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Letter to the Editor

Rhabdomyolysis Following SARS-CoV-2 Vaccination in Hyperlipidemia is more Likely Due to the Statin than the Vaccine

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Letter to the Editor

We read with interest the article by Hazari *et al.* about a 53-year-old woman with a history of diabetes and hyperlipidemia who developed 45 days after receiving the second dose of an mRNA-based anti-SARS-CoV-2 vaccine (BNT162b2) [1]. The muscle weakness was attributed to vaccine-induced rhabdomyolysis, and treatment with adequate hydration, glucocorticoids, and immunoglobulins had a positive effect [1]. The study is interesting, but some points should be discussed.

The first point is that rhabdomyolysis in the index patient was not necessarily attributable to the active ingredients of the vaccine (e.g., antigens) themselves, but rather to one of the additives in the manufacturer's drug, such as adjuvants, stabilizers, preservatives, antioxidants, and production residues (e.g., egg protein, formaldehyde, antibiotics). Before attributing rhabdomyolysis to the active ingredient itself, all other possible triggers of rhabdomyolysis must be thoroughly ruled out.

The second point is that any rhabdomyolysis requires a thorough investigation of the underlying cause. Even if rhabdomyolysis has been attributed to the vaccine, an underlying primary or secondary muscle disease must be ruled out. Since an external co-trigger (e.g., medication, fever, electrolyte disturbances, seizures) can trigger rhabdomyolysis in patients with known or unknown primary or secondary myopathy, it is important to consider myopathy or susceptibility to malignant hyperthermia (MHS) as the underlying cause of rhabdomyolysis. There are further studies showing that SARS-CoV-2 vaccination in combination with statin myopathy can trigger rhabdomyolysis [2].

The third point is that rhabdomyolysis can occur in particular when a patient is taking certain medications that contain compounds known to cause rhabdomyolysis, such as fibrates, statins, cocaine, amphetamines, heroin, tricyclic antidepressants, benzodiazepines, colchicine, levetiracetam, or lithium [3]. It is therefore important to be aware of all medications that a patient takes regularly. Since the index patient had been taking atorvastatin for 3 years and statins often trigger rhabdomyolysis in conjunction with fever, infections, or immunological disorders [4], it is more likely that the rhabdomyolysis in the index patient was due to the statin than to the vaccination. In this respect, vaccination can be considered similar to an infection.

The fourth point is that it is unclear why the patient underwent cerebrospinal fluid (CSF) testing [1]. The patient suffered from proximal tetraparesis and myalgia with no evidence that the symptoms and signs originated in the central nervous system (CNS). An increase in CK can, of course, originate in the brain, but in this case it is advisable to perform brain imaging to determine whether or not there is a lesion in the CNS. It is also surprising in this context that no cerebral imaging was performed prior to the lumbar puncture [1]. In order to rule out contraindications for a lumbar puncture, it would have been essential to either perform a fundoscopy or assess whether there were indirect indications of increased intracranial pressure.

The fifth point is that the muscle biopsy was performed immediately after the onset of rhabdomyolysis and did not provide any meaningful results. Since a muscle biopsy shortly after rhabdomyolysis usually only shows necrotic muscle fibers and is therefore not meaningful, it is generally recommended to wait a few months before performing the biopsy until the muscle has had sufficient time to regenerate [5].

One limitation of the study is that no reference ranges for laboratory values were provided, making it difficult to assess what was normal and what was abnormal.

Overall, it is unlikely that the SARS-CoV-2 vaccination was the primary cause of rhabdomyolysis. It is more likely that the patient had subclinical secondary myopathy due to atorvastatin and that the vaccination was the final straw. Statin myopathy often only becomes symptomatic in the presence of fever, infections, newly occurring immunological diseases, or vaccinations.

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