patient carefully while considering other serious diseases even within a limited period of time and with limited access to imaging studies.

The second important finding was that we encountered cases where patients with a necrotizing fasciitis and a peritonsillar abscess required urgent treatment. Appropriate and relevant patient care in the era of the COVID-19 pandemic requires the following: (1) appropriate infection prevention and control, (2) multidisciplinary cooperation among specialists (6). A fever clinic should be established in or near facilities that meet these two elements.

Another important finding was that 23 patients among non-COVID-19 hospitalized patients (59%) were diagnosed to have cardiac and pulmonary diseases. According to a study by Sahu et al., it is reported that cardiac and pulmonary diseases were common COVID-19 mimickers (7). Our study results were consistent with this. Those epidemiological data would help us to consider differential diagnoses when seeing a patient suspected with COVID-19.

There are three limitations associated with our study, which are as follows: (1) This study was conducted at a single institution, and thus may not reflect the situation in other facilities, (2) we did not investigate the final diagnosis of coinfections with SARS-CoV-2. Thus, there may have been

life-threatening diseases in hospitalized patients with COVID-19, (3) it was not known whether patients who visited our fever clinic and were not admitted to our hospital subsequently developed any severe symptoms and were admitted to other healthcare facilities.

Conclusion

In conclusion, we exploratorily investigated the final diagnosis among non-COVID-19 hospitalized patients who visited the fever clinic in the NCGM. Among them there were nine patients (23%, 9/39) with life-threatening diseases. Physicians should be aware of this fact, and evaluate each patient carefully while considering other life-threatening conditions even in this era of a global pandemic. This research helps to meet the scope of providing a feedback on the current plight of the patients who are ailed with life-threatening diseases. The findings of the study will help physicians evaluate and eventually treat patients carefully with a detailed focus on their overall health and not just screening for COVID-19.

The authors state that they have no Conflict of Interest (COI).

Acknowledgement

We thank the medical staff at the National Center for Global Health and Medicine (NCGM) for their support.

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