Hypersensitivity myocarditis and COVID-19 vaccines

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Myocarditis is an inflammatory cardiac disorder induced by a wide spectrum of infectious agents, including viruses, bacteria, chlamydia, rickettsia, fungi, and protozoans. The so-called eosinophilic myocarditis includes types associated with systemic disease (e.g, hypereosinophilic syndrome, Churg-Strauss syndrome, and malignancies), parasitic infections, like *Toxocara canis*, and idiopathic acute necrotizing eosinophilic myocarditis. A specific type of myocarditis called hypersensitivity myocarditis is induced by hypersensitivity reactions to a variety of drugs including vaccines with their components. Atopic individuals are predominantly prone to develop this type of myocarditis. In the very interesting report published in *Kardiologia Polska* (*Kardiol Pol*, *Polish Heart Journal*) [1], a 21-year-old man with a previous history of atopic asthma in childhood, pollen, and pet allergy developed chest discomfort lasting about 3 hours following the first dose of mRNA COVID-19 vaccination (Comirnaty, Pfizer, New York, NY, USA). Whereas coronary computed tomography angiography demonstrated normal coronary arteries, cardiac magnetic resonance imaging revealed increased signal intensity on T2-weighted images, increased values on both T1 and T2 mapping, and the presence of diffuse subepicardial late gadolinium enhancement compatible with typical active myocarditis. Whereas this report raises important issues on COVID-19 vaccine-induced myocarditis, the type of myocarditis, and the potential measures of how to prevent such vaccine-induced cardiovascular events, the authors do not specify the type of myocarditis and the relative treatment this patient received in addition to the painkillers for the chest pain.

Indeed, rare cases of myocarditis following COVID-19 vaccination have been reported recently. The first reports described young men who presented with chest pain, usually 2–3 days after the second dose of mRNA vaccination. Very late-onset myocarditis after the second dose of mRNA vaccination has also been induced. Apart from the mRNA COVID-19 vaccine (Comirnaty, Pfizer), myocarditis has been induced following the mRNA-1273 COVID-19 (Moderna, Cambridge, MA, USA) and AstraZeneca vaccines. So far, no reports have associated the Johnson & Johnson vaccine with myocarditis. The previous history of cardiovascular disease or myocarditis may increase the risk for COVID-19 vaccine-related myocarditis.

The exact mechanism by which SARS-CoV-2 leads to myocardial damage has not been elucidated. It has been postulated that direct damage to the cardiac myocytes, interferon-mediated immune response leading to systemic inflammation might be potential mechanisms. However, histological or immunohistological evidence of inflammatory cell infiltrate is of paramount importance for elucidating the mechanism of myocarditis. The mRNA vaccine Pfizer-BioNTech contains polyethylene glycol (PEG), and the mRNA-1273 vaccine (Moderna) contains PEG and tromethamine that can induce hypersensitivity reactions. The latter constitutes an excipient of gadolinium-based contrast agents. Surprisingly, gadolinium is a substance used in cardiac magnetic resonance imaging for diagnosing myocarditis!

Very few cases of myocarditis associated with the COVID-19 vaccines have been subjected, so far, to endomyocardial biop-

sies. Indeed, due to the mild clinical course of myocarditis and the lack of myocardial biopsies, its pathogenesis is poorly understood. In 2 cases of myocarditis following COVID-19 vaccination in the United States and one in Israel, the endomyocardial biopsies revealed eosinophils and other interacting and interrelated inflammatory cells, such as macrophages, T-cells, and B-cells compatible with hypersensitivity myocarditis [2].

The described young patient [1] had an atopic diathesis due to his previous history of atopic asthma, pollen, and pet allergy, therefore, the induced myocarditis was presumably hypersensitivity myocarditis. Indeed, this type of myocarditis is particularly difficult to recognize because the clinical features characteristic of a drug hypersensitivity reaction — including non-specific skin rash, malaise, fever, and eosinophilia — are absent in most cases [3].

Most patients respond well to steroid administration or drug removal. Hypersensitivity myocarditis is seen in 3% to 10% of cardiac explants and patients on ventricular assist devices. The PEG excipient contained in mRNA vaccines is also part of creams, ointments, lotions, cosmetics, dental materials, and might have sensitized their users. Indeed, 1%–5.4% of the population is already sensitized to cosmetics or dental materials. In the USA, it is estimated that 2% to 5% of the population have experienced hypersensitivity or anaphylaxis; most commonly to drugs, food, or insect stings [4]. Therefore, hypersensitivity to the above COVID-19 excipients could induce hypersensitivity and consequently hypersensitivity myocarditis. This has forced researchers to suggest alternatives in vaccine manufacturing if vaccine component-induced hypersensitivity is confirmed by more systematic future investigations [4]. Prevention of thrombotic and cardiovascular events may be achieved by alternative agents that reduce immunogenicity, improve stability, and suppress oxidative damage [5]. We have the feeling that COVID-19 free allergenic vaccines might prove more suitable, more beneficial, and not induce cardiovascular events.

Article information

Conflict of interest: None declared.

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