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Letter to Editor

LETTER TO EDITOR

Rare acute hypersensitivity myocardial infarction (Kounis syndrome) and hypersensitivity myocarditis following COVID-19 vaccination

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In the important pooled analysis of the study cohort and systematic review published in *QJM*,[1] the authors evaluated the temporal association between coronavirus disease 2019 (COVID-19) vaccinations and adverse cardiac events. They demonstrated that among 77 patients, 35 presented acute myocardial infarction and (AMI), and 42 suffered from myocarditis. The authors speculation on the mechanism of AMI following vaccination was autoimmune response against platelets, autoimmune heparin-induced thrombocytopenia, vaccination stress, polymorbid vaccination stress and Kounis syndrome. Moreover, non-specific inflammatory response or autoimmune response due to similarities between the vaccine and cardiac cell proteins could cause myocarditis. These results raise important issues on Kounis hypersensitivity AMI, hypersensitivity myocarditis and future measures in order to avoid and prevent the rare COVID-19 vaccine hypersensitivity.

Kounis hypersensitivity-associated AMI

Indeed, the Kounis syndrome is an entity associated with hypersensitivity reactions caused by drugs, metals, environmental exposures, conditions and foods. Recent reports have incriminated Kounis type hypersensitivity-associated AMI to be associated with all types of COVID-19 vaccines.[2] Especially, Kounis syndrome occurred in an 86-year-old and a healthy 96-year-old female post the first dose of BNT162b2 (Pfizer–BioNTech) and Moderna COVID-19 vaccine respectively, in a 62-year-old woman post the first dose of the AZD1222 vaccine (Oxford University and AstraZeneca), in a 41-year-old woman after the first dose of inactivated coronavirus vaccine (Sinovac Life Sciences, Beijing, China) and in a healthy 63-year-old man post the first dose of Covishield vaccine (similar to AstraZeneca and manufactured in India). All above vaccines contain excipients that could potentially induce hypersentitivity reactions. For example, the Pfizer-BioNTech vaccine contains polyethylene glycol, the Moderna vaccine contains polyethylene glycol and tromethamine, also known as trometamol, the AstraZeneca and Covishield vaccines consist of polysorbate 80, disodium edetate dihydrate (ethylenediaminetetraacetic acid) and aluminum hydroxide and finally the CoronaVac contains disodium hydrogen phosphate, sodium dihydrogen phosphate monohydrate and sodium chloride.

Hypersensitivity myocarditis

The pathogenesis of COVID-19 vaccine-associated myocarditis is poorly understood due to the lack of myocardial biopsies. In order to establish definite diagnosis histological or immunohistological evidence of an inflammatory cell infiltrate is of paramount importance. Indeed, in one fatal case from Korea,[3] in two patients from the USA[4] and in one patient from Israel[5] who demonstrated mRNA COVID-19 vaccination-induced-myocarditis, myocardial biopsy revealed myocardial infiltration by

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eosinophils and other inflammatory cells. Therefore, COVID-19 vaccination-associated myocarditis seems similar to hypersensitivity myocarditis. One-third of patients may have not peripheral eosinophilia and most patients respond well to drug removal or steroid administration.

Future perspectives

Polysorbate and polyethylenglycol are also ingredients in creams, ointments, lotions, cosmetics and dental materials able to sensitize their users. Sensitization to cosmetics or dental materials has been found in 1–5.4% of the population. Therefore, hypersensitivity myocarditis could be induced by the above materials. Fact that has forced researchers to suggest alternative ingredients in vaccine manufacturing if vaccine component-induced hypersensitivity is confirmed by further systematic future investigations.[6] Promising agents that reduce immunogenicity, improve stability, suppress oxidative damage and may prevent thrombotic and cardiovascular events constitute the alkylsaccharides. We believe that COVID-19 free allergenic vaccines might prove more suitable, and more beneficial without inducing hypersensitivity myocarditis.

Conflict of interest. None declared.

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