Journal of Cardiology Cases 26 (2022) 242–243

Contents lists available at ScienceDirect

Journal of Cardiology Cases

journal homepage: www.elsevier.com/locate/jccase

Letter to the Editor

Hypersensitivity coronary myocardial infarction (Kounis syndrome) and COVID-19 vaccines

Rare cases of acute myocardial infarction have been reported following coronavirus disease 2019 (COVID-19) vaccination. In a recent report [1] evaluating the short-term risk of severe cardiovascular events, among people aged 75 years or older after the administration of the BNT162b2 mRNA vaccine in the 14 days following either dose of vaccine, no significant increased risk was found for myocardial infarction and the relative incidence for the first dose was 0.97 (95% CI, 0.88–1.06) and for the second dose, 1.04 (95% CI, 0.93–1.16). Recent reports, however, have speculated on Kounis type hypersensitivity-associated acute myocardial infarction as the type of COVID-19 vaccine-induced acute myocardial infarction. Several vaccine types [2] have been incriminated as causes for this event, including (Pfizer–BioNTech, Marburg, Germany), (Covishield vaccine, Serum Institute, Pune, Maharashtra, India), (Sinovac (Coronovac), *Sinovac* Biotech Ltd., Beijing, China), in addition to (AstraZeneca, Oxford, England) and (Moderna, Cambridge, Massachusetts, USA). No allergies or atopic diathesis have been reported in any of these patients. In the important case published in *Journal of Cardiology Cases* [3], a 59-year-old male, suffering from rheumatoid arthritis, atrial fibrillation, and stent implantation, developed precordial pain, 20 min after the ChAdOx1 (AstraZeneca) vaccine, accompanied by sweat, discrete micropapular rash on his chest, and eosinophilia. An ST-elevation myocardial infarction was diagnosed and a new stent was implanted in the proximal margin of the previous one. Detailed past medical history revealed the same symptomatology after influenza vaccine administration (Influvac Tetra®Abbott Biologicals B.V., Olst, Overijssel, *Netherlands*). Based on the skin reaction, eosinophilia, catheterization results and the fact that both vaccines, Covid-19 and influenza contain a common excipient polysorbate-80 (PS80), the authors diagnosed that the patient had suffered a Kounis syndrome type III. The skin tests with intravenous amiodarone, that contains PS80, were negative. Therefore, this report raises important issues on causality, thrombosis, allergy, and negative skin test. Polysorbate is derived from polyethylene glycol (PEG), is of lower molecular weight (PS80 has a molecular weight of 1310 Da) and rarely induces allergic hypersensitivity reactions. However, the described patient had suffered the same symptomatology following influenza vaccine which also contains PS80 which means that the patient was sensitized to PS80. Polysorbate 80 can induce systemic reactions including IgE immediate reactions as well as non-immunologic anaphylactoid reactions but also local reactions such as vein thrombus formation, pain, erythema. The adenoviral vector ChAdOx1 nCov-19 (AstraZeneca) is associated with rare, delayed manifestations, mainly in women of less than 60 years, resembling autoimmune heparin-induced thrombocytopenia with thrombosis and especially serious cerebral venous sinus thrombosis, in the absence of heparin administration. The contained PS80 can enhance membrane permeability, penetrate the blood–brain barrier, and facilitate the passage of drugs from the blood compartment to the brain for therapeutic purposes, especially in oncology. These PS80 actions make one wonder whether the adenoviral vector vaccine-induced cerebral venous sinus thrombosis is a simple coincidence. Indeed, the classical heparin-induced thrombocytopenia, which is not related to PS80, is not complicated with cerebral venous sinus thrombosis. The patient underwent emergent coronary angiography and large occluding thrombus was aspirated. In a recent report concerning a 22-year-old female patient with a previous history of egg and tomato allergy, the development of coronary vasospasm compatible with type I Kounis syndrome occurred 15 min after the first dose of COVID-19 vaccine BNT162b2 (Pfizer–BioNTech). The patient developed infero-anterior electrocardiographic ST elevations, treated successfully with anti-allergic medications and had normal coronary arteries during catheterization. Therefore, an atopic background advocates an allergic reaction. Furthermore, this patient was suffering from rheumatoid arthritis. Increased prevalence of allergic symptoms in patients with this chronic disease requires further investigation as chronic inflammation can lead to posttranslational modification of proteins and autoantigen formation. The authors correctly pointed out that negative results do not exclude PS80 non-IgE mediated hypersensitivity reactions. Indeed, the false-negative rate for skin testing ranges from 2.3% to 6.97%, depending on the used reagent. Several materials such as creams, ointments, lotions, cosmetics that are used frequently by individuals and dental materials contain also PS80 that is able to sensitize its users. Surprisingly, PS80 was found to be the second important allergen for dental students with sensitization rate of 27.5% – significantly higher compared to *myroxylon pereirae* resin, hydroperoxides of limonene, isopropyl myristate, and triclosan [4]. In general, 1–5.4% of the general population is sensitized to cosmetics or dental materials and 2% to 5% of the population, in the USA, have experienced hypersensitivity or anaphylaxis, to drugs, food, or insect stings. However, recent reports [5,6] have demonstrated that most individuals were able to receive the second mRNA COVID-19 vaccine dose safely despite the first-dose mRNA COVID-19 vaccine reactions, regardless of excipient skin testing result. Alternative excipients in vaccine manufacturing, if vaccine component-induced hypersensitivity is confirmed by systematic future investigations, have been already suggested. In a recent report [7] the authors concluded that hypersensitivity to such excipients constitutes risk to patients with allergy to PEG or polysorbates. After diagnostic evaluation, safe COVID-19 vaccines could be offered to most patients, but the authors of this report suggested “the remainders will await new vaccines containing different excipients”. Despite all of the above, myocardial infarction after vaccination is very rare and the benefits of vaccination should be taken into account and continue to be recommended to all those who are eligible.

Declaration of competing interest

The authors declare that there are no conflicts of interest.

Acknowledgments

None.

https://doi.org/10.1016/j.jccase.2022.05.001

Funding

None.

References

[1] Jabagi MJ, Botton J, Bertrand M, Weill A, Farrington P, Zureik M, et al. Myocardial infarction, stroke, and pulmonary embolism after BNT162b2 mRNA COVID-19 vaccine in people aged 75 years or older. JAMA 2022;327:80–2.

[2] Kounis NG, Koniari I, Mplani V, Kouni SN, Plotas P, Tsigkas G. Acute myocardial infarction within 24 hours after COVID-19 vaccination: is Kounis syndrome the culprit? Am J Cardiol 2022;162:207.

[3] Fialho I, Mateus C, Martins-Dos-Santos G, Pita J, Cabanelas N, Batista SB, et al. Recurrent Kounis syndrome - a life-threatening event after COVID-19 vaccine administration. J Cardiol Cases 2022. https://doi.org/10.1016/j.jccase.2022.01.014. [Feb 7, Epub ahead of print].

[4] Lyapina MG, Stoyanova Dencheva M. Contact sensitization to ingredients of dental materials and cosmetics in dental students: a pilot study. Cent Eur J Public Health 2019;27:73–7.

[5] Wolfson AR, Robinson LB, Li L, McMahon AE, Cogan AS, Fu X, et al. First-dose mRNA COVID-19 vaccine allergic reactions: limited role for excipient skin testing. J Allergy Clin Immunol Pract 2021;9:3308–3320.e3.

[6] Fernandez-Davila N, Taylor MG, Anvari S. Hypersensitivity reactions to COVID-19 vaccines-identify high-risk children and vaccinate the rest. JAMA Pediatr 2022;176:443–4.

[7] Mortz CG, Kjaer HF, Rasmussen TH, Rasmussen HM, Garvey LH, Bindslev-Jensen C. Allergy to polyethylene glycol and polysorbates in a patient cohort: diagnostic work-up and decision points for vaccination during the COVID-19 pandemic. Clin Transl Allergy 2022;12:e12111.

Nicholas G. Kounis (MD, PhD)*
Department of Cardiology, University of Patras Medical School, Patras, Greece
Virginia Mplani (MD)
Intensive Care Unit, University of Patras Medical School, Patras, Greece

Ioanna Koniari (MD, PhD)
Department of Cardiology,
University Hospital of South Manchester NHS Foundation Trust,
Manchester, United Kingdom

Sophia Kouni (MSc, PhD)
Panagiotis Plotas (MD, PhD)
Grigorios Tsigkas (MD, PhD)
Department of Cardiology, University of Patras Medical School, Patras, Greece

Dimitrios Velissaris (MD, PhD)
Department of Internal Medicine, University of Patras, Patras, Greece

*Corresponding author at: Department of Cardiology,
University of Patras Medical School, Queen Olgas Square,
7 Aratou Street, Patras 26221, Greece.
E-mail address: ngkounis@otenet.gr (N.G. Kounis).

18 March 2022