SARS-CoV-2 mRNA vaccination and subsequent herpes zoster: Possible immune reconstitution by mRNA vaccination

INTRODUCTION

To the Editor: I read with great interest the manuscript by Etaee et al.[1] Herpes zoster (HZ) is caused by reactivation and shedding of latent varicella-zoster virus (VZV). However, direct reactivation of VZV by messenger (m)RNA vaccination has never been proven.[2] Another question is why HZ occurs almost exclusively with mRNA-based COVID-19 vaccines and not with viral vector or inactivated COVID-19 vaccines.[2] Here, I present a HZ case that raises awareness of potential immune reconstitution triggered by mRNA vaccination in an immunosuppressed patient.

A 74-year-old man who had been receiving chemotherapy for rectal cancer presented with a 2-day history of HZ in the left T4 dermatome (Fig 1). He had not been vaccinated against HZ. He had received the first dose of the BNT162b2 mRNA vaccine (Pfizer–BioNTech) 7 days before the rash appeared. VZV-specific immunoglobulin (Ig)G titers in his serum specimens at the first visit and 4 weeks before that were >128 and 25.9, respectively (negative titer value, <2). He was treated with oral valacyclovir (3000 mg/day). His rash completely crusted in a week, and postherpetic neuralgia did not develop (Fig 2). This case highlighted the mild severity of HZ, even though the patient had risk factors of developing severe HZ symptoms, namely aging and immunosuppression. Moreover, his VZV-specific IgG elevation started prior to HZ onset. VZV-specific IgG boosts attributed to subclinical VZV reactivation can be observed.[3] Subclinical VZV reactivation occurs commonly in immunosuppressed patients and even in healthy individuals under stressful circumstances.[4]

HZ is a common manifestation as an immune reconstitution inflammatory syndrome in immunosuppressed individuals.[5] It is thought that as a consequence of the host immune reconstitution, vigorous VZV-specific cytotoxic T cells target keratinocytes infected with subclinically reactivated VZV, causing full-blown HZ as an immune reconstitution inflammatory syndrome.[6] It is notable that the HZ usually produces mild inflammation.[5]

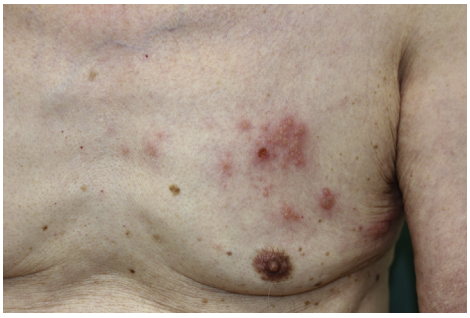

Fig 1. Mild vesicular rash on the left part of the chest on the second day postonset (at the first visit).

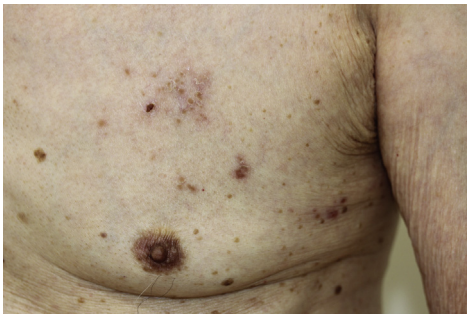

Fig 2. Complete healing of the rash without expanding on the 9th day after onset.

When VZV is subclinically reactivated or injected as an attenuated vaccine,[1] the question remains whether HZ can develop by mRNA vaccination in a similar manner as immune reconstitution inflammatory syndrome. Exogenous mRNA stimulates innate immunity through cellular sensors, such as toll-like receptors, and strongly induces type I interferons and proinflammatory cytokines, which instigate adaptive immunity. BNT162b2 and mRNA-1273 vaccines use modified RNA, which drastically reduce immune reaction to foreign mRNA.[7] However, mild-to-moderate reactogenicity (eg, injection site reaction, fatigue, headache. and fever) has often been reported in both vaccines. Therefore, there is a possibility that mRNA vaccines could trigger immune reconstitution.

A nationwide study in Israel revealed a correlation between BNT162b2 mRNA vaccination and HZ occurrence associated with a risk ratio of 1.43 (95% confidence interval, 1.20 to 1.73).[8] Furer et al suggested a correlation between BNT162b2 mRNA vaccination and HZ occurrence, especially in patients treated with immunosuppressants for rheumatic diseases in Israel. Although serologic tests for

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VZV were not described, the result that 5 out of 6 cases of HZ following the vaccination exhibited mild severity is remarkable.[9]

In conclusion, this case offers additional evidence of a correlation between mRNA vaccination and HZ occurrence. Larger studies, however, are required to further elucidate possible mechanisms of this correlation.

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Conflicts of interest

None disclosed.

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