



ELSEVIER

Contents lists available at ScienceDirect

International Journal of Infectious Diseases

journal homepage: www.elsevier.com/locate/ijid

Case Report

Simultaneous co-infection with Omicron (B.1.1.529) and Delta (21A/478K.V1) SARS-CoV-2 variants confirmed by whole genome sequencing

Souheil Zayet^{1,*}, Jean-Baptiste Vuillemenot², Laurence Josset³, Vincent Gendrin¹,
Timothée Klopfenstein¹

¹ Infectious Disease Department, Nord Franche-Comté Hospital, 90400, Trevenans, France

² Microbiology Department, Nord Franche-Comté Hospital, 90400, Trevenans, France

³ GenEPII sequencing platform, Institut des Agents Infectieux, Laboratoire associé au Centre National de Référence des virus des infections respiratoires, Hospices Civils de Lyon, F69004, Lyon, France

ARTICLE INFO

Article history:

Received 17 June 2022

Revised 31 August 2022

Accepted 1 September 2022

Keywords:

COVID-19

SARS-CoV-2

Omicron variant

Delta variant

Co-infection

ABSTRACT

We reported herein a simultaneous co-identification with Omicron (B.1.1.529) and Delta (21A/478K.V1) SARS-CoV-2 variants, confirmed by whole genome sequencing in an 83-year-old French patient.

© 2022 The Author(s). Published by Elsevier Ltd on behalf of International Society for Infectious Diseases.

This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>)

Introduction

The national data of the epidemiological survey of COVID-19 variants carried out in France has shown a predominance of the Delta variant (21A/478K.V1) since June 29, 2021 ([Santé publique France 2021](#)). Since the SARS-CoV-2 Omicron variant (B.1.1.529) was first reported ([WHO, 2021](#)), it has rapidly spread worldwide. Preliminary evidence suggests an increased risk of reinfection with this variant compared with other variants of concern (VOCs) ([WHO, 2021](#)) but no simultaneous co-infection. We described herein a case of SARS-CoV-2 Omicron and Delta VOCs co-infection, confirmed by whole genome sequencing (WGS).

Case report

On January 5, 2022, an 83-year-old woman with a past history of atrial fibrillation presented for critical lower limb ischemia, requiring lower extremity amputation. On January 10, she sought care for fever and cough. Real-time reverse transcription-polymerase chain reaction (RT-PCR) on a nasopharyngeal swab

specimen confirmed SARS-CoV-2 infection (TaqPath™ COVID-19 CE-IVD RT-PCR Kit, ThermoFisher Scientific). Detection of RNA nucleocapsid encoding gene (N) and specific open reading frame 1ab at cycle threshold (Ct) values of 9.2 and 10.2, respectively, suggested a recent COVID-19 infection. The absence of S gene detection (S gene dropout) suggested a SARS-CoV-2 infection with the Omicron variant (B.1.1.529) ([WHO, 2021](#)). The patient only received supportive treatment (antipyretics and heparin), with no steroids, antiviral, or monoclonal antibody treatments. On January 17, a systematic SARS-CoV-2 RT-PCR follow-up test was positive, and the S gene was detected at Ct value of 17.4, in contrast to the first PCR. The detection of S gene and the presence of a 3.2/3.3 cycle gap with N and open reading frame 1ab (Ct of 14.2 and 14.3, respectively) made us suspect an Omicron and Delta variant co-infection. No change in symptoms has been noted after the Delta infection was suspected to have been acquired. A RT-PCR assay designed for the qualitative detection and discrimination of S gene mutations (K417N, E484K, and L452R) was performed on both swabs to differentiate Omicron from other VOCs, Beta, Gamma, and Delta (GSD NovaType IV SARS-CoV-2/NovaTec Immundiagnostica GmbH). As expected, the K417N substitution was identified in the first sample, whereas both K417N and L452R were identified in the second sample ([Figure](#)).

* Corresponding author: Souheil Zayet, Department of Infectious Disease, Nord Franche-Comté Hospital, 90400 Trevenans, France. Tel: +33384983659
E-mail address: souhail.zayet@gmail.com (S. Zayet).

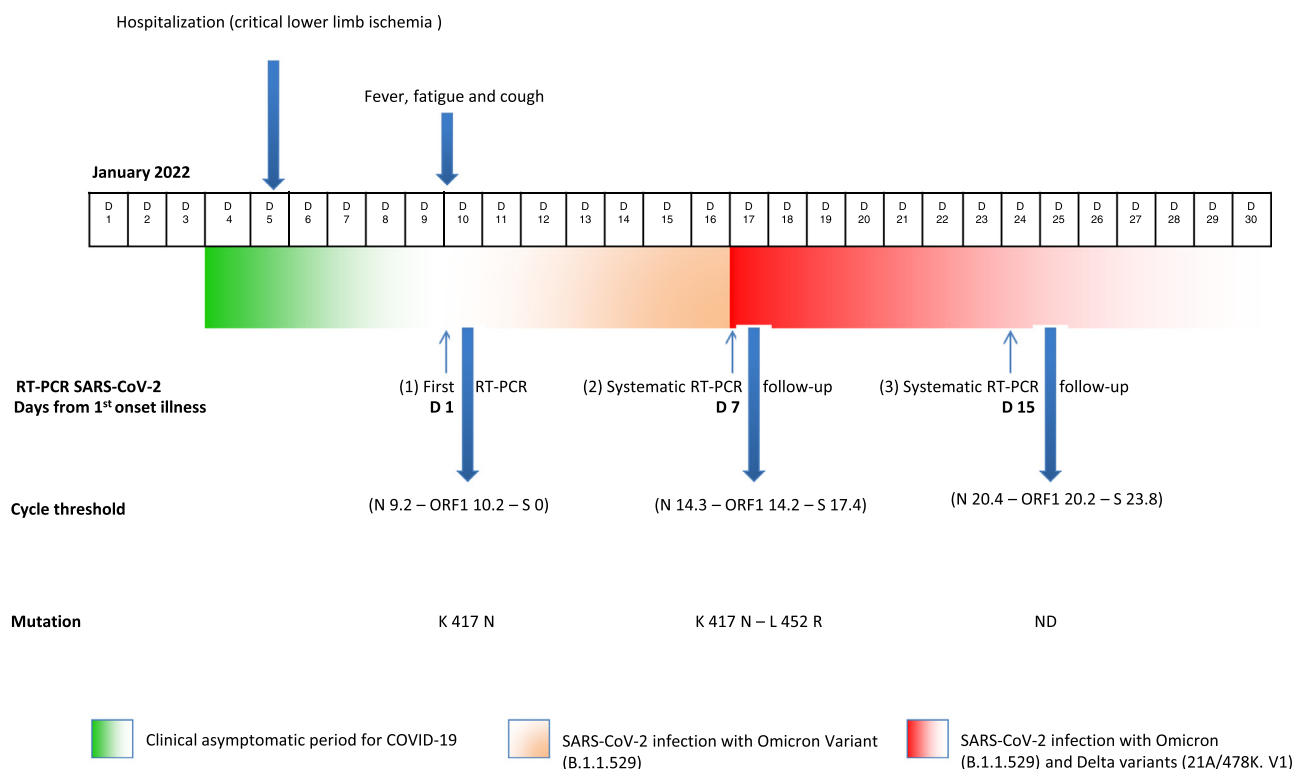


Figure. Timeline in COVID-19 patient with co-infection with Omicron (B.1.1.529) and Delta SARS-CoV-2 variants (21A/478K. V1). N, nucleocapsid encoding gene; ND, not determined; ORF1, specific open reading frame 1ab; RT-PCR, real-time reverse transcription-polymerase chain reaction; S, Spike gene.

To confirm the co-infection, a WGS using the COVIDSeqTest™ and the NovaSeq 6000 (Illumina, San Diego, CA, USA), was performed on the second sample (Bal et al., 2022) by applying an unbiased bioinformatics method (“seqmet,” 2022); both 21K Omicron and 21J Delta variants were identified. No evidence of recombination event was observed. Our anamnestic survey and investigations revealed that this patient was not vaccinated against SARS-CoV-2, nursed initially in a side room, with a likely recent contact with other patients with COVID-19 and visitors during this hospitalization. On January 24, the patient was discharged.

Discussion

We emphasized the possibility of a SARS-CoV-2 infection with more than one strain in the era of multiple VOCs. National data from epidemiologic surveillance showed that the Delta variant was predominant (21A/478K.V1) from June 29 to November 15, 2021 in France, and Omicron (B.1.1.529) was currently the predominant circulating variant in all French regions (Coronavirus, n.d.). Due to partial bed saturation during the different waves, we were faced with having to hospitalize patients in the same room, disregarding the difference in their VOCs, which may be a misleading approach, whereas two variants with different pathogenicity were circulating. Previous research has reported patients infected with different influenza strains (Garigliany et al., 2010). Fransico et al. reported that two patients had been simultaneously infected with two different lineages of COVID-19: the Brazilian variant, known as B.1.1.28 (E484K), and a second variant, VUI-NP13L, which had previously been discovered in Rio Grande do Sul (Francisco et al., 2021). Furthermore, Wawina-Bokalanga et al. also reported a genomic evidence (using ONT GridION sequencing) of co-identification with Omicron and Delta SARS-CoV-2 variants in two patients from the United Kingdom (Wawina-Bokalanga et al., 2022). In a large cohort, Zhou et al. suggested that 0.18% (53/29,993 samples) of co-

infection events were identified with NGS. Only one sample with co-infections of three SARS-CoV-2 lineages was first noted (Zhou et al., 2022). In France, Delta/Omicron SARS-CoV-2 co-infection was detected and confirmed during the fifth wave of the COVID-19 pandemic in seven immunocompetent and epidemiologically unrelated patients (Combes et al., 2022). Another recent study using WGS data reported prevalence for Delta/Omicron (BA.1) and Omicron BA.1/BA.2, estimated at 0.18% and 0.26%, respectively (Bal et al., 2022). To confirm the co-infections, some studies/tools used appropriate and specific pipelines (Molina-Mora et al., 2022). We highlighted the need for more studies to determine whether infection with multiple VOCs affects the clinical course of COVID-19 and the importance to continue to isolate patients.

Funding

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Ethical approval statement

Not applicable. Written informed consent has been given and retained by authors.

Declaration of competing interests

The authors have no competing interests to declare.

CRediT authorship contribution statement

Souheil Zayet: Conceptualization, Investigation, Methodology, Project administration, Resources, Software, Writing – original draft, Writing – review & editing. **Jean-Baptiste Vuilleminot:** Formal analysis, Funding acquisition, Resources. **Vincent Gendrin:**

Supervision, Validation, Writing – review & editing. **Timothée Klopfenstein**: Conceptualization, Supervision, Validation, Writing – review & editing.

Acknowledgments

The authors would like to thank the members of the GenEPII sequencing platform and the national reference center of respiratory viruses who contributed to this investigation.

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:[10.1016/j.ijid.2022.09.002](https://doi.org/10.1016/j.ijid.2022.09.002).

References

- Bal A, Simon B, Destras G, Chalignac R, Semanas Q, Oblette A, et al. Detection and prevalence of SARS-CoV-2 co-infections during the Omicron variant circulation, France, December 2021 - February 2022. medRxiv 2022. doi:[10.1101/2022.03.24.22272871](https://doi.org/10.1101/2022.03.24.22272871).
- Combes P, Bisseux M, Bal A, Marin P, Latour J, Archimbaud C, Brebion A, Chabrolles H, Regagnon C, Lafolie J, Destras G, Simon B, Izopet J, Josset L, Henquell C, Mirand A. Evidence of co-infections during Delta and Omicron SARS-CoV-2 variants co-circulation through prospective screening and sequencing. Clin Microbiol Infect Forthcoming 2022.
- Francisco RDS, Benites LF, Lamarca AP, de Almeida LGP, Hansen AW, Gularte JS, Demoliner M, Gerber AL, de C Guimarães AP, Antunes AKE, Heldt FH, Mallmann L, Hermann B, Ziulkoski AL, Goes V, Schallenberger K, Fillipi M, Pereira F, Weber MN, de Almeida PR, Fleck JD, Vasconcelos ATR, Spilki FR. Pervasive transmission of E484K and emergence of VUI-NP13L with evidence of SARS-CoV-2 co-infection events by two different lineages in Rio Grande do Sul, Brazil. Virus Res 2021;296.
- Garigliany MM, Habyarimana A, Lambrecht B, Van de Paar E, Cornet A, van den Berg T, Desmecht D. Influenza A strain-dependent pathogenesis in fatal H1N1 and H5N1 subtype infections of mice. Emerg Infect Dis 2010;16:595–603.
- Molina-Mora JA, Cordero-Laurent E, Calderón-Osorno M, Chacón-Ramírez E, Duarte-Martínez F. Metagenomic pipeline for identifying co-infections among distinct SARS-CoV-2 variants of concern: study cases from Alpha to Omicron. Sci Rep 2022;12:9377.
- Santé publique France, Coronavirus: circulation des variants du SARS-CoV-2. <https://www.santepubliquefrance.fr/dossiers/coronavirus-covid-19/coronavirus-circulation-des-variants-du-sars-cov-2>, n.d. (accessed 23 September 2021).
- seqmet, 2022.
- Wawina-Bokalanga T, Logist AS, Sinnesael R, Van Holm B, Delforge ML, Struyven P, Cuypers L, André E, Baele G, Maes P. Genomic evidence of co-identification with Omicron and Delta SARS-CoV-2 variants: a report of two cases. Int J Infect Dis 2022;122:212–14.
- World Health Organization, Classification of omicron (B.1.1.529): SARS-CoV-2 variant of concern. [https://www.who.int/news/item/26-11-2021-classification-of-omicron-\(b.1.1.529\)-sars-cov-2-variant-of-concern](https://www.who.int/news/item/26-11-2021-classification-of-omicron-(b.1.1.529)-sars-cov-2-variant-of-concern), 2021 (accessed 26 January 2022).
- Zhou H-Y, Cheng Y-X, Xu L, Li J-Y, Tao C-Y, Ji C-Y, Han N, Yang R, Li Y, Wu A. Genomic evidence for divergent co-infections of SARS-CoV-2 lineages. Comput Struct Biotechnol J 2022;20:4015–24.