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Importation of SARS-CoV-2 Omicron variant in Beijing, China

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A B S T R A C T

Omicron (B.1.1.529), the fifth variant of concern (VOC) of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), was firstly identified in November 2021 in South Africa. Omicron contains far more genome mutations than any other VOCs ever found, raising significant concerns about its increased transmissibility and immune evasion. Here, we report the importation of the Omicron variant into Beijing, China, in December 2021. Full-length genome sequences of five imported strains were obtained, with their genetic features characterized. Each strain contained 57 to 61 nucleotide substitutions, 39 deletions, and 9 insertions in the genome. Thirty to thirty-two amino acid changes were found in the spike proteins of the five strains. The phylogenetic tree constructed by the maximum likelihood method showed that all five imported genomes belonged to Omicron (BA.1) (alias of B.1.1.529.1), which is leading to the current surge of coronavirus disease 2019 (COVID-19) cases worldwide. The globally increased COVID-19 cases driven by the Omicron variant pose a significant challenge to disease prevention and control in China. Continuous viral genetic surveillance and increased testing among international travellers are required to contain this highly contagious variant.

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1. Introduction

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) variant B.1.1.529 was initially detected in South Africa in a specimen collected on November 9, 2021, and was soon designated as the fifth variant of concern (VOC) by the World Health Organization (WHO) on November 26, 2021, and named Omicron [1,2]. More than 30 amino acid mutations were detected in the spike protein of Omicron, including 15 amino acid mutations located in the receptor-binding domain (RBD), which raises significant concerns about the increase in pathogenicity transmissibility and immune escape of this variant [3]. Recently, the Omicron variant has replaced the Delta variant as the predominant strain in many countries and areas. As of February 22, 2022, the Omicron variant has been identified in almost all countries and is driving a new wave of coronavirus disease 2019 (COVID-19) cases worldwide [4].

2. Case presentation and results

Our study reported five overseas passengers or flight crew members arrived at Beijing Capital International Airport from December 17 to December 21, 2021. The first patient (Patient 1) was a Russian flight crew member who arrived in Beijing on December 17, 2021. The second patient (Patient 2), a 27-year-old female Chinese international student, returned from England to Beijing, China on December 18, 2021. On June 28 and August 23, 2021, she received two doses of the Pfizer/BNT162b2 vaccine and tested negative for SARS-CoV-2 nucleic acid and IgM antibody on December 15 and 17, 2021. On December 18, 2021, the patient complained of dry throat accompanied by mild fever and tested positive for SARS-CoV-2 nucleic acid on the same day. Patient 3 was a 26-year-old male company employee who took a business trip to Budapest, Hungary, on September 4, 2021, and returned to Beijing on December 19, 2021. The patient was tested negative for SARS-CoV-2 nucleic acid on December 17, 2021, before leaving for China. On December 19, 2021, the patient complained of sore throat and dry throat and was tested positive for SARS-CoV-2 nucleic acid. The patient received two doses of inactivated SARS-CoV-2 vaccine in China on March 15 and May 18, 2021. Both Patient 2 and 3 were transferred to designated hospitals for treatment and isolation by closed-loop transportation after the onset. Passengers in the same row, the three rows before and after the patient, and the passengers on the same airport shuttle bus were recognized as close contacts. Finally, 55 and 60 close contacts of Patient 2 and 3 were identified and centrally quarantined. As of February 11, 2022, all the close contacts tested negative for SARS-CoV-2 nucleic acid. Patient 4, a 39-year-old male, and Patient 5, a 37-year-old male, were flight crew members of Ethiopia, who arrived in Beijing on December 18 and 21, 2021. No additional clinical manifestations or vaccination information was collected as they were flown back on return flights, respectively.

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Fig. 1. Genomic analysis of the five imported severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) Omicron strains. A) Phylogenetic tree constructed using the full-length SARS-CoV-2 genome sequences. The names of the imported strains were highlighted in red, and the clades of the current SARS-CoV-2 variants of concern (VOCs)/variants of interest (VOIs) were color-coded. The patients' numbers were represented in Arabic numerals. B) Amino acid mutations of the five imported SARS-CoV-2 strains, compared to the reference genome Wuhan-Hu-1. The Omicron (BA.1) defining mutations were highlighted in red. Private mutations of each imported strain, compared with the Omicron (BA.1) variant strain SARS-CoV-2/human/BEL/rega-20174/2021 (GenBank accession number OL672836.1), were highlighted in green.
Nasopharyngeal swab samples were collected from these five individuals for SARS-CoV-2 nucleic acid tests, and all of them showed positive results in ORF1ab and N gene testing. The samples were then transferred to the Beijing Center for Disease Prevention and Control for genome sequencing. Viral RNA was extracted by the Viral RNA/DNA Extraction Kit (X‘ian TianLong Science and Technology Co., Ltd, Xi’an, China). First-strand cDNA was synthesized and amplified using the ULSEN® SARS-CoV-2 Whole-Genome Capture Kit (Beijing MicroFuture Technology Co., Ltd, Beijing, China). Sequencing libraries were prepared with the Nextera® XT Library Prep Kit and sequenced using the Illumina MiniSeq platform (Illumina, San Diego, CA, USA).

Finally, all five imported genomes belonged to the VOC/Omicron (Pango lineage BA.1) (alias of B.1.1.529.1). The strains from Ethiopia’s two flight crew members (Patient 4 and 5) were clustered into the same sub-clade, with only two distinct nucleotides, suggesting that they might link with the same chain of transmission (Fig. 1A). However, further investigation is needed to confirm the epidemiological relation. Sequence analysis showed that each of the five imported strains contained 57 to 61 nucleotide substitutions, 39 deletions, and 9 insertions, compared to the reference genome Wuhan-Hu-1 (GenBank accession number NC_045512.2). All strains had 64 to 68 amino acid mutations, involving spike (S), envelope (E), membrane (M), nucleocapsid (N) proteins, and non-structural proteins. Thirty to thirty-two amino acid changes were detected in the spike proteins of the five strains. All strains shared 30 amino acid substituions (A67V, T95I, Y145D, L212L, G339D, S371L, S373P, S375F, K417N, N440K, G446S, S477N, T478K, E484A, Q493R, G496S, Q498R, N501Y, V505H, T547K, D614G, H655Y, N679K, P681H, G694K, Q768K, N856K, Q945H, N969K, and L981F), six deletions (H69del, V70del, G142del, G143del, V144del, and N211del), and one insertion (214insEPE) in the spike protein, corresponding to the genetic features of the Omicron (BA.1) (Fig. 1B). Among these mutations, 15 to 16 mutations were located in the RBD of the spike proteins. Several private mutations were also found in these strains’ spike, nucleocapsid, and nonstructural proteins.

3. Discussion and conclusion

Imported Omicron variant strains have recently been identified and have caused outbreaks in several Chinese megacities [6,7], posing a significant challenge to the dynamic clearing strategy. In addition, the first five imported Omicron variant infected cases in Beijing were detected in overseas travellers and flight crew members from four countries in a relatively short period of four days, suggesting that Omicron can quickly spread through international travel.

Omicron contains numerous mutations in the spike, envelope, membrane, nucleocapsid, and non-structural proteins that lead to increased viral transmissibility and immune evasion. A particular cluster of mutations (H655Y, N679K, and P681H) adjacent to the S1/S2 furin cleavage site could facilitate spike protein cleavage, which contributes to enhanced transmissibility [8]. Four amino acid mutations (A67V, T95I, Y145D, and L212I), six deletions (H69del, V70del, G142del, V143del, Y144del, and N211del), and one insertion (214insEPE) in the N-terminal domain (NTD) of spike protein are expected to reduce the sensitivity of Omicron to immune responses elicited by either natural infection or vaccination [9,10]. It’s worth noting that many mutations in the RBD region of Omicron may affect the binding of receptors and neutralizing antibodies. Five RBD mutations, including G339D, N440K, G446S, T478K, and N501Y, have been shown to enhance ACE2 receptor binding [11]. Seven RBD mutations, including K417N, G446S, E484A, Q493R, G496S, Q498R, and N501Y, were associated with the reduced binding affinity of RBD-targeted neutralizing antibodies [12]. We also found that two strains from Patient 4 and 5 carried a private mutation, R346K, in the RBD region, which was found to be prevalent in the newly designated sub-lineage BA.1.1 of Omicron (Fig. 1B). The R346K mutation has altered the interactions with monoclonal antibodies from class 2 [13]. Thus, further research should investigate whether the R346K mutation in the RBD region leads to increased immune escape.

Since the outbreak of the COVID-19 pandemic, SARS-CoV-2 has continuously evolved into a variety of VOC mutants [14]. Phylogenetic analysis showed that Omicron was phylogenetically distinct from other SARS-CoV-2 VOCs and evolved into three main sub-lineages consisting of BA.1, BA.2, and BA.3. Furthermore, five imported strains in the study belonged to different subclades, showing Omicron’s current genetic diversity. This emphasizes the significance of enhancing global SARS-CoV-2 genomic surveillance to provide evidence for the continuous evolution of circulating variants.

In conclusion, a timely risk assessment should be conducted to adjust international travel-related control measures to slow down the global spread of Omicron. Continuous genomic surveillance is also required to contain this highly contagious variant.

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Conflict of interest statement

The authors declare that there are no conflicts of interest.

Author contributions

Fu Li: Conceptualization, Data Curation, Writing – Original Draft, Writing – Review & Editing. Zhichao Liang: Data Curation. Shujuan Cui: Formal Analysis. Bing Lv: Formal Analysis. Zhaomin Feng: Formal Analysis. Hui Xu: Formal Analysis. Lei Jia: Data Curation. Peng Yang: Data Curation, Conceptualization. Quanyi Wang: Conceptualization. Yang Pan: Data Curation, Conceptualization. Daitao Zhang: Data Curation, Conceptualization.

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