LETTER

Renal Complications Following COVID-19 Vaccination

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COVID-19 vaccines provide a powerful strategy against coronavirus pandemic. They prevent the spread of disease, and reduce hospitalization and disease severity. Despite the clear benefits of vaccination programs, COVID-19 vaccines are not risk-free and adverse events can sometimes occur after vaccination. Most of these adverse reactions are mild and are more common. The array of mild symptoms can include fever/chills, headache, lethargy, or injection site reactions like edema, erythema, or pain and usually disappear within a few days. Nonetheless, there have been some reports of new-onset or exacerbation of glomerular diseases following COVID-19 vaccines. Based on the available literature, IgA nephropathy (IgAN) or minimal change disease(MCD) are the most common forms of COVID-19 vaccine-associated glomerular disease. But, a small number of vaccine recipients also develop other diseases such as membranous nephropathy, anti–neutrophil cytoplasmic antibody–associated vasculitis, anti–glomerular basement membrane disease, and IgG4 renal disease.[1]

The exact molecular pathogenesis of kidney side effects of COVID-19 vaccines remains unclear. Immune derangement would seem to play an important role in the onset and progression of these complications. Interestingly, different types of immune response seems to be a critical determinant of the ultimate progression of glomerular disease. For instance, dysregulation of antibody-mediated humoral immune response plays important roles in the development and progression of IgAN after vaccination. In contrast, dysregulated T-cell is essential for podocyte injury as a hallmark of MCD. Molecular mimicry is another possible mechanism for the induction of vaccine-associated autoimmunity.[2] Sequence homology between certain viral proteins and human proteins, may contribute to immune attack against self antigens. Bystander activation may also offer a plausible explanation for vaccine-induced autoimmune activation. Immune system's reaction to the vaccine may trigger cellular damage and exposure of self-hidden (sequestered) antigens. The detection of these antigens by the immune system can result in antigen presentation to autoreactive cells and development of glomerular diseases.

Another point that must be kept in mind is a probable relationship between the appearance of glomerular complications and the different forms of technology that have been applied for the production of COVID-19 vaccines. At present, the four main types of COVID-19 vaccines are available: mRNA-based, viral vector, inactivated and protein subunit. All of them rely on the viral spike protein (S) of SARS-CoV-2 but there are differences between these four different categories of vaccines with respect to the presentation of S protein to the immune system. S protein is essential for viral replication and is important for inducing long-lived neutralizing antibodies. Among these four types of vaccines, mRNA vaccines have shown to induce more potent immune responses than others. This ability can strengthen virus-specific responses and vaccine efficacy that is important in disease prevention. But at the same time, host immune response against mRNA vaccines is accompanied by increased production of T cell cytokines such as interferon γ, tumor necrosis factor α and interleukin 2. The early T cell activation and the overproduction of inflammatory cytokines in disease-susceptible individuals, can be considered as part of mechanisms that may trigger podocytopathies and production of disease-specific antibodies.[3,4]

Vaccine-related adverse events in patients with renal failures like patients with autoimmune kidney diseases is another point of focus. Such individuals are considered to be good vaccine candidates because they are at higher risk of severe illness from the coronavirus. On the other hand, these patients with weak immune systems (immunocompromised) often have to be treated with immunosuppressive drugs.[5] Unfortunately, currently there are not enough data to show the safety, efficacy and immunogenicity of COVID-19 vaccines in these patients as a result of their exclusion from all major clinical trials of vaccine candidates against COVID-19. Therefore, there are different questions needed to be addressed, such as the effect of immunosuppression on immune responses against SARS-CoV-2 vaccination, the potential of COVID-19 vaccine in inducing autoimmunity or relapse of the autoimmune diseases. It seems that timing of vaccination is an important concern in patients who have been treated with immunosuppressive drugs because these medication can weaken the immune response of patients.

Overall, renal adverse effects following COVID-19 vaccination are not abundant but can lead to serious health problems. There are controversies about the causal
relationship between COVID-19 vaccination and these adverse events. Therefore, more studies are required to further elucidate whether these associations are plausible.

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