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Co-infection with SARS-CoV-2 omicron BA.1 and BA.2 subvariants in a non-vaccinated woman

Circulation of contagious SARS-CoV-2 variants and suboptimal vaccine protection create the conditions for simultaneous infections with multiple strains, which could generate inter-lineage SARS-CoV-2 recombinants with novel unpredictable features.^{1,2} Mixed infections have been reported since the first epidemic waves.^{3,4} Co-infection with omicron and delta have been found in immunocompetent and immunocompromised patients living in different geographical areas.^{5,6} Because these variants are characterised by different genomic sequences, their co-presence can be identified promptly. However, recombination between closely related variants is difficult to identify but can also occur. A total of 637 cases of the omicron BA.1 and BA.2 recombinant, known as XE, have been confirmed in the UK up to now, and the number is increasing.⁷ These data also suggest that intralinear recombination generates highly transmissible chimeric strains. It is necessary to detect all co-infections to minimise the risk of recombination.

Here, we report a non-vaccinated woman, aged 63 years and with mild respiratory symptoms, who had a nasopharyngeal swab on Jan 31, 2022. The sample scored positive for the E,

N, and RdRp or genes using the Allplex SARS-CoV-2 assay (Arrow and Seegene, Seoul, South Korea; appendix p 3). This case was found fortuitously, as it was randomly picked along with 68 other acute infections to do a molecular survey requested by *Istituto Superiore di Sanità*. All isolates were preliminarily examined with a multiplex PCR to detect the mutation signatures of major circulating variants and were found to belong to the omicron variant (appendix p 2). 54 samples were then chosen at random, 24 of which were whole-genome sequenced and 30 of which were Sanger sequenced in the region of the Spike gene. The case sample fell into the Sanger group and the resulting electropherogram showed various polymorphisms and unreadable sequences close to the 142–144 amino acid deletion of omicron variant BA.1. The sample was then examined by whole-genome sequencing and showed 67 mutations defining the omicron variants. Of these, 15 were of BA.1 sublineage and 20 were of BA.2 sublineage (appendix p 2). Nextclade (version 1.14.0) analysis confirmed the presence of two distinct isolates (appendix p 2).

The woman promptly isolated herself, had no other contacts since then, and resolved the infection within 9 days. These results suggest that omicron co-infection induces mild symptoms, even in non-vaccinated individuals, and can go unnoticed. This work underlines the need for effective genomic surveillance to reduce the risk of generating SARS-CoV-2

recombinants with novel pathogenic and immunological properties.

We declare no competing interests.

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Maria Linda Vatteroni, Anna-Lisa Capria, Pietro Giorgio Spezia, Susi Frateschi, *Mauro Pistello
mauro.pistello@unipi.it

Virology Unit (MLV, A-LC, PGS, SF, MP) and Retrovirus Centre and Virology Section (PGS, MP), University of Pisa, I-56127 Pisa, Italy

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