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Case Report

Imported and locally transmitted mild SARS-CoV-2 pneumonia cases in Japan

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Here, we describe two mild SARS-CoV-2 pneumonia cases. One was imported from Wuhan, and the other was locally transmitted in Japan without recent travel to China. In both cases, lower respiratory tract symptoms were observed first, and high fever progressed in about one week. The laboratory findings revealed normal WBC and CRP despite apparent lung infiltrations, and typical observations on CT imaging were important diagnostic clues. In the domestic endemic situation, a comprehensive evaluation of the clinical course, and laboratory and radiological findings was required for diagnosis.

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1. Introduction

In December 2019, a cluster of acute respiratory illnesses, now known as the coronavirus disease 2019 (Covid-19) in Wuhan (Hubei Province, China) occurred [1]. The causative virus was categorized as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) by World Health Organization (WHO). Until May 1, a total of 3,175,207 patients and 224,172 deaths were reported in the world, but the number is rapidly increasing. Covid-19 has been confirmed all over the world including Japan (14,281 cases), with 712 international conveyance (Diamond Princess) passenger cases [2]. Some reports describe Covid-19 patients in the U.S, Korea, Germany, Nepal, and Italy [3–7], but case reports and detailed epidemiology are scarce in Japan. Herein, we report two mild SARS-CoV-2 pneumonia cases with good clinical response in Japan.

2. Case reports

2.1. Patient 1

On January 28, 2020, a 25-year-old Chinese woman presented to an emergency hospital in Kyoto with 5 days’ history of cough and 38 °C fever on the same day. Originally from Wuhan, she was a university student, lived in Japan, and visited Wuhan from 16th to 22nd January, 2020. During her stay, she met her grandmother who presented with respiratory symptoms. She had no previous history and no medication. During examination, she showed no abnormal findings. A chest X-ray was performed, but the results were normal. Because of contact history and symptoms, she was suspected of SARS-CoV-2 infection. Oropharyngeal swab specimen was sent to an administrative laboratory for real-time reverse-transcriptase–polymerase-chain-reaction (rRT-PCR) assay. Since her symptoms were stable, she stayed at home while waiting for the test results. On 30th January, 2020, the rRT-PCR test was reported to be positive, and thus she was transferred to our hospital on 31st January, 2020.

On admission to our hospital, she had a fever, cough, slight dyspnea, appetite loss, and fatigue. Her vital signs were normal, and lung sound was clear. Laboratory findings also showed no abnormality (Table 1). Nevertheless, chest computed tomography (CT) revealed ground-glass opacity in the right lower lobe (Fig. 1). Although she had pneumonia, her respiratory status was stable. Therefore, we continued symptomatic treatment such as acetaminophen for fever and dextromethorphan for cough. On days 3 and 6, she had mild diarrhea with spontaneous relief. Fever and cough gradually improved, and her temperature dropped below 37.5 °C on day 6.

Based on the Japanese Ministry of Health, Labour and Welfare (MHLW) criteria, we performed oropharyngeal swab rRT-PCR on days...
whether the customers also comprised some traveler from Wuhan. It was unclear approximately 300 customers from China in a day. It was unclear years and a shop sales assistant in Kyoto had contact with her arrival to Japan on 22nd January; therefore, no infected cases have been identified around him.

2.2. Patient 2

A 26-year-old Chinese man, who has been living in Japan for 5 years and works as a shop sales assistant in Kyoto had contact with approximately 300 customers from China in a day. It was unclear whether the customers also comprised some traveler from Wuhan.

He was careful and used a mask during work from January 21st, 2020, to prevent SARS-CoV-2 infection. He presented with fatigue on January 24th, 2020. Because his body temperature raised up to 37.5 °C and he developed a cough on January 25th, he was absent at the workplace. On January 27th, he visited a hospital, but the results of influenza rapid antigen test were negative. On January 29th, he visited the same hospital because he developed a fever of 38.2 °C with a persistent dry cough. The chest radiography showed no infiltrations. On January 31st, 2020, he presented to our hospital with a deteriorating dry cough and fever over 7 days and diarrhea from the day before. The vital signs revealed a body temperature of 37.7 °C, and respiratory status was normal. The physical examination results were generally unremarkable. The laboratory tests showed no abnormalities (Table 2). The chest radiography showed ground-glass opacities in the right lower lung. The CT showed multiple, ground-glass opacities located in both subpleural spaces of the lower lobe (Fig. 3). He was suspected of pneumonia associated with SARS-CoV-2, and an oropharyngeal swab specimen was sent for rRT-PCR assay to an administrative laboratory. He was admitted for observation to an airborne-isolation unit at our hospital and received only symptomatic treatment. On February 2nd, fever and cough started to improve. On February 4, the specimen obtained on admission was revealed to be positive for SARS-CoV-2 through rRT-PCR assay. Oropharyngeal swab PCR test on the same day was also positive. On February 6 and 7, the oropharyngeal and nasopharyngeal swab PCR tests, respectively, were negative for SARS-CoV-2. The patient was discharged on February 8. The corresponding clinical course is described in Fig. 2. He lived with a colleague in the same house, but until now, no infected cases have been identified around him.

3. Discussion

We report herein two cases with mild SARS-CoV-2 pneumonia, which were successfully treated for the symptoms presented. As in

8 and 11, and both results were negative. She was discharged on day 12, and chest CT on that day showed reduced ground-glass opacity and some scar formation. Her clinical course is shown in Fig. 2.

She was careful to stay home to avoid contact with others since her arrival to Japan on 22nd January; therefore, no infected cases have been identified around her.

![Fig. 1. Chest computed tomography (CT) findings of patient 1, who was diagnosed with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection, revealed ground-glass opacity in her right lower lobes.](image-url)

![Table 1](image-url)

| Measure                        | Reference range | day 6 | day 9 | day 13 | day 16 |
|--------------------------------|-----------------|-------|-------|--------|--------|
| White-cell count (per μl)      | 3500–8500       | 5900  | 4230  | 5300   | 5280   |
| Red-cell count (× 10^6, per μl)| 380–490         | 451   | 469   | 475    | 427    |
| Absolute neutrophil count (per μl) | 2559 | 3159  | 3369  | 3369   |
| Absolute lymphocyte count (per μl) | 1011 | 1511  | 1510  | 1510   |
| Platelet count (× 10^4, per μl) | 13–35           | 27.8  | 24.7  | 27.2   | 35.8   |
| Hemoglobin (g/dl)              | 11.5–15.0       | 13.4  | 14.4  | 14.4   | 13.0   |
| Hematocrit (%)                 | 34–45           | 39.3  | 41.0  | 40.6   | 36.6   |
| Sodium (mEq/liter)             | 135–147         | 140   | 138   | 140    | 141    |
| Potassium (mEq/liter)          | 3.3–4.8         | 3.3   | 3.6   | 3.7    | 4.2    |
| Chloride (mEq/liter)           | 98–109          | 106   | 104   | 105    | 107    |
| Calcium (mg/dl)                | 8.2–10.2        | 8.9   | 9.3   | 9.3    | 9.2    |
| Glucose (mg/dl)                | 70–110          | 100   | 90    | 107    | 111    |
| Blood urea nitrogen (mg/dl)    | 8–21            | 6     | 10.2  | 7.2    | 6.9    |
| Creatinine (mg/dl)             | 0.3–1.1         | 0.62  | 0.62  | 0.64   | 0.69   |
| Total protein (g/dl)           | 6.7–8.3         | 7.8   | 7.9   | 7.9    | 6.8    |
| Albumin (g/dl)                 | 3.9–4.9         | 4.5   | 4.6   | 4.2    | 3.6    |
| Total bilirubin (mg/dl)        | 0.2–1.2         | 0.3   | 0.3   | 0.3    | 0.4    |
| Alanine aminotransferase (U/liter) | 0–30 | 12   | 13    | 13     | 13     |
| Aspartate aminotransferase (U/liter) | 0–35 | 13   | 18    | 17     | 13     |
| Alkaline phosphatase (U/liter) | 110–350         | 175   | 168   | 183    | 171    |
| Lactate dehydrogenase (U/liter) | 120–230 | 144  | 194   | 231    | 205    |
| Activated partial thromboplastin time (sec) | 25.0–38.0 | 32.8  | 37.6  | 37.6   |         |
| Prothrombin time (sec)         | 10.0–14.0       | 14.1  | 13.1  | 13.1   |         |
| International normalized ratio | 1.12            | 1.14  | 1.14  | 1.14   |         |
| D-dimer (μg/ml)                | 0–0.99          | <0.50 | <0.50 |         |         |
| Creatine kinase (U/liter)      | 0–200           | 52    | 50    | 41     | 33     |
| Venous lactate (mmol/liter)    | 0.5–2.0         | 1.09  | 1.09  | 1.09   |         |
| C-reactive protein (mg/dl)     | 0–0.3           | 0.2   | 0.51  | 1.68   | 0.84   |
previous reports, the patients' symptoms were mainly cough, fever, and no rhinorrhea [8]. Both cases progressed to a high fever (over 38°C) on the sixth day after the appearance of cough. However, it was difficult to distinguish it from the usual viral upper respiratory tract infection in the early days of the disease. Laboratory findings showed that both white blood cell count (WBC) and C-reactive protein (CRP) were within the normal range at the first visit, and the results were not compatible with bacterial pneumonia. Radiological findings showed ground-glass opacity in the airway dissemination non-segmental pneumonia, similar to previous reports [9].

Patient 1 had a travel history to Wuhan, and the diagnosis was relatively easy, but Patient 2 had only a contact history with many usual Chinese travelers. For that reason, we hesitated to perform the rRT-PCR test. However, we noted that 1) he had a contact with many Chinese travelers, 2) lower respiratory tract symptoms preceded high fever in about one week, 3) laboratory findings showed normal WBC and CRP values despite apparent lung infiltrations, 4) typical findings on CT imaging were important diagnostic clues, which enabled us to diagnose without critical delay. Recently unlinked cases were reported in many countries, including Japan. In such a situation, contact with patients or travel history is useless. It is necessary to shift to a strategy to perform rRT-PCR test for the patients with unexplained pneumonia. We believe the diagnostic clues described above can be helpful for appropriate evaluation.

According to a report of 1099 patients from China, only 3.8% of patients with COVID-19 had diarrhea on admission [8]. However, our two patients had diarrhea during the clinical course. Even if there is no diarrhea at the onset of pneumonia, it may appear later. It has been reported that one patient with atypical abdominal symptoms was admitted to a surgical ward, and may have contaminated more than 10 healthcare workers in Wuhan [10]. We are not able to exclude COVID-19 just because of the presence of diarrhea. Several studies have demonstrated the presence of viral RNA in stool or anal/rectal swabs of COVID-19 patients [11].

![Fig. 2. Clinical course of two mild severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia case-patients. A) patient 1, a 25-year-old Chinese woman, returned from Wuhan. B) patient 2, 26-year-old Chinese man locally transmitted in Japan.

Table 2
Clinical laboratory results at the time of hospital admission, day 8, 12 post-illness onset, for patient 2 of mild severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pneumonia.

| Measure                        | Reference range | day 8 Jan 31 | day 12 Feb 4 |
|-------------------------------|-----------------|--------------|--------------|
| White-cell count (per μl)     | 3500–8500       | 4650         | 3940         |
| Red-cell count (× 10⁶, per μl) | 380–490        | 522          | 485          |
| Absolute neutrophil count (per μl) | 11.5–15.0       | 14.9         | 16.8         |
| Absolute lymphocyte count (per μl) | 13–35         | 46.0         | 43.1         |
| Platelet count (× 10⁴, per μl) | 135–147       | 137          | 140          |
| Hemoglobin (g/dl)             | 8.2–10.2       | 9.5          | 8.9          |
| Sodium (mEq/liter)            | 110–130        | 113          | 104          |
| Potassium (mEq/liter)         | 3.3–4.8        | 4.2          | 4.1          |
| Chloride (mEq/liter)          | 98–109         | 103          | 107          |
| Calcium (mg/dl)               | 0.2–1.2        | 0.4          | 0.4          |
| Creatinine (mg/dl)            | 0.3–1.1        | 0.83         | 0.75         |
| Total protein (g/dl)          | 0.3–1.1        | 0.83         | 0.75         |
| Albumin (g/dl)                | 6.7–8.3        | 7.6          | 6.8          |
| Total bilirubin (mg/dl)       | 0.3–1.1        | 0.83         | 0.75         |
| Alanine aminotransferase (U/liter) | 0–30        | 12           | 12           |
| Aspartate aminotransferase (U/liter) | 0–35      | 15           | 13           |
| Alkaline phosphatase (U/liter) | 110–350       | 165          | 150          |
| Lactate dehydrogenase (U/liter) | 120–230       | 192          | 150          |
| Creatine kinase (U/liter)     | 0–200          | 68           | 43           |
| C-reactive protein (mg/dl)    | 0–0.3          | 0.23         | 0.11         |
should be careful and take contact precautions against patients with digestive symptoms. It has been reported that severely ill patients had more digestive symptoms than those showing non-severe illness, but some reports have denied this.[12] The two patients in our report did not show severe illness and responded well to the clinical course.

There have been few reports describing the time until viral RNA becomes undetected. In our cases, SARS-CoV-2 became undetected by rRT-PCR at day 16 (Patient 1) and day 14 (Patient 2) of illness. According to reports from 18 COVID-19 confirmed patients in China, viral RNA became undetected in 3–17 days of illness.[13] However, other reports described the case in which viral RNA persisted detectable after 21 days of illness, or reoccurrence of viral detection was observed after rRT-PCR negative confirmation [14,15]. The detectable duration of viral RNA may vary from case to case. However, it should be noted that the negative conversion of rRT-PCR does not necessarily indicate a loss of infectivity. Moreover, it was reported that the nasopharyngeal specimen showed rRT-PCR-positive result longer than that of the oropharyngeal sample, but we used only either the nasopharyngeal or the oropharyngeal specimen. Further research is needed to analyze infectivity by using appropriate specimens.

**Ethical approval**

Written informed consent was obtained from the patients and for the publication of this case report.

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**Declaration of Competing Interest**

None declared.

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