Two cases of breakthrough SARS-CoV-2 infections caused by the Omicron variant (B.1.1.529 lineage) in international travelers to Japan

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Abstract

In November 2021, the World Health Organization designated a new SARS-CoV-2 variant of concern, Omicron (PANGO lineage B.1.1.529). We report on first two cases of breakthrough COVID-19 caused by Omicron in Japan among international travelers returning from the country with undetected infection. The spread of infection by Omicron were considered.

Keywords: COVID-19, SARS-CoV-2, Omicron, variant of concern, spike mutation

Background

Since December 2019, coronavirus disease 2019 (COVID-19) has been a major health threat worldwide. On November 26, 2021, the World Health Organization (WHO) designated B.1.1.529 lineage of the SARS-CoV-2 as a new variant of concern (VOC), Omicron. The first known case of this variant, detected in South Africa [1], was reported to the WHO on November 24 [2]. Since then the virus has spread rapidly across the globe. [3] Preliminary evidence suggests an increased risk of reinfection [4], and recently, it has reported that Orf9b mutations outside spike in Omicron likely contribute to adaptation [5]. Further clinical characterizations effective screening system of this newly found VOC are urgently needed [6]. Herein, we report the first two known mild COVID-19 cases infected with Omicron in Japan.

Case 1 was a healthy male in his 30s. He had been vaccinated with two doses of mRNA-1273 SARS-CoV-2 five months before. He was a resident of Japan who traveled to Namibia on November 12. On November 27, before his departure, he was tested for SARS-CoV-2 via real-time reverse transcriptase PCR (rRT-PCR) with a negative result. On November 28, he presented with a fever on the airplane, and arrived at an international airport in Japan on the same day. He was tested positive for SARS-CoV-2 via quantitative antigen test at the airport quarantine procedure and was isolated in an isolation facility. On November 29, he was transferred to our hospital. He presented with a mild fever, a cough, and a sore throat. On day 3, the results of viral genome sequencing confirmed

infection with Omicron variant (GISAID Accession ID: EPI_ISL_6913953). He became afebrile on day 5 and improved without medication.

Case 2 was a healthy male in his 20s. He had been vaccinated with two doses of BNT162b2 mRNA COVID-19 vaccine two months before. He was a resident of Japan who traveled to Peru in late October. He departed Peru on November 24 and transited via an international airport in Brazil, where he stayed for approximately 30 hours according to him. Before his departure, he was tested negative for SARS-CoV-2 via rRT-PCR. On November 27, he arrived at a major airport in Japan, where he tested positive for SARS-CoV-2 by quantitative antigen test. The sample was sent to the National Institute of Infectious Diseases for viral genome sequencing and confirmed as Omicron variant on November 30 (GISAID Accession ID: EPI_ISL_6914908). He was first isolated in an isolation facility managed by Japanese Quarantine Stations. On November 28, he developed with a mild fever and a sore throat. On November 30, he was transferred to our hospital. At admission, he already improved his symptoms, and he had no symptoms after hospitalization. These two cases reported here were fully vaccinated prior to onset. They had a mild clinical course and improved their symptoms without medication for COVID-19 (Table 1).

Discussion

Cases 1 and 2 were travelers from countries no Omicron variant had been identified. Haogao Gu et al, reported the detection of infection with the Omicron variant between two fully vaccinated individuals across the corridor of a quarantine hotel [6]. There has been an explosion in the number of Omicron variants registered in GISAID around the world, especially in Africa and Europe [7]. The potential spread of infection by Omicron variant were considered. The Omicron variant is characterized by many changes, including three small deletions and one small insertion in the spike protein. Of these, fifteen alterations are in the receptor binding domain. The Omicron variant is the

most divergent variant detected in significant numbers during the pandemic thus far, raising concerns that this variant may be associated with increased transmissibility, a meaningful reduction in vaccine effectiveness, and an increased risk for reinfections [8]. Further epidemiological and clinical investigation of Omicron variant cases and evaluation of the relationship between virological characteristics are needed.

E484K mutations (amino acid substitution) in the spike protein (S) gene within the Delta variant may cause immune escape and reduce vaccine efficacy. E484A and K417N mutations in Omicron may also reduce vaccine efficacy [9,10]. Recently, it was reported demonstrates that vaccine-induced immune protection might more likely be escaped by Omicron compared to prototypes and other VOCs. [11]. The two cases reported here were fully vaccinated prior to the onset. This suggests that the two doses vaccine might be less effective against infection with Omicron variant and that individuals who have been fully vaccinated might develop breakthrough infections.

On December 3, the Ministry of Health, Labour and Welfare (MHLW) issued a notice requesting that all COVID-19 cases with a travel history within 14 days undergo viral genome sequencing to identify Omicron variant. MHLW also requested that the other COVID-19 cases be screened with PCR assay for the L452R, which had been widely used for Delta variant screening in Japan until recently, and if the result is negative, viral genome sequencing is required because of the possibility of an Omicron variant [12]. In our two cases, we performed an in-house L452R PCR screening with the respiratory samples obtained from the cases and got negative results. (See supplementary Figure 1, supplementary Table 1). It would also be worth pointing out that case1 patient was rapid test negative on departure and became symptomatic during the flight. Thus, while pre-departure screening might detect some cases of early infection, it is still a porous control approach.

We have been able to identify cases infected with Omicron variant among travelers from undetected areas. This strain reached Japan within 48 hours of the designation of the Omicron strain as a VOC. During an early phase of global lineage shift with Omicron variant, it is essential to update epidemiological information and effectively introduce a simple screening test system to efficiently detect cases infected with Omicron variant. The rapidity of spread points clearly to the fact that that each new strain with selective advantages over prior strains cannot be geographically contained by travel restrictions. Thus, concerted and coordinated global action to expand access to effective vaccines will be critical to global disease mitigation.

NOTES

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Consent for Publication

The two cases provided written informed consent for the publication of their anonymized case descriptions.

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100 **Conflicts of Interest**

101 TS reports grant-in-aid from Japan Society for the Promotion of Science outside of the conduct of the

102 study. Other authors have no conflicts.

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142 Table 1. Descriptive statistics for case medical and demographic characteristics.

	Case 1	Case 2
Age	30s	20s
Sex	Male	Male
Country of travel	Namibia	Peru
Number of transit airport	One	Two
Date of return to Japan	Nov. 28, 2021	Nov. 27, 2021
Date of onset	Nov. 28, 2021	Nov. 28, 2021
Date of hospitalization	Nov. 30, 2021	Dec. 1, 2021
Previous COVID-19 vaccination history	Two times	Two times
Type of SARS-Cov-2 Vaccine	mRNA-1273 SARS-CoV-2 vaccine	BNT162b2 mRNA COVID-19 vaccine
Date of 1st vaccine	Jul. 1, 2021	2021 (mid-September)
Date of 2nd vaccine	Jul. 30, 2021	2021 (early October)
Contact with a known COVID-19 case	Yes	Unknown
Comorbidities	None	None
Smoking	None	None
Symptoms during the course of the disease	Fever for four days, cough, sore throat	Fever for three days, cough, sore throat
BMI	22.2	28.8
Maximum body temperature (°C)	38.8	39.1
SpO_2 (%), room air	98	98
Chest imaging test	Unremarkable	Unremarkable
Severity of disease	Mild	Mild
Therapeutic agent for COVID-19	None	None
WBC (/μL) / Neu (%) / Lym (%)	3,580 / 52.6 / 20.9	7,530 / 63.6 / 25.5
Hb (g/dL) / Ht (%) / Plt (10*4 /μL)	14.4 / 42.7 / 18.5	14.7 / 43.2 / 19.6
D-dimer (μg/dL)	<0.5	<0.5
Total bilirubin (mg/dL)	0.9	0.3
AST / ALT (U/L)	21 / 19	23 / 29
Lactate dehydrogenase (U/L)	137	157
C-reactive protein (mg/dL)	1.5	3.52
Blood urea nitrogen / creatinine (mg/dL)	13.4 / 0.91	12.0 / 0.55

Cq value / date / number of days since onset	36.2 / Nov. 29 2021 / day 2 22.2 /Dec. 1, 2021 / day 4 24.2 /2021 Dec 5/ day 8 33.9/2021 Dec 7/day10	26.4/ Dec. 1 2021 / day 4 25.7/ Dec. 2, 2021 / day 5 28.4/ Dec. 3, 2021 / day 6 38.0 /Dec. 5, 2021 / day 8 35.4 /Dec. 6, 2021 / day 9 36.7/Dec 7, 2021/ day10

143 NOTE- ALT, alanine transaminase; AST, aspartate aminotransferase; BMI, body mass index; COVID-19, coronavirus disease

144 2019; Cq, cycle of quantification; Lym, lymphocytes; Neu, neutrophils; SARS-CoV2, severe acute respiratory syndrome

145 coronavirus 2; WBC, white blood cell count