

Dr. Kitajima et al reply

To the Editor:

We thank Mutoh et al¹ for their interest in our study on anti-melanoma differentiation-associated gene 5 antibody-positive interstitial lung disease (anti-MDA5-ILD) after vaccination with coronavirus disease 2019 (COVID-19) mRNA vaccines² and for sharing their clinical experience.

Mutoh et al¹ reported a case of anti-MDA5-ILD that developed 8 weeks after COVID-19 mRNA vaccination in Japan. This case is similar to the cases that we have encountered. A recent literature review also reported 7 cases of anti-MDA5-ILD after COVID-19 vaccination.³ Collectively, these cases provide evidence of an association between vaccination with COVID-19 mRNA vaccines and anti-MDA5-ILD, and suggest the possibility of COVID-19 mRNA-vaccine-induced anti-MDA5-ILD. However, these cases do not explain the relationship between vaccination with COVID-19 mRNA vaccines and anti-MDA5-ILD. In our single-center retrospective analysis, we did not find a statistically significant difference in the annual number of cases of anti-MDA5-ILD before and after the COVID-19 vaccination campaign in Japan.² We agree with Mutoh et al¹ that further large epidemiological population-based studies are needed to clarify the relationship between anti-MDA5-ILD and vaccination with COVID-19 mRNA vaccines.

Mutoh et al¹ pointed out the possibility that COVID-19 vaccination could lead to early diagnosis of anti-MDA5-ILD, as patients are likely to seek medical attention if they develop symptoms shortly after being inoculated with a new vaccine. However, the cases in our study were not diagnosed early. All 4 cases of anti-MDA5-ILD in our study had multiple poor prognostic indicators on admission (hypoxia, hyperferritinemia, computed tomography findings, and high lactate dehydrogenase levels), suggesting advanced disease.⁴ We are concerned about the delay in the diagnosis of cases of anti-MDA5-ILD during the COVID-19 pandemic. Anti-MDA5-ILD is often regarded as a form of pneumonia, similar to COVID-19, rather than as a connective tissue disease complicated by ILD and a dermatomyositis (DM)-specific rash.⁵ Therefore, it is important to rule out anti-MDA5-ILD in patients with COVID-19-like lung disease. Delayed diagnosis of anti-MDA5-ILD may further delay the initiation of aggressive immunosuppressive therapy needed to control anti-MDA5-ILD and may worsen the prognosis.⁴ In particular, the widespread use of telemedicine during the COVID-19 pandemic may lead to a lack of a full physical examination, and the DM-specific rash, which is necessary for the diagnosis of anti-MDA5-ILD, may be missed. In addition, patients with suspected COVID-19 are often examined by general physicians, and not by rheumatologists or respiratory physicians. Therefore, physicians should consider

anti-MDA5-ILD in the differential diagnosis of patients with COVID-19-like lung disease.

COVID-19 vaccination has changed the course of the pandemic and has saved tens of millions of lives globally.⁶ In addition, third or fourth vaccinations have been approved because of the emergence of new Omicron subvariants and the reduced protection provided by 2 doses of COVID-19 vaccines.⁷ Without an ongoing large-scale vaccination campaign, the healthcare system could become overwhelmed. Therefore, COVID-19 vaccination campaigns should continue. In clinical practice, it is difficult to determine the risk of developing anti-MDA5-ILD based on the associated genetic factors.⁸ Therefore, in patients with pneumonia and a rash after COVID-19 vaccination, anti-MDA5-ILD should always be considered in the differential diagnosis.

In order to improve our understanding of anti-MDA5-ILD after COVID-19 vaccination, further case reports are required, and further studies are needed to clarify the pathogenesis of anti-MDA5-ILD after COVID-19 vaccination and its association with the type of vaccine.

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The authors declare no conflicts of interest relevant to this article.

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