Breakthrough infection after three doses of COVID-19 mRNA vaccine in systemic autoimmune rheumatic diseases: two cases in patients on TNF inhibitor monotherapy

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Despite COVID-19 vaccination, immunocompromised patients may be particularly susceptible to SARS-CoV-2 breakthrough infections,1 defined by the US Centers for Disease Control and Prevention (CDC) as positive test results 14 or more days after initial vaccine series completion (https://www.cdc.gov/vaccines/Covid-19/health-departments/breakthrough-cases.html). On 13 August 2021, the US Food and Drug Administration and CDC authorised immunocompromised patients to receive a third dose of SARS-CoV-2 mRNA vaccine, defining this as the completion of their initial series (rather than a ‘booster’). Studies have evaluated breakthrough infections in patients with systemic autoimmune rheumatic diseases (SARDs) after the second but not third dose of mRNA (messenger ribonucleic acid) vaccine.2,3 Therefore, we aimed to provide an early description of two cases of breakthrough infections occurring after three mRNA vaccine doses.

Mass General Brigham (MGB) is a large, multicentre healthcare system in the greater Boston, Massachusetts area. As previously described,4 we systematically identify all patients with SARDs at MGB with confirmed COVID-19 (by PCR or antigen testing). As of 25 October 2021, we identified two cases of breakthrough infections at least 14 days after receipt of three mRNA vaccine doses (table 1).

The first case is a 31-year-old woman with a history of juvenile idiopathic arthritis diagnosed at age 8 that evolved into seronegative inflammatory arthritis in adulthood. Her inflammatory arthritis was in remission on adalimumab. She had no other comorbidities, never smoked and was on no other medications. She received mRNA-1273 (Moderna) vaccine doses on 29 January 2021, 26 February 2021 and 22 August 21. Thirty days later, she developed cough, headache, malaise, fever, diarrhoea, anosmia and dysgeusia. She presented and tested positive for SARS-CoV-2 by antigen test. Given her immunocompromised state, she received monoclonal antibody treatment (casirivimab/imdevimab) 2 days after the positive test. Symptoms resolved without need for hospitalisation.

The second case is a 51-year-old man with seropositive rheumatoid arthritis of 14 years duration. He was in remission on certolizumab pegol. He also had hypertension, hyperlipidaemia, obesity and obstructive sleep apnoea. Other medications were gabapentin, olmesartan/hydrochlorothiazide, rosuvastatin and finasteride. He received Pfizer-BioNTech (BNT162b2) doses on 21 January 2021, 11 February 2021 and 25 August 2021. Fourteen days later, he developed chest pain and then fever, sore throat and dry cough that prompted PCR testing for SARS-CoV-2 that was positive 16 days after the third vaccine dose. His spouse also had COVID-19 that was diagnosed the day before his test. He received supportive care and never required hospitalisation.

To our knowledge, these are the first reports of SARS-CoV-2 infection after three doses of mRNA, the current standard initial vaccine series for immunocompromised individuals. Our findings may be reassuring since both patients had a mild COVID-19 course. Some breakthrough infections are expected for any vaccine. The number of patients with SARD within MGB who had received three mRNA doses is too small to determine if people already on immunomodulation are at increased risk for breakthrough infections. Further studies are needed to determine whether patients on TNF inhibitors are more likely to develop breakthrough infections with mRNA vaccines.
TNF users at time of COVID-19 vaccination may mount insufficient immune responses to the SARS-CoV-2 delta variant, the predominant circulating strain in Massachusetts (and worldwide) at the time of both patients' infections. The American College of Rheumatology COVID-19 Vaccine Clinical Guidance Task Force recently ‘could not achieve consensus’ on whether to hold cytokine inhibitors such as TNFi at the time of third mRNA vaccine dose. These findings support further research into determining whether biological disease-modifying antirheumatic drugs such as TNFi should be temporarily discontinued around COVID-19 vaccination to optimise immune response to the delta as well as future variants.

Acknowledgements We thank each patient and their providers.

Contributors All authors made substantial contributions to the conception or design of the work and in the acquisition, analysis and interpretation of the data. All authors drafted or revised the work for critically important intellectual consent. All authors provided final approval of the version to be published.

Funding NUP is supported by the National Institutes of Health Ruth L. Kirschstein Institutional National Research Service Award (T32 AR007258). ZSW is funded by NIH/NIAMS K23AR073334 and R03AR078938. JAS is funded by NIH/NIAMS (grant numbers R01 AR077607, P30 AR070253, and P30 AR072577) and the R. Bruce and Joan M. Mickey Research Scholar Fund.

Competing interests ZSW reports research support from Bristol Myers Squibb and Principia/Sanofi and consulting fees from Viela Bio and MedPace. All other authors report no competing interests. JAS has received research support from Bristol Myers Squibb and performed consultancy for AbbVie, Boehringer Ingelheim, Bristol Myers Squibb, Gilead, Innova Diagnostics, Janssen, Optum and Pfizer unrelated to this work.

Patient consent for publication Consent obtained directly from patient(s)

Ethics approval This study was approved by Mass General Brigham IRB (Protocol #: 2020P000840).

Provenance and peer review Not commissioned; externally peer reviewed.

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REFERENCES


