Letter to the editor

Cardiovascular complications after COVID-19 vaccination

The SARS-CoV-2 pandemic revealed a disastrous global emergency with tremendous medical, financial and social consequences. Since December 2019 science has been fighting against a corona-viral enemy with a high transmission and relative low fatality rate[1]. The worst clinical scenario is a respiratory infection with ARDS-like manifestation and adverse outcome mainly as for age, male gender and obesity. Several other clinical scenaria has been described worldwide in combination with the inflammatory and thrombogenic activation provoked by the virus. Pulmonary embolism, peri-myocarditis, acute renal failure and degenerative neurological syndromes confirm an impressive range of diseases[2] accompanied by an infection with up to 5000000 deaths globally.

The main pathophysiological way which causes the increased morbidity is the high binding affinity of spike protein of the virus to the ACE2 enzyme of endothelium[3]. The latter permits the entry of the virus in the cell and the modification of many molecular mechanisms. The vaccines developed against SARSCoV-2 provide in different ways the ultimate goal of production of neutralizing antibodies against spike- protein and activation of humoral and cellular immunity. As for the primary randomized studies there is a wide range of observational ones as well, which underline the relatively preserved efficacy against death, severe disease but not transmission over months[4]. New strains reduce the capability of vaccines to control the pandemic. Furthermore, a spread of adverse events disproportionately huge compared with the entire registration of all vaccines according to the main databases of VAERS and EudroVigilance. So, since endothelial ACE2- enzyme is a key target-molecule of Covid-19 and relates to spike-protein (SP) antibodies of the vaccines, cardiovascular complications should be investigated under a possibly direct pathophysiological pathway. As Covid-19 disease tends to be endemic, registration of adverse events of the vaccines become more important.

Kounis N. et al. explained fatal cardiovascular events by activation of

coagulation and allergic hypersensitivity caused by macrophages and mast cells[5]. The same mechanism provokes clinical identities in other vascular beds like coronary, mesenteric, pulmonary and cerebral vessels[6]. Such events have already recorded after Covid-19 vaccination[7]. Although myocardial infarction has not yet shown a clear hazard ratio after covid-19 vaccination, plethora of sudden deaths revealed an questionable coincidence. Elevated thrombogenicity of activated platelets could give an answer to the scenario. Pulmonary embolism and thromboses of extremities were registered as a result of thrombosis thrombocytopenia syndrome (TTS) with the prevailing mechanism of cross reactivity of antibodies against SP and PF4 factor[8]. Moreover, cerebral venous thrombosis after vaccination confirms an unique cardiovascular complication severe and fatal with preference in younger population[9]. Not rare, proportion of cerebral ischemic events are accompanied by bleeding findings.

There is a suspicion of exacerbation of heart failure, hypertension and arrythmias due to the documented downregulation of the endothelial ACE-2 enzyme by SP and vaccines in relation to the latter[10]. Although there is no strong verification in the current literature, pivotal study after vaccination showed increased levels of inflammatory and thrombogenic factors in blood samples consisting a cardiovascular negative prediction (PULS score)[11].

Myocarditis is more frequent among young males with an incidence from 1 to 37 after the second shot per 100000 vaccinations. Pericarditis has an incidence of 1.8 per 100000. The possible mechanism is immune- related, but the manifestation 5 days after shot remarks a direct idiopathic toxicity against myocardial mitochondria[12]. Specific groups like male adolescents[13] and military staff[14] present high incidence of myo-, pericarditis with mild to moderate severity.

On the whole, covid-19 vaccines need to be investigated as for cardiovascular complications, since SP-related pathophysiology and specific clinical syndromes are

verified, documented and on official databases in large numbers registered. More observational studies accompanied by strict pharmacovigilance would contribute to clear epidemiological conclusions. In addition, such findings could offer the appropriate literature for making decisions about mandatory vaccination.

Keywords : Complication; cardiovascular disease; COVID-19 vaccine; myocarditis; pulmonary embolism

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