Concerted efforts toward genomic surveillance of viral pathogens in immunocompromised individuals

Whether prolonged SARS-CoV-2 active infection in immunocompromised individuals favours the emergence of new variants of concern through a prolonged host–viral arms race continues to be extensively debated. Although this theory is considered sound by many experts, only a few related case reports have been published thus far. The scarceness of robust scientific evidence likely stems from the practical challenges of conducting such complex longitudinal patient-based studies. In this context, the study by Raglow and colleagues[1] brought to attention notable findings regarding the intra-host SARS-CoV-2 evolution in a large prospective cohort of immunocompromised individuals.

The identification of specific conditions, such as HIV and B-cell malignancies, which increase the risk for prolonged SARS-CoV-2 infection, provides key information for public health policy makers. Moreover, Raglow and colleagues[1] describe increased spike mutations in individuals with prolonged active infection. However, we identified some compelling aspects that should not be overlooked. For several mutations acquired at positions Ser255, Arg346, Ser371, Thr376, Asn450, Lys444, Gly446, and Leu452 in the spike protein, many of which occur within the receptor binding domain and its immunodominant motifs[2,3], a discernible pattern of expansion of viral populations harbouring minor variants at these sites was seen, which eventually outcompeted the original virus. Collectively, these observations substantiate that prolonged exposure to selective pressure in immunocompromised individuals allows the virus to explore the mutational landscape before viral clearance, leading to the emergence of new variants with enhanced immune escape or antigen–receptor fitness properties.

The results of the study conducted by Raglow and colleagues[1] underscore the crucial need to closely monitor immunocompromised individuals with prolonged SARS-CoV-2 infections for emerging variants and investigate their phenotypic implications. Sequencing the genomes of the viruses from these cases would marginally elevate the cost in the whole COVID-19 genomic surveillance effort, and many countries with universal health systems could effectively integrate the tracking of prolonged COVID-19 infections in people living with HIV into their primary care programmes.

Nonetheless, most sequencing laboratories are likely to face logistical difficulties in obtaining serial samples from individuals with prolonged SARS-CoV-2 infection outside the scope of a research project. Although some guidelines mention surveillance of prolonged infections, they provide only vague instructions on this topic. Therefore, discussions on the implementations of a comprehensive strategy for targeted surveillance of these groups in public health guidelines are essential. Furthermore, fostering the integration of stakeholders from epidemiology, laboratory, and clinic is key to implementing effective public health policies and workflows to strengthen genomic surveillance in immunocompromised individuals.

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