A 48-Year-Old Immunocompetent Female Resident of Southern Florida with Confirmed Reinfection with P.1 (Gamma) Variant of SARS-CoV-2

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Patient: Female, 48-year-old
Final Diagnosis: COVID 19 infection

Symptoms: Cough • diarrhea • dyspnea • fatigue • fever • headache • lightheadedness • nausea • sore throat • vomiting

Medication: —

Clinical Procedure: —

Specialty: Infectious Diseases

Objective: Unusual clinical course

Background: During the global Coronavirus Disease-2019 (COVID-19) pandemic, the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO) have identified and monitored variants of concerns (VOCs) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). P.1 (Gamma) variant was initially identified in northern Brazil but has now spread worldwide. This is a report of a 48-year-old female resident of southern Florida with confirmed reinfection with P.1 variant 9 months following the initial infection. This patient was not immunocompromised and was not vaccinated.

Case Report: A 48-year-old woman residing in southern Florida presented with symptoms of COVID-19 and tested positive for SARS-CoV-2 with oral swab polymerase chain reaction (PCR) in September 2020. Her symptoms resolved spontaneously after 5 days. Nine months later, the patient again presented with respiratory, digestive, and constitutional symptoms. The nasopharyngeal swab SARS-CoV-2 PCR was positive. At that time, she had not received any vaccinations against SARS-CoV-2. Whole-genome sequencing (WGS) of viral RNA from the patient’s second infection confirmed that the viral strain was P.1 variant 9 months following the initial infection. This patient was not immunocompromised and was not vaccinated.

Conclusions: This report has identified a confirmed case of reinfection with P.1 variant of SARS-CoV-2 outside Brazil. This case supports recent epidemiological findings that indicate this VOC may have increased infectivity and virulence, and highlights the importance of SARS-CoV-2 vaccination for everyone.

Keywords: COVID-19 • COVID-19 Vaccines • Reinfection • SARS-CoV-2 • SARS-CoV-2 Variants

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Background

The emergence of a variant of concern (VOC) posed a great challenge in the global effort to manage the Coronavirus Disease-2019 (COVID-19) pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection [1]. The World Health Organization (WHO) has been monitoring and assessing the genomic evolution of SARS-CoV-2 since January 2020 [2]. More specifically, the WHO Virus Evolution Working Group, established in June 2020, coordinates international efforts to monitor and counteract the evolution and spread of SARS-CoV-2 variants [2]. The WHO defines a variant of interest (VOI) as “a SARS-CoV-2 variant (i) with genetic changes that are predicted or known to affect virus characteristics such as transmissibility, disease severity, immune escape, diagnostic or therapeutic escape, and (ii) identified to cause significant community transmission or multiple COVID-19 clusters, in multiple countries with increasing relative prevalence alongside increasing number of cases over time, or other apparent epidemiological impacts to suggest an emerging risk to global public health” [1]. A variant of concern (VOC) is defined as “a SARS-CoV-2 VOI that has been demonstrated to be associated with increased transmissibility, increased virulence, or decreased effectiveness of public, social, or medical measures, at a degree of global public health significance” [1].

Among VOCs circulating in the USA, P.1 (Gamma) variant was first detected in November 2020 in northern Brazil, when there was a second surge of infections in the city of Manaus [3]. An epidemiological study in Brazil identified changes in the pattern of infection and mortality due to COVID-19 in patients of different ages and genders associated with the emergence of the P.1 strain [4]. The study reported a higher incidence of infection and a higher case fatality rate in younger age groups [4]. In addition, as genetic variants of VOCs reduce neutralization by antibodies from prior infection or vaccination [5], the concern for reinfection is higher.

Cases of the P.1 variant were identified in Florida as early as February 2021 by the Florida Bureau of Public Health Laboratories via whole-genome sequencing (WGS) [6]. SARS-CoV-2 variant data for Florida from the Centers for Disease Control and Prevention (CDC) website showed the prevalence of P.1 at 9.8% in early June 2021 and increasing to 18% in mid-July until the arrival of B.617.2 (Delta variant), which became the predominant strain in Florida by early August 2021 [7] (Table 1). During the week of August 1st to August 7th, the prevalence of P.1 in Florida dropped to 2.2% of all SARS-CoV-2 strains sequenced [7]. During the week of August 8th to August 14th, 0.2% of new SARS-CoV-2 infections with variant strains in the USA were attributed to P.1 variant [7].

Here, we present a case of a 48-year-old female resident of southern Florida with confirmed reinfection with P.1 variant 9 months following the initial infection. This patient was not immunocompromised and was not vaccinated. To the best of our

Table 1. Proportion of VOCs and other lineages in Florida [7].

| Date       | Alpha (B.1.1.7) | Beta (B.1.351) | Delta (B.617.2) | Gamma (P.1) | Delta (AY.1) | Delta (AY.2) | Delta (AY.3) | Other lineages |
|------------|----------------|----------------|----------------|-------------|--------------|--------------|--------------|---------------|
| 06/02/2021 | 69%            | 0.4%           | NR             | 9.8%        | NR           | NR           | NR           | 19.4%         |
| 06/09/2021 | 67.4%          | 0.3%           | NR             | 10.4%       | NR           | NR           | NR           | 21%           |
| 06/16/2021 | 67.2%          | 0.3%           | 1.3%           | 11.8%       | NR           | NR           | NR           | 18.5%         |
| 06/23/2021 | 63.1%          | 0.2%           | 2.3%           | 14.7%       | NR           | NR           | NR           | 19.2%         |
| 06/30/2021 | 62.3%          | 0.2%           | 2.8%           | 15%         | NR           | NR           | NR           | 19.3%         |
| 07/07/2021 | 48.6%          | NR             | 13.2%          | 18%         | NR           | NR           | NR           | 20.2%         |
| 07/14/2021 | 48.4%          | NR             | 13.4%          | 18.1%       | NR           | NR           | NR           | 20.2%         |
| 07/21/2021 | 34%            | 0%             | 36.1%          | 13.7%       | NR           | NR           | NR           | 16.2%         |
| 07/28/2021 | 33.8%          | 0%             | 36.8%          | 13.4%       | NR           | NR           | NR           | 16%           |
| 08/04/2021 | 14.3%          | 0%             | 65.4%          | 7.3%        | NR           | NR           | NR           | 0.2%          |
| 08/11/2021 | 11.8%          | 0%             | 69%            | 6%          | NR           | NR           | NR           | 10.2%         |
| 08/18/2021 | 3.4%           | 0%             | 86.4%          | 2.2%        | 0%           | 0.2%         | 3.8%         | 4%            |

NR – not reported. * AY.1, AY.2, AY.3, and B.617.2 are sub-lineages within Delta. ** Independent classification may be assigned in the future to AY.1 through AY.12.
knowledge, there have been no previously published cases of reinfection with the P.1 variant of SARS-CoV-2 outside of Brazil.

Case Report

A 48-year-old female resident of southern Florida who is obese with body mass index (BMI) of 38.10 kg/m², and has history of hepatosteatosis, hypothyroidism, osteoarthritis, and malignant melanoma excised in 2018 and 2019 with no documented recurrence, acutely developed fever, cough, malaise, diarrhea, anosmia, and ageusia in mid-September of 2020. The oral swab SARS-CoV-2 polymerase chain reaction (PCR) resulted positive on September 16, 2020. Specific genomic sequencing of this viral isolate was not performed. Her symptoms lasted 5 days and resolved spontaneously without any complications. She did not require any hospital visits, oxygen supplementation, or specific COVID-19-directed treatments.

On June 26, 2021, the patient presented to the Emergency Department of our institution reporting worsening shortness of breath, productive cough, sore throat, fever, fatigue, light-headedness, headaches, nausea, vomiting, and diarrhea. The patient specifically endorsed that these symptoms started on June 17th. The nasopharyngeal swab SARS-CoV-2 PCR performed on the day of presentation was positive. At that time, she had not received any vaccinations against SARS-CoV-2. Initial vital signs included blood pressure of 111 mmHg/55 mmHg, heart rate of 106 beats/min, respiratory rate of 30/min, temperature of 38.0°C, and oxygen saturation of 67% on room air. Physical exam revealed tachycardia, conversational dyspnea, increased work of breathing, and decreased breath sounds and crackles in all lung fields. She was found to have acute kidney injury with blood urea nitrogen (BUN) of 43 mg/dL, creatinine of 2.17 mg/dL, Aspartate transaminase (AST) was elevated at 68 units/L, White blood cell count was 4000/uL, and D-dimer was 0.74 mg/L. A chest X-ray revealed bilateral diffuse patchy opacities.

The patient was admitted to Intermediate Care Unit (IMCU) and was placed on bi-level positive airway pressure (BiPAP) with fraction of inspired oxygen (FiO2) of 100% and inspiratory positive airway pressure (IPAP)/expiratory positive airway pressure (EPAP) of 18 mmHg/8 mmHg. Three days later, she was placed on high-flow nasal cannula (HFNC) with FiO2 of 60%. She received intravenous corticosteroid, a 10-day course of remdesivir, and 1 dose of tocilizumab. She was discharged home with an oxygen tank on July 8 (day 22 after symptom onset).

WGS of viral RNA from the patient's second infection showed the viral strain to be P.1 variant containing the E484K spike protein substitution, which is considered a substitution of therapeutic concern (SOTC) by the CDC. This patient’s specimen was selected for submission to the Florida Department of Health laboratory for WGS under a genomic surveillance program due to the history of a reinfection of SARS-CoV-2. Of note, serologic analysis of the patient's serum dated June 29, 2021 was negative for SARS-CoV-2 nucleocapsid IgG and positive for SARS-CoV-2 spike protein IgG.

Discussion

This case report aligns with recent study by Freitas et al that found P.1 variant has increased infectivity and virulence in females and in younger age groups [4]. The study compared COVID-19 cases during the peak of the first wave (from April 2020 to May 2020), and the second wave (January 2021) when P.1 variant was predominant in Amazonas state of Brazil [4]. They reported that the proportion of women among severe infection cases was increased during the second wave [4]. Also, mortality among people between 20 and 59 years old has increased in both sexes [4]. In our case, the patient was female, immunocompetent, and 48 years old. Also, the second infection led to a more severe illness requiring non-invasive ventilation, indicative of higher virulence.

Early in the pandemic, it was anticipated that the large number of people who recovered from natural infection would assist an effective vaccination strategy by promoting herd immunity and bringing an end to the pandemic. In a study done using data from Manaus, Brazil, previous non-P.1 infection provided an estimated 54% to 79% protection against infection with the P.1 variant [8], implying herd immunity solely through natural infection would not likely be achieved. As more new infections occur with the current variant, the opportunity for a novel variant arises with each new infection. This presents a potentially insurmountable challenge in facing an increasing number of new variants entering pandemic circulation, which may emerge and spread at an increasingly quicker rate.

SARS-CoV-2 infection induces a humoral immune response, meaning production of virus-specific antibodies. Deeks et al reported that by the fifth week after infection, seroconversion rates reached 96.0% [9]. However, multiple studies have found that the titer of anti-SARS-CoV-2 antibodies decline progressively over time [10-17]. In our case, the patient tested negative for SARS-CoV-2 nucleocapsid IgG when she presented with the second infection 9 months after the first infection. This finding suggests that natural infection may not confer consistent immunity against reinfection, particularly by variant strains.

Compared to natural infection, currently available SARS-CoV-2 vaccines induce humoral immunity through a different biological mechanism. Vaccines available in the USA are BNT162b2
(Pfizer-BioNTech), mRNA-1273 (Moderna), and Ad26.Cov2.S (J&J/Janssen). Comirnaty (BNT162b2) and mRNA-1273 are nanoparticle-formulated mRNA vaccines, and Ad26.Cov2.S is an adenovirus-vector-based vaccine. All induce immunity by expression of SARS-CoV-2 spike protein. Whether vaccination-induced humoral immunity is more robust and provides longer protection than the immunity obtained by natural infection is still unknown and is an area of active research. We performed a literature search in the PubMed database using keywords “COVID-19”, “reinfection”, and “variant”. Our search found 18 case reports or series reporting cases of reinfection with genetic study-confirmed distinct strains of SARS-CoV-2. None of the patients in these cases were fully vaccinated against SARS-CoV-2 (a person is considered fully vaccinated if >14 days have passed after the final dose of vaccination). In a case-control study with 738 subjects who had prior SARS-CoV-2 infection, Cavanaugh et al reported that individuals who were not vaccinated had a 2.34 times higher risk of reinfection compared to fully vaccinated persons (odds ratio [OR]=2.34; 95% confidence interval [CI]=1.58-3.47) [18]. These findings suggest that vaccination in addition to natural SARS-CoV-2 infection leads to more robust and longer-lasting immune response, providing better protection against reinfection. The accumulated data suggests that the best strategy against the COVID-19 pandemic is increasing the vaccination rate globally. By decreasing reinfection, we will be able to better control the total number of new infections, which will subsequently decelerate the evolution of new variants and limit the chance of the emergence of vaccine-resistant VOCs.

Conclusions

This report has identified a confirmed case of reinfection with P.1 variant of SARS-CoV-2 outside Brazil. This case supports recent epidemiological findings that indicate this VOC may have increased infectivity and virulence, and highlights the importance of SARS-CoV-2 vaccination for everyone.

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