Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Letter to the Editor

Covid-19 vaccine and autoimmunity: Awakening the sleeping dragon

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To the editor

Coronavirus disease 2019 (COVID-19), has affected millions of people globally, since it was declared a global emergency in March 2019 by World Health Organization. Its clinical spectrum varies, from asymptomatic disease to involvement of lower respiratory tract infection and uncontrolled inflammatory response, culminating in severe respiratory distress syndrome. Hence, the recent reports of effective and safe vaccines were welcomed with great joy [1], followed by FDA and EMA emergency approvals. Nonetheless, COVID-19 vaccines have raised a number of concerns regarding their reactogenicity, while a large proportion of the field remains unexplored, especially among patients with autoimmune conditions. The association of immune hyperactivation and excessive cytokine release, leading to multiorgan failure and death in COVID-19 patients, has been well established [2]. A variety of mechanisms has been proposed to contribute to the rise of acute autoimmune response [3]. As recently shown by Vorjani et al. [4], molecular mimicry, i.e. antibodies against SARS-CoV-2 spike glycoproteins cross-react with structurally similar host peptide protein sequences, could play an important role is this response. On top of that Talotta et al. [5] argues that especially in young female individuals who are already predisposed to autoimmune or autoinflammatory disorders, the administration of a nucleic acid vaccine may put them at risk of unwanted and unprecedented immunological side-effects. However, even in the context of population with autoimmune diseases, severe adverse events did not seem to exceed that of other regular vaccinations [1].

We hereby report the case of a 32y/o health care worker, with no prior medical history presenting with an itchy annular granulomatous rash over both her elbows 48 h following 1st dosage of COVID-19 mRNA vaccination (BNT162b2 *Pfizer*, Inc. as per manufacturer's instructions). The patient was in good condition, afebrile, in absence of systemic symptoms, while no other lesions were noted in trunk, palms, soles or genitals (Fig. 1). Laboratory tests were unremarkable. She reported a similar incident approximately a year ago, following an upper respiratory infection, biopsy of which revealed cutaneous small cell vasculitis, possibly of leukocytoclastic origin, without any other clinical or laboratory findings at that time. The patient has never tested positive during regular nucleic acid SARS-CoV-2 tests, among health care personnel, nor showed respective antibody positivity prior to immunization. The current lesions resolved spontaneously with no medical intervention, approximately 72–96 h following their initial presentation. Despite lack of experience, we chose to proceed with second dosage and close monitoring thereafter. We observed identical lesions, followed by spontaneous resolution without any need for further action.

In line with Talotta et al. [5], we hypothesize that, even though, COVID-19 vaccination does not provoke de novo immune mediated adverse events, it is possible that, the immunologic response triggers pre-existing underlying dysregulated pathways. This could be mirrored in a polyclonal B-cell expansion, resulting in immune complex formation and respective vasculitis phenomena. Of note, in genetically susceptible individuals, this kind of dysregulation may be enhanced by other autoimmune mechanisms, including epitope spreading and bystander activation, which could also lead to chronic autoimmunity following COVID-19 infection [6]. It remains an open question, when these phenomena do occur and if they do, whether a second dose should be administered. At the same time, one cannot help wondering what the relative response would unveil, in the context of non-specific organ vasculitis, eg in the case of systemic lupus erythematosus. We need more data to assess immune implications in patients with prior history of autoimmune associated manifestations, not only in terms of efficacy but also in terms of immune mediated adverse events, that could jeopardise disease flair. In this case, the clinical implications described should be weighted against the larger impact of vaccination, and by no means should hamper global efforts, if non-severe symptoms are exacerbated. Similar to other vaccines and existing literature, a causative link between vaccination and vasculitides cannot be established, since strict definitions do not currently exist [7]. However, its better to err on the side of caution, in order to provoke more observations and promote better understanding of disease itself, and optimize management and prevention, rather than find ourselves in awe of unexpected stumbling blocks.

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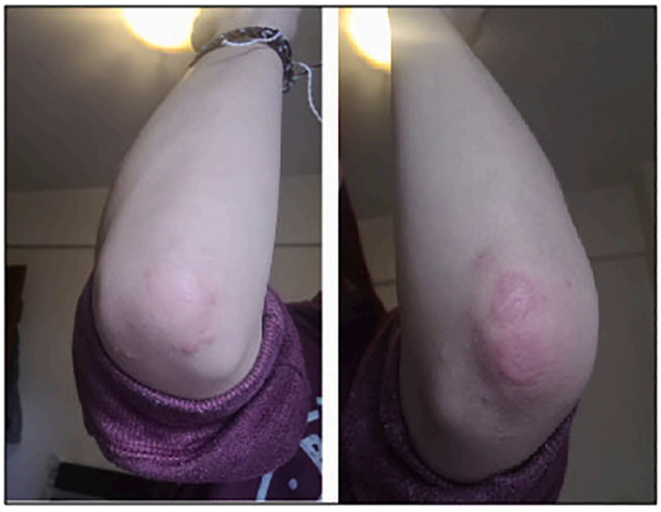

Fig. 1. Annular granulomatous rash on left and right elbow of a patient, 48 h following COVID-19 immunization.

Ethics approval

This study has been conducted according to declaration of Helsinki and approved by local ethics committee.

Consent to participate

The patient has consented to have his data anonymously used and published.

Availability of data and material

Data can be made available upon reasonable request from corresponding authors.

Authors' contributions

KA & IT performed literature search and collected patient's data, KA wrote the manuscript, KA & MM oversaw patient's management.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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Karolina Akinosoglou[a,b,*], Ilektra Tzivaki[a], Markos Marangos[a,b]

[a] *Department of Internal Medicine, University General Hospital of Patras, 26504 Rio, Greece*

[b] *Department of Infectious Diseases, University General Hospital of Patras, 26504 Rio, Greece*

[*] Corresponding author at: Specialist in Internal Medicine and Infectious Diseases, University General Hospital of Patras, 26504, Greece.

E-mail address: akin@upatras.gr (K. Akinosoglou).