Changes in RT-PCR test results and symptoms during the menstrual cycle of a female individual infected with SARS-CoV-2: a case report

Hua Zheng (hzheng@hust.edu.cn)

Department of anesthesiology, Tongji hospital of Tongji Medical college, Huazhong University of science and Technology, Wuhan, China

Juan Tan

Department of anesthesiology, Tongji hospital of Tongji Medical college, Huazhong University of science and Technology, Wuhan, China

Ke Ma

Department of Infectious Disease, Tongji Hospital of Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China

Weihua Meng

Division of Population Health Sciences, School of Medicine, University of Dundee, Dundee, UK

Case Report

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Abstract

Background: The implications of the menstrual cycle for disease susceptibility, development, and severity of acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection are largely unknown.

Case presentation: We report a 37-year-old woman infected with SARS-CoV-2 who showed a 16-day incubation period. She developed a fever on the first day of her menstrual period, and again on the first day of her next menstrual period after hospital discharge. RT-PCR test results were positive during the first menstrual period before admission, turned negative during hospitalization, and then positive again during the second menstrual period after hospital discharge.

Conclusions: This case indicates sex hormones may play an important role in SARS-CoV-2 infection. For women with history of exposure to SARS-CoV-2, the management protocol should include assessment of the menstrual status.

Background

The 2019 novel coronavirus infection (COVID–19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV–2), has emerged as a major global health threat since December 2019 [1–4]. As of April 2, 2020, the pandemic had registered 896450 cases and 45525 deaths worldwide [5]. A population level observational study by Sun and colleagues [6] revealed that a sharp increase of COVID–19 was reported among people aged between 30 and 50 years, and 40% of the patients were female, indicating women of childbearing age are at high risk of infection. Growing evidences indicate that female immunity changes over the menstrual cycle [7, 8]. However, the implications of the menstrual cycle for disease susceptibility, development, and severity of COVID–19 are largely unknown. Here, we report the epidemiologic and clinical features of a female individual with SARS-CoV–2 infection and the infection's association with the menstrual cycle.

Case Presentation

A 37-year-old, previously healthy (gravida 2, para 2, regular menstrual cycle, no history of hormonal therapies), woman had dinner with her relative on January 12, 2020. Five days later, her relative had a fever and was confirmed to be infected with SARS-CoV–2. The woman had no fever or any other gastrointestinal or respiratory symptoms until January 28, 2019, the first day of her menstrual period (Figure 1). At first, she had only a slight and intermittent fever. The next afternoon, she developed high fever, tiredness, and lack of appetite. Because of the possibility of infection with SARS-CoV–2, she was prescribed ibuprofen, oseltamivir (75 mg every 12 h orally), arbidol (0.2 g every 8 h orally), and moxifloxacin (0.4 g every day orally) by a community physician. Lopinavir and Ritonavir tablets (200 mg/50 mg every 12 h orally) were added to her antiviral regimen two days later. Her symptoms did not improve, prompting her to come to the emergency department on February 2, 2020. Although chest auscultation was normal, chest CT scans showed bilateral lower lobe infiltrates (Figure 2A). Real-time

reverse transcriptase–polymerase chain reaction (RT-PCR) test for nucleic acid of SARS-CoV–2 on an oropharyngeal swab was performed as described in a previous study [2]. The same technician and brand of test kit (Novel Coronavirus PCR Fluorescence Diagnostic Kit, BioGerm Medical Biotechnology), which was recommended by the Chinese Center for Disease Control and Prevention, was used in this report. The result of RT-PCR test was positive. The patient was asked to self-quarantine at home because of limited hospital beds in Wuhan at that time. Her temperature dropped to normal one day later, the last day of her menstrual period.

On February 4, 2020, the patient was hospitalized with COVID–19. On admission, the physical examination revealed body temperature of 97.5℉(36.4℃), blood pressure of 98/61 mmHg, pulse rate of 78 beats per minute, respiratory rate of 20 breaths per minute and oxygen saturation of 95% on room air. The results of her laboratory testing showed a C-reactive protein count 12.3 mg/L (< 1 mg/L indicates low risk of cardiovascular disease; 1 - 3 mg/L indicates medium risk of cardiovascular disease; > 3 mg/L indicates high risk of cardiovascular disease; > 10 mg/L indicates infection or inflammation) and erythrocyte sedimentation rate of 30 mm/H (normal range 10 - 30 mm/H). Other pertinent laboratory tests, including complete blood count, coagulation tests, liver function tests, kidney function tests, metabolic panel tests, and high-sensitivity cardiac troponin tests did not reveal any clinically significant results. A follow-up chest CT scan on February 8, 2020, showed the shadow on bilateral lung was partly absorbed (Figure 2B). Thus all of her antiviral and antibacterial medications were canceled. RT-PCR tests for nucleic acid of SARS-CoV–2 on oropharyngeal swabs were performed 3 and 6 days after admission and the results were positive. The RT-PCR tests on oropharyngeal swabs were repeated 10 and 12 days after admission, and both showed negative results. On February 14, 2020, a repeated chest CT scan showed a further improvement of ground-glass opacification (Figure 2C). Her temperature remained normal during hospitalization. According to the criteria for hospital discharge in China including: (1) normal temperature for at least 3 days, (2) resolution of respiratory symptoms, (3) substantially improved radiological signs, and (4) negative results in two consecutive RT-PCR tests performed ≥ 24 h apart, this patient was discharged on February 18, 2020.

After hospital discharge, the patient was asked to continue home quarantine for 14 days. She felt well until February 24, 2020, the first day of her menstrual period. The patient did not report contact with any other person but had fever again, peaking at 100.2℉(37.9℃). Except for tiredness, she had no other symptoms at that same time. She took arbidol (0.2 g every 8 h orally) and moxifloxacin (0.4 g every day orally) for three days. The results of a RT-PCR test on February 25, 2020 and a repeated test on oropharyngeal swabs four days later were both positive. However, chest CT scans showed no changes from the previous results (Figure 2D). The patient still had a slight and intermittent fever until February 29, 2020, the last day of her menstrual period. Since then, her temperature has remained normal. The RT-PCR test on oropharyngeal swab was performed on March 10, 2020, and the result was negative. However, her blood was positive for both IgG and IgM antibodies against SARS-CoV–2.

Discussion And Conclusion

There are reported sex differences in the susceptibility and outcomes of infectious disease [9, 10]. A recent epidemiological study of the COVID–19 outbreak shows that SARS-CoV–2 might have a longer incubation period and less pronounced symptoms in women than in men [11]. However, the mechanism underlying these differences remains unclear. Here, we report a female patient infected with SARS-CoV–2 who showed a 16-day incubation period. She developed a fever on the first day of her menstrual period, and again on the first day of her next menstrual period after hospital discharge. RT-PCR test results were positive during the first menstrual period before admission, turned negative during hospitalization, and then positive again during the second menstrual period, which occurred after hospital discharge. This case indicates sex hormones may play an important role in SARS-CoV–2 infection.

In female humans, the levels of sex hormones, largely estrogens and progesterone, vary during the menstrual cycle and decrease sharply before menstruation [12]. The dramatic fluctuation in sex hormone levels is associated with changes in immune function and response to respiratory virus infections [13]. In an animal model of influenza A virus infection, estrogen is reported to be a potent anti-inflammatory hormone and to reduce adaptive immune responses and protect hosts from influenza A virus-mediated pathogenesis [14]. In another animal model of the severe acute respiratory syndrome coronavirus (SARS-CoV) infection, treatment with an estrogen receptor antagonist or ovariectomy can increase mortality in females, indicating a critical role of estrogen receptor signaling in protecting females from severe SARS-CoV infection [15]. Consistent with these previous studies, our findings in the current case showed a close association between symptoms, positive RT-PCR test results and the menstruation. Future studies exploring the role and mechanism of sex hormones in the pathogenesis of SARS-CoV–2 infection are warranted.

In the current case, the incubation period is 16 days after exposure to SARS-CoV–2, which is longer than the 14-day of observation period recommended by WHO. This finding is consistent with the results of a recent study, which showed that SARS-CoV–2 might have a longer incubation period in women than in men [11]. Thus, differential control measures for women need to be considered. For women with history of exposure to SARS-CoV–2, the observation period might be longer than 14 days. Furthermore, the menstrual status need to be included in the observation period. During the observation period, the identification of potentially infected patients should be based on the results of RT-PCR tests or CT scans rather than symptoms.

The patient in this report had a recurrence of fever and positive RT-PCR test results on the first day of her first menstrual period after hospital discharge. There are increasing reports regarding positive RT-PCR test results in convalescent COVID–19 patients [16–18]. These observations suggest that some of the recovered patients still might be virus carriers. The management protocol for hospital discharge might need to be reevaluated, and the 14 days of home quarantine should include assessment of the menstrual status of female patients.

In summary, our report provides an initial view of the association between the menstrual cycle, symptoms and RT-PCR test results. Future studies in large cohorts are necessary to address the effect of sex

hormones on the clinical course of COVID–19.

Abbreviations

COVID–19: the 2019 novel coronavirus infection; SARS-CoV–2: severe acute respiratory syndrome coronavirus 2; RT-PCR: Real-time reverse transcriptase–polymerase chain reaction; SARS-CoV: severe acute respiratory syndrome coronavirus

Declarations

Ethics approval and consent to participate

Institutional Review Board (IRB) approval for this report was granted through the ethic committee of Tongji hospital, Tongji Medical College, Huazhong University of Science and Technology (TJ-C20200142).

Consent for publication

The signed consent has been obtained from the patient in this case report.

Availability of data and materials

All data generated or analysed during this study are included in this published article.

Competing interests

All authors declare that they have no conflicts of interest.

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Authors' contributions

All authors discussed the results and commented on the manuscript. Specifically, HZ and JT contributed to the conception of the idea and the study design. HZ prepared the data set, performed the analysis and wrote the manuscript. KM contributed to analysis and interpretation of data. WM provided intellectual inputs for the project and critical comments on the manuscript.

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Author details

[1] Department of Anesthesiology, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

[2] Department of Infectious Disease, Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, Wuhan, China.

[3] Division of Population Health Sciences, School of Medicine, University of Dundee, Dundee, UK.

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Figures

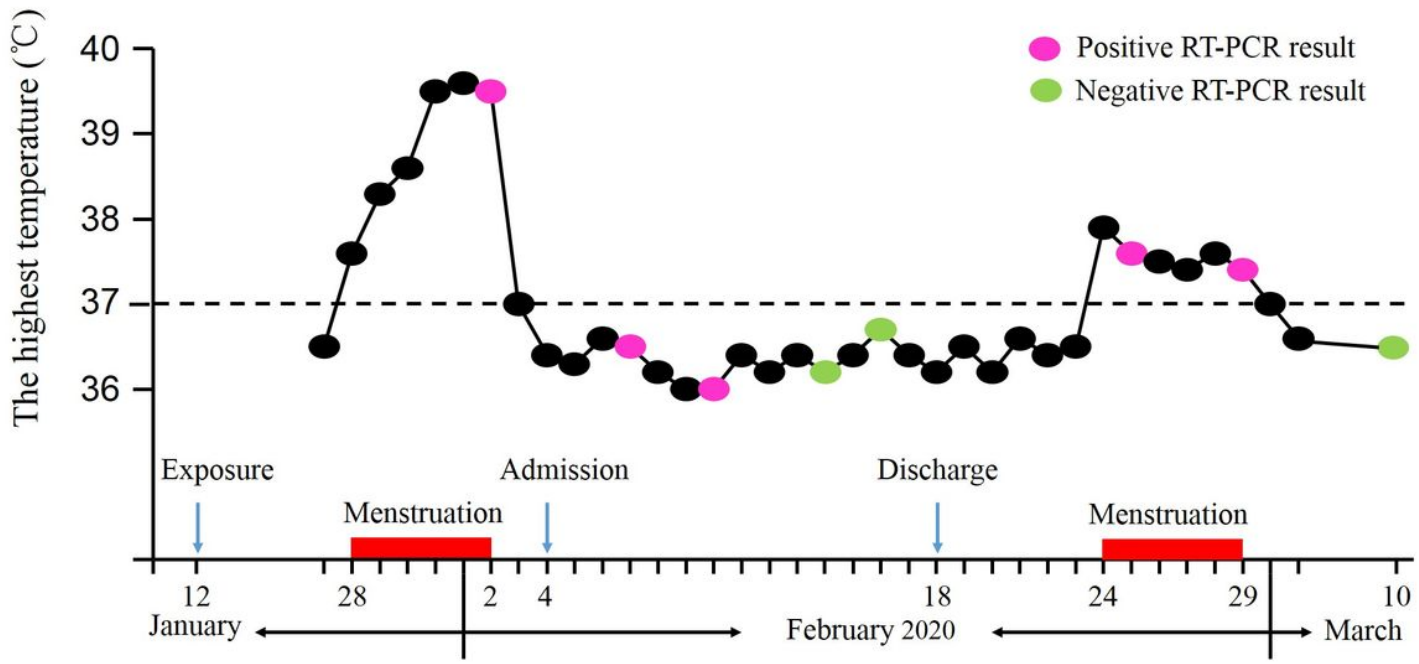

Figure 1

Timeline of changes of RT-PCR test results and symptoms during the menstrual cycle of a female individual infected with SARS-CoV-2. Sixteen days after exposure to SARS-CoV-2, fever occurred on the first day of her menstrual period, and again on the first day of her next menstrual period after hospital discharge. RT-PCR test results were positive during the first menstrual period before admission, turned negative during hospitalization, and then positive again during the second menstrual period, which occurred after hospital discharge. RT-PCR indicates real time polymerase chain reaction test for the coronavirus disease 2019 (COVID-19) nucleic acid.

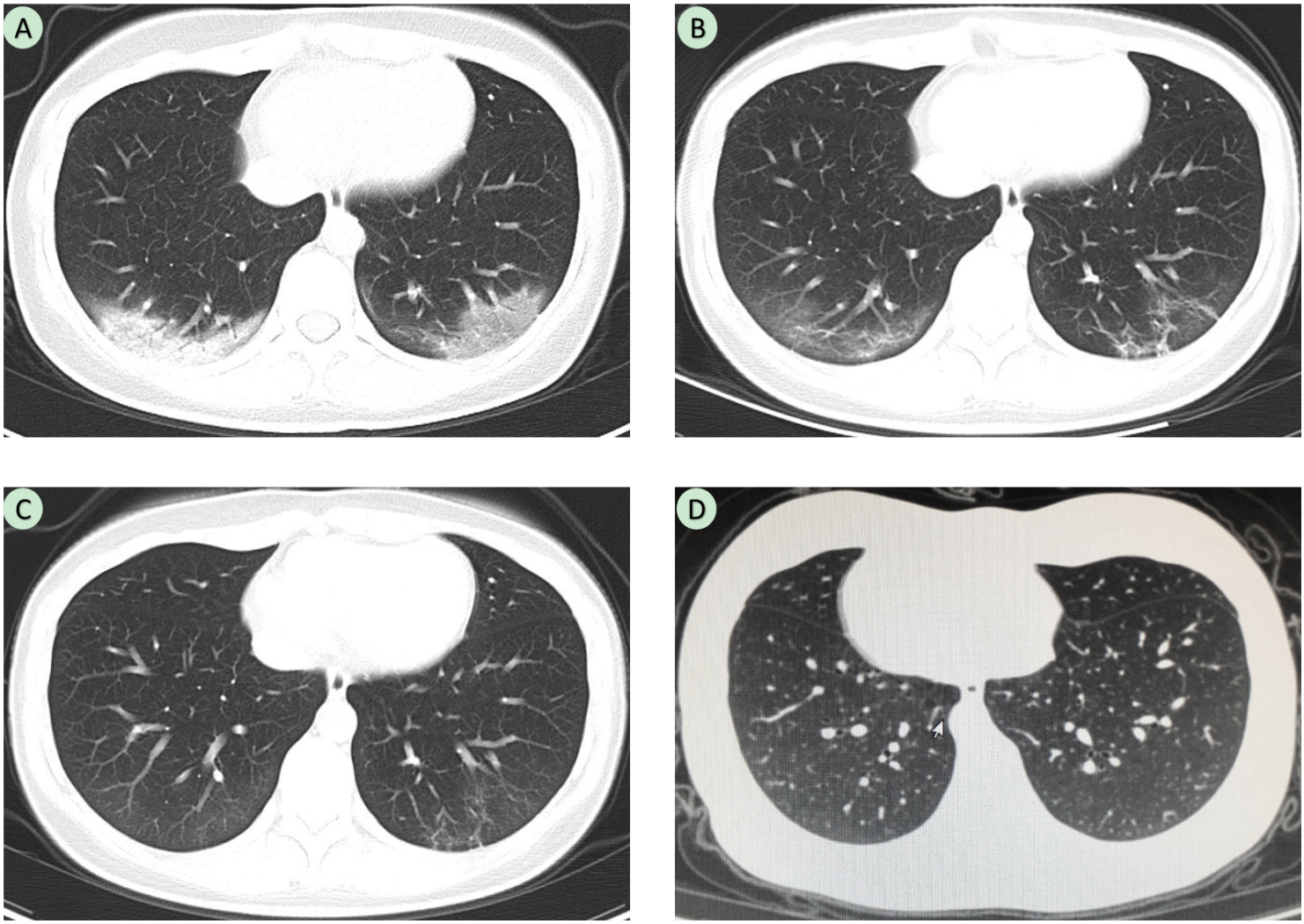

Figure 2

Transverse chest CT images of a 37-year-old woman infected with SARS-CoV-2. Representative images of the chest CT scans showing (A) bilateral ground-glass opacity and subsegmental areas of consolidation on day 6 after symptom onset, (B) bilateral ground-glass opacity on day 12 after symptom onset, (C) bilateral patchy ground-glass opacity on day 18 after symptom onset, and (D) focal ground-glass opacity on day 29 after symptom onset.