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BRIEF REPORT

First Identification of the New Severe Acute Respiratory Syndrome Coronavirus 2 Omicron Variant (B.1.1.529) in Italy

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We identified the first case in Italy of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) B.1.1.529 variant, using whole-genome sequencing in an Italian subject traveling from Mozambique. Specific mutation profiles deserve further investigations to clarify potential effects on vaccination efficacy. This case highlights the crucial role of rapid and continuous surveillance of SARS-CoV-2 variant circulation.

Keywords. SARS-CoV-2; viral variants; Omicron; B.1.1.529; COVID-19.

Since the worldwide emergence of the coronavirus disease 2019 (COVID-19) outbreak, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has been characterized by subsequent waves of viral propagation sustained by different viral strains with peculiar transmissibility, disease severity, risk of death, and potential escape from the immune response. The strong sequencing effort put in place by the international scientific community allowed characterization of numerous lineages differing in abundance and type of amino-acidic mutations. Particular attention was directed to the so-called variants of concern (VOCs), for which evidence of significant impact on epidemiological and clinical consequences are currently available. The lineages classified as VOCs until October 2021 were B.1.351 (Beta), P.1 (Gamma), and B.1.617.2 (Delta) [1]. Starting from summer 2021, the Delta variant overcame the Alpha variant, establishing itself as the globally dominant strain with its rapid diversification into several sublineages (AY.X).

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The most recent identified VOC was Omicron (B.1.1.529), isolated in November in Botswana and South Africa, presenting 32 aminoacidic changes in the surface (S) protein: to date, a total of 189 sequences were available in the GISAID database [2], mainly from Africa (144 of 189), while information on possible alteration in immunity and natural infection course has still to be generated [3]. The arising concerns about the Omicron variant are based on its unprecedentedly large mutation pattern and its rapid diffusion, which have strongly stimulated containment measures and travel policy strategies worldwide to prevent global spread.

According to the Italian SARS-CoV-2 surveillance program indication for travelers of 2 March 2021 (updated on 22 October 2021), the countries are classified into 5 classes of risk, and only inbound travelers from specific places are tested for SARS-CoV-2. In particular, persons coming from Africa are requested to fill in a passenger locator form, to have a negative result of a molecular or antigenic SARS-CoV-2 test within 72 hours, and to observe a 10-day isolation period or stay in Italy for <120 hours [4].

Here we report the first case of SARS-CoV-2 B.1.1.529 identified in Italy, in an Italian subject traveling from Mozambique. After the Belgian case, this is the second patient harboring Omicron variant in Europe, according to GISAID. Other cases have been reported in the Netherlands, the United Kingdom, Germany, and Austria.

CASE REPORT

A 48-year-old man, who had undergone full vaccination with heterologous CAZD1222 (ChAdOx1; AstraZeneca-Oxford) and BNT162b2 prime-boost vaccination (Comirnaty; Pfizer-BioNTech) in June 2021, tested positive for SARS-CoV-2 RNA in November 2021. He reported recent business travel to Mozambique, with 2 stopovers in Johannesburg and Doha. Before leaving Mozambique, he had a negative SARS-CoV-2 RNA result (day 0); 2 days later, on arrival in Italy, he visited his family in Southern Italy. On day 5 he traveled to Milan because of another scheduled trip to Africa; for this reason, another nasopharyngeal swab sample was collected, which revealed SARS-CoV-2 infection. Later, the patient started to experience fever (38°C), myalgia, fatigue, and headache. According to the rules of contact tracing, his 5 relatives were tested, and their results were positive for SARS-CoV-2 RNA. No one in the family required hospitalization, and at this writing nearly all of the patient's relatives are fully recovered.

Thanks to the national SARS-CoV-2 surveillance program indication for travelers, a nasopharyngeal swab sample was

collected from the patient and tested positive using the SARS-CoV-2 ELITe MGB Kit on the InGenius platform (EliTech Group), with a cycle threshold value of 21 for both RNA-dependent RNA polymerase and open reading frame 8 targets. At the Clinical Laboratory of Microbiology, Virology and Bioemergencies of L. Sacco University Hospital, a regional reference center for SARS-CoV-2 emergency and viral variant surveillance, we received an aliquot from this sample for genotyping analysis.

According to the national surveillance program on variant circulation, the criteria for genotyping include arrival from area at risk of variants, cluster of outbreak, potential cases of reinfection, and vaccinated subjects. As initial screening, a specific variant reverse-transcription polymerase chain reaction–based test assay was performed, using the Allplex SARS-CoV-2 Variants I + II Assays kit (Seegene), which detected N501Y and K417N mutations plus 69/70 deletions in the S gene a mutation pattern inconclusive for the well-known Alpha, Beta, Gamma, and Delta VOCs and suggestive of a new VOC [5].

To assign the definitive lineage, whole-genome sequencing analysis was conducted on the iSeq platform (Illumina), using the CleanPlex SARS-CoV-2 Panel kit (Paragon Genomics); the FASTQ file was then processed on the Sophia bioinformatic platform (SOPHiA GENETICS), and the resulting FASTA file was uploaded on the Italian web-based portal I-Co-Gen (https://irida.iss.it/), as coordinated by the Istituto Superiore di Sanità (National Institute of Health).

I-Co-Gen first reported the presence of an early warning, owing to the presence of amino acid substitution S371L, specific for the new lineage B.1.1.529, and the lineage was then assigned by the I-Co-Gen platform. The sequence is also present on GISAID, with code EPI_ISL_6777160. Lineage assignment was confirmed by the Pangolin COVID-19 lineage assigner (https://pangolin.cog-uk.io/). This result allowed sharing of data with the Istituto Superiore di Sanità and the network of laboratories participating in the genomic surveillance program. In addition to molecular analyses, viral isolation was performed on Vero E6 cells (Vero C1008; American Type Culture Collection CRL-1586).

DISCUSSION

The availability of isolated virus would enable the antibody response against the new variant to be evaluated using in vitro serum neutralization tests, in persons convalescing from COVID-19 as well as in vaccinated persons [6]. Because mutations in the S gene were associated with higher infectivity, escape from monoclonal antibodies and immune response, as well as syncytium formation, it is crucial to identify aminoacidic alterations and test their effect on human antibodies activity [7–9]. Moreover, comparison with other VOCs can help us estimate the Omicron variant's level of concern [10], and the in vitro results could strengthen third-dose COVID-19 vaccine recommendations, considering also the dangers of potential waning immunity [11].

The multistep approach—based on reverse-transcription polymerase chain reaction assays for a specific variant and subsequent whole-genome sequencing of samples with an atypical pattern of mutations—could be a powerful algorithm for first-step screening before sequencing of the entire SARS-CoV-2 genome, in order to report new SARS-CoV-2 variants to public health authorities. Prompt and accurate surveillance of SARS-CoV-2 variants at the national level could play a crucial role, not only for quickly identifying new variants but also for public health purposes.

Thanks to this rapid report, health authorities on 26 November 2021 released an urgent update to manage arrivals from sub-Saharan Africa. In addition to following previous rules, it is now necessary to undergo molecular or antigenic testing at the airport or harbor on arrival and then undergo a 10-day isolation period, followed by another molecular test. The excellent integrated surveillance system implemented in Italy allowed us to rapidly identify the new variant and limit its circulation, even if—in an interconnected world—travel bans might slow but unfortunately will not eliminate global spread.

Notes

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