「Study highlights risk of new SARS-CoV-2 mutations emerging during chronic infection」

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The world is watching the evolution of SARS-CoV-2 as it moves around the globe, with new variants becoming important factors in the path of the pandemic. But how does the virus evolve over the course of one infection is still mysterious. Recently, scientists sought to answer that question by analyzing the genomes of the virus over the course of the infection in one immunosuppressed (with a weakened immune system) patient. Writing in Nature, a team led by Cambridge researchers report how they were able to observe SARS-CoV-2 mutating in the case of an immunocompromised patient treated with convalescent plasma. In particular, they saw the emergence of a key mutation also seen in the new variant that led to the UK being forced once again into strict lockdown, though there is no suggestion that the variant originated from this patient. [1, 2]

In this study, the authors collected samples of the virus on 23 occasions during treatment from this immunocompromised patient who was a man in his 70s who had been diagnosed with marginal B cell lymphoma in 2012 and had received various forms of chemotherapy. The man was admitted to a tertiary hospital in the summer of 2020 and had tested positive for SARS-CoV-2 at a local hospital 35 days previously. Computed tomography of the chest revealed abnormalities consistent with COVID-19 pneumonia.

Virus genomic comparative analysis of 23 sequential respiratory samples was performed over 101 days. Little change was observed in the structure of the overall viral population following two courses of remdesivir administered during the first 57 days.

However, following the administration of CT, large, dynamic shifts in the viral population occurred between days 66 and 82. A dominant viral strain emerged bearing the D796H mutation in subunit 2 of the spike protein and the ΔH69/ΔV70 deletion in the NTD of subunit 1.

On days 86 and 89, the deletion-mutation pair observed on day 82 had fallen to frequencies of 10% or less and viruses were instead characterized by mutations Y200H and T240I in the spike protein.

In a final effort to reduce the viral load, a third course of remdesivir was administered on day 93, and a third dose of CP was administered on day 95, which resulted in the re-emergence of the D796H + ΔH69/ΔV70 viral population. [3]

These data reveal strong correlation on convalescent plasma therapy with the emergence of viral variants, and spike mutants emerging post convalescent plasma impair neutralizing antibody potency. Based on the findings, the authors believe repeated increase in the frequency of this viral population after plasma therapy could mean the observed mutations may be conferring these variants a survival advantage over others. This study reveals for the first time the dynamic process of the novel coronavirus mutations in patients with weakened immunity, thereby reducing the sensitivity of neutralizing antibodies. Infected patients showing low immunity may be an important source of mutated strains of the new coronavirus. The researchers also emphasized in the study that this phenomenon only applies to infected people with low immunity. For patients with strong immunity, due to better immune control, the virus diversity may be low. At the same time, this study also shows that some adjustments may be needed in the clinical treatment of people with low immunity and Covid-19 infection.

Reference:

1. Steven A. Kemp et al. 5 Feb 2021. "SARS-CoV-2 evolution during treatment of chronic infection" *Nature.*
2. 8 Feb 2021. "The Evolution of SARS-CoV-2 in a Single Patient" *Genetic Engineering and Biotechnology News.*
3. Sally Robertson. 11 Feb 2021. "SARS-CoV-2 evolves antibody resistance in immunocompromised patient" *Medical Life Science News.*