Case of a pregnant woman with probable prolonged SARS-CoV-2 viral shedding 221 days after diagnosis

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ABSTRACT

We describe a case of probable prolonged severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Alpha (B.1.1.7) variant shedding for 221 days from the diagnosis, in a healthy 20-year-old Japanese pregnant woman with a normal delivery. To our knowledge, this is the longest duration of SARS-CoV-2 shedding reported in an immunocompetent individual to date.

1. Introduction

In the era of the coronavirus disease (COVID-19) pandemic, medical institutions are struggling to prevent the spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) in their facilities. Prehospital screening protocols of pregnant women for SARS-CoV-2 infection vary by country, region, and epidemic status. Before admission, pregnant women are generally asked about the presence of fever and upper respiratory symptoms, travel and occupational history, and history of close contact and involvement with clusters [1]. In settings where there is a moderate to high risk of infection, pregnant women should be tested. As there are concerns that asymptomatic pregnant woman may be missed with these protocols, some health care facilities perform real time reverse-transcription polymerase chain reaction (RT-PCR) testing of all pregnant women on admission.

We recently observed the case of a woman admitted to our hospital for a normal delivery who was initially diagnosed with SARS-CoV-2 infection during pregnancy and tested positive for SARS-CoV-2 by RT-PCR 221 days after the diagnosis of COVID-19.

2. Case

At the end of May 2021, a 20-year-old nulliparous woman sought medical attention for a fever. She was diagnosed with COVID-19 after a positive SARS-CoV-2 antigen test result. She showed no symptoms other than fever during the treatment course; thus, her quarantine was completed in 10 days (as scheduled). She had no episode of visiting crowded places and denied any fever or upper respiratory symptoms since her previous COVID-19 diagnosis. None of her family members had any symptoms of COVID-19. She subsequently discovered that she had been about 8 weeks pregnant at the time of her fever. She received two doses of a COVID-19 mRNA vaccine in September and October 2021.

In December 2021, she was admitted to our hospital due to frequent contractions (every 10 min) at 38 2/7 weeks gestation. Apart from COVID-19 in May 2021, her pregnancy had been uneventful, and she did not have gestational diabetes. On admission, she underwent an uncomplicated vaginal delivery of a 3320 g female neonate, with 1- and 5-min Apgar scores of 8 and 9, respectively.

The results of routine SARS-CoV-2 RT-PCR performed on a nasopharyngeal specimen collected on admission was positive (cycle threshold [Ct] = 36.4). Screening tests for variant strains revealed the

presence of the N501Y mutation, an indicator of the Alpha (B.1.1.7) variant; however, L452R, an indicator of the Delta (B.1.617.2) variant, and G339D and E484A, which are indicators of the Omicron (B.1.1.529) variant, were negative. Viral genomic sequencing of the specimens was attempted, but due to the small amount of virus contained in the specimens, no analysis was possible.

2.1. Microbiological investigations

MagLEAD 12gC (Precision System Science Co., Ltd., Chiba, Japan) and MagDEA® Dx SV (Precision System Science Co., Ltd.) were used to extract viral RNA from nasopharyngeal swab specimens. To detect SARS-CoV-2, QuantStudio™ 5 Dx (Life Technologies Japan Ltd., Tokyo, Japan) and Takara SARS-CoV-2 Direct PCR detection kit (Takara Bio Ltd., Shiga, Japan) were used for RT-PCR. Testing for the Alpha, Delta, and Omicron variants was performed with Applied Biosystems® 7500 Real-Time PCR System (Thermo Fisher Scientific Ltd., Tokyo, Japan) using Primer/Probe N501Y (Takara Bio Ltd.), Primer/Probe L452R Ver.2 (Takara Bio Ltd.), Primer/Probe G339D (Takara Bio Ltd.), and Primer/Probe E484A (Takara Bio Ltd.). All procedures were performed according to the protocols of the National Institute of Infectious Diseases (Japan) [2].

3. Discussion

We reported the case of a pregnant woman who was admitted to our hospital for a normal delivery who tested positive for SARS-CoV-2 by RT-PCR 221 days after a COVID-19 diagnosis. We detected the SARS-CoV-2 Alpha variant in a nasopharyngeal swab specimen, although the SARS-CoV-2 Alpha variant was no longer circulating in Japan at the time of her admission. Thus, based on the following reasoning, we concluded that this was a case of prolonged viral shedding: 1) The patient had no acute symptoms and no known contacts with SARS-CoV-2 infection; 2) the Ct value of 39.2 suggests a very low viral load; and 3) the wave in Japan dominated by the Alpha variant ended in July 2021 [3].

The epidemiological data of the predominant variant strains in Ibaraki Prefecture, where the patient lives and where our hospital is located, are available on the website [4]. The Alpha (B.1.1.7) variant was the predominant strain from April to July 2021, but had been almost completely replaced by the Delta variant by mid-September 2021. The Omicron variant epidemic started in Ibaraki Prefecture in late December 2021, just after the patient tested SARS-CoV-2-positive on RT-PCR testing, and accounted for almost all SARS-CoV-2 infections in January and February 2022. Assuming that our patient was re-infected with SARS-CoV-2 in December 2021, the strain that infected her should have been the Delta or Omicron variant. This epidemiological data supports our conclusion that it is unlikely that the pregnant woman would have been infected with the Alpha variant in Ibaraki Prefecture in late December 2021.

Patients with mild to moderate and severe COVID-19 have been reported to test positive by RT-PCR for up to 17.2 days and 19.8 days after the onset, respectively [5]. Prolonged viral shedding beyond these periods has been reported. According to a meta-analysis of 79 articles involving 5340 patients, the average duration of SARS-CoV-2 shedding in specimens collected from the upper airway was 17.0 days, with a maximum of 83 days [6]. Another meta-analysis found that risk factors for prolonged viral shedding included older age, hypertension, coronary artery disease, and diabetes mellitus [5]. Pregnant women are not considered a high-risk group for prolonged viral shedding, and as far as we are aware, there has been only one case report of prolonged viral shedding during pregnancy [7]. Molina et al. [7] described a case of a pregnant woman who continued to shed virus for up to 104 days after her initial positive test. Our case is unique as it documents probable prolonged viral shedding 221 days after the diagnosis of SARS-CoV-2 infection in a healthy pregnant woman.

The mechanism of prolonged viral shedding during pregnancy remains unclear. Dashraath et al. [1] suggested that as the maternal body physiologically shifts to a Th2-dominant environment during pregnancy, the attenuation of cell-mediated immunity by Th1 cells increases maternal susceptibility to intracellular pathogens, including viruses, and contributes to overall morbidity from infectious diseases. Littauer et al. [8] reported that the viral load of influenza virus in the lungs of pregnant mice was eight times higher than that in those of non-pregnant mice, suggesting that viral clearance is inhibited during pregnancy. Conversely, this physiological shift to a Th2-dominant state, which promotes the expression of anti-inflammatory cytokines, may serve as the predominant immune response to SARS-CoV-2, resulting in less severe COVID-19 than in non-pregnant individuals [1,9]. Thus, it has been hypothesized that the physiological change of the maternal immune system to a Th2-dominant state causes prolonged viral shedding while preventing severe COVID-19.

In the past year, laboratory equipment for rapid RT-PCR testing of SARS-CoV-2 has been developed and has been widely used in many healthcare institutions to perform testing in a shorter time, without requiring special knowledge or skills for operation. The results of such tests are consistent with those of conventional methods with a high level of accuracy [10]. However, these instruments are often qualitative and do not report Ct values. In addition, information on the variant strains cannot be obtained. Therefore, using these instruments alone does not allow viral shedding to be distinguished from acute infection. This is a shortcoming of rapid RT-PCR methods.

A limitation of this study is that due to the small amount of virus, genomic sequencing of the specimen was not successful. Therefore, we were unable to confirm that the strain was the Alpha variant. However, based on the results of the variant strain screening PCR test (N501Y positive, L452R negative, G339D negative, E484A negative), it is likely to have been the Alpha variant.

Authorship statement

Consent for publication

The patient provided written informed consent for the publication of her anonymized case description.

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Declaration of competing interest

None.

Acknowledgment

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