

Cardiovascular Events After Coronavirus Disease 2019 Vaccinations: Hypersensitivity Myocarditis After Coronavirus Disease 2019 Vaccines, Diagnostic and Long-term Considerations

To the Editor,

Myocarditis is an inflammatory condition of the myocardium with absence of acute or chronic coronary artery disease. The correct terminology and distinction between myocarditis brought on by vaccinations, medications, or other substances are still up for debate. There are various forms of myocarditis¹ according to causative, histological, and clinicopathological criteria. In the interesting report published in the *Anatolian Journal of Cardiology*,² the author described a 65-year-old Russian patient who had an almost asymptomatic coronavirus disease 2019 (COVID-19) infection and a year later was vaccinated with Gam-COVID-Vac vaccination. He then experienced symptoms consistent with asthenia, dyspnea, cardiac arrhythmia, limb numbness, and herpes zoster. The author emphasized the need to be aware of potential late side effects from COVID-19 vaccinations, including cardiovascular issues.

Indeed, several factors have been proposed as potential causes of vaccine-induced myocarditis and its long-term COVID-19 complications. Immune messenger ribonucleic acid (mRNA) reactivity, sex-related hormonal differences, the amount of mRNA antigen in each vaccine,³ and molecular mimicry⁴ between the cardiac self-antigens and the spike protein of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) are associated with myocarditis. The diagnosis of myocarditis is based on results from cardiac MRI, which showed myocardial edema on T1 and T2-based images. Presumably, due to the disease's self-limiting and mild course, cardiac biopsies have not been performed.⁵ However, the gold standard for diagnosing myocarditis is histological evidence of an inflammatory cell infiltrate, with or without myocardial damage. We have reviewed the literature and found that a 21-year-old man with a history of childhood atopic asthma, pollen, and pet allergy has been reported to have developed myocarditis following the first dose of the SARS-CoV-2 mRNA vaccine.⁶ The perspective that SARS-CoV-2 mRNA vaccine-associated myocarditis is hypersensitivity myocarditis⁷ is based on the presence of histiocytes and giant cells.⁸ Because nonspecific skin rash, malaise, fever, and eosinophilia—clinical features typical of a hypersensitivity reaction—are typically absent in hypersensitivity myocarditis cases, it is particularly challenging to diagnose it clinically. Although the precise process by which SARS-CoV-2 vaccinations cause myocarditis remains unclear, the presence of even infrequent histiocytes indicates a hypersensitivity reaction. Excipients used in SARS-CoV-2 vaccines, including polyethylene glycol (PEG) in PEGylated lipid nanoparticles and trometamol or tromethamine in common practice items, have been identified as potentially hypersensitive substances in the past. Polyethylene glycol can sensitize users of creams, ointments, lotions, cosmetics, dental materials, and even laxatives, which are frequently used by young people, particularly females.⁹ Between 1% and 5.4% of the general population is sensitized to dental or cosmetic materials.⁹ In the event that systematic

LETTER TO THE EDITOR

Nicholas G. Kounis 

Division of Cardiology, Department of
Medicine, University Hospital of Patras,
Patras, Greece

Corresponding author:

Nicholas G. Kounis
✉ ngkounis@otenet.gr

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future investigations confirm vaccine component-induced hypersensitivity, alternative excipients have been proposed for use in vaccine manufacturing. According to several authors, patients who have a PEG allergy run the risk of developing hypersensitivity to excipients; as a result, these patients will likely wait for new vaccines that use different excipients. Though thankfully still extremely rare, the current recommendations made in a recent position paper¹⁰ will aid in our understanding of the mechanisms underlying hypersensitivity reactions to SARS-CoV-2 vaccines.

In order to more fully characterize long-term outcomes, continuous monitoring of COVID-19 complications will be necessary for years to come. It is important to remember that myocarditis can cause dilated cardiomyopathy, which can lead to end-stage heart failure and necessitate cutting-edge treatments like orthotopic heart transplantation.¹¹

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