



Response to: Before blaming SARS-CoV-2 vaccinations for rhabdomyolysis, other potential triggers should be considered

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Received: 4 August 2022 / Revised: 4 August 2022 / Accepted: 5 August 2022 / Published online: 23 August 2022
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Dear Editors,

We thank Dr. Josef Finsterer for his interest and questions regarding our case, ‘A child with crescentic glomerulonephritis following SARS-CoV-2 mRNA (Pfizer-BioNTech) vaccination’ [1], and for giving us a chance to have a more in-depth discussion. We will herein endeavor to address as many of his questions as possible.

Dr. Finsterer indicated that the latency between the vaccination and the ‘onset’ of kidney disease, which was approximately 6 weeks, was too long. We reported that the interval between the second vaccination and the ‘detection’ of the kidney disease was 6 weeks, rather than the ‘onset.’ He also queried how we knew acute kidney injury (AKI) started 2 weeks after vaccination, and as he rightly noted, we cannot precisely identify the date of onset given our lack of laboratory data. The initial presentation of rapidly progressive glomerulonephritis (RPGN) is non-specific, such as fatigue or edema. Additionally, RPGN can progress over a comparatively short period, and progression to kidney failure can occur within as little as several weeks. We postulated that kidney disease might have started within 2 weeks of the second vaccination based on the previously reported adult cases of RPGN [1]. Further discussion below will add some additional support to our assumptions.

Dr. Finsterer highlighted that kidney disease could have been present before vaccination and that other potential triggers should be considered before attributing this to the vaccination. Once again, we would like to emphasize that the provocations of kidney disease associated with immune responses to vaccinations or infections are not rare events. ANCA-associated vasculitis and other glomerular diseases have been associated with SARS-CoV-2 vaccinations [1] and

SARS-CoV-2 infections [2, 3]. Additionally, several types of vasculitis have developed after other vaccines, including the influenza vaccination. The provocation of glomerulonephritis, such as IgA nephropathy, is also associated with viral and bacterial infections and vaccinations, including the SARS-CoV-2 vaccines. In our case, we could not find any possible provoking event outside of the vaccination.

Dr. Finsterer disagreed that our patient had myocarditis. Indeed, the diagnosis of myocarditis was unclear in this case. We did not describe the diagnosis of myocarditis in detail because this was a brief report, and myocarditis itself was not a major concern. The patient had elevated cardiac markers, including B-type natriuretic peptide and cardiac myocyte-specific troponin-I. Dr. Finsterer also asked if cardiac magnetic resonance imaging (MRI) was carried out with gadolinium, to which the answer is yes. Cardiac MRI revealed the fuzzy and faint subepicardial late gadolinium enhancement in the mid-lateral and inferior interventricular junction, suspicious of early minimal fibrosis. Thus, we described the diagnosis as ‘suspicious’ myocarditis rather than ‘definite’ myocarditis in our report. Electrocardiographic (ECG) findings indicated non-specific T-wave abnormality with prolonged QT interval, and elevated cardiac enzymes and abnormal ECG findings returned to normal on follow-up. Although we did not perform a follow-up MRI, we conducted echocardiography, which persistently showed normal bilateral ventricular function without morphologic abnormality.

Dr. Finsterer queried if we performed a brain MRI to rule out several central nervous system-associated complications corresponding to the vaccination. We believe this recommendation is reasonable. We did not perform a brain MRI because the patient had complained of headaches previously, but this symptom was not present on admission to our hospital. We also considered the risk of nephrogenic systemic fibrosis.

The type of edema was peripheral pitting combined with pulmonary edema confirmed on the chest radiography. Our

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patient's weight decreased from 76 to 63 kg after 2 weeks of hemodialysis. We suspect that the cause of the edema might have been AKI because the echocardiography on admission indicated that her cardiac function was normal. Nevertheless, the patient could have had undetected heart failure before admission, which might have contributed to her edema.

Our patient appears to have had vaccination-associated myositis. There have been several reports on rhabdomyolysis associated with SARS-CoV-2 vaccination, as Dr. Finsterer stated. However, serum creatinine-kinase (CK) level was elevated to several hundred IU/L in this case, which seemed to be relatively low compared with the values typically associated with AKI. We cannot be certain whether that patient had had a higher CK level before admission. Regardless, renal pathology revealed minimal tubular interstitial changes, which is crucial evidence for denying the possibility of AKI caused by rhabdomyolysis. Initially, the possibility of multisystem inflammatory syndrome in children (MIS-C) was ruled out because the diagnostic criteria were not met (no persistent fever lasting more than 24 h, normal levels of C-reactive protein [0.55 mg/dL, normal range 0–0.6] and procalcitonin [0.19 ng/mL, normal range <0.5]). However, it is possible that the diagnostic criteria were satisfied before hospitalization, and vaccination-induced MIS-C has also been reported. Therefore,

we agree that the possibility of MIS-C cannot be excluded in this case.

Finally, we are thankful for the comments that initiated valuable discussion around the association between SARS-CoV-2 vaccination and RPGN.

Declarations

The authors declare no conflicts of interest.

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