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Polymyalgia rheumatica and polymyalgia-like syndromes as adverse events following immunisation with COVID-19 vaccines: a 15 months update

Ciro Manzo[1], Alberto Castagna[2], Arvind Nune[3], Marco Isetta[4]

[1]Division of Rheumatology, Internal and Geriatric Medicine Department, Azienda Sanitaria Napoli 3 sud, Sant' Agnello, Italy
[2]Department of Primary Care, Health District of Soverato, Azienda Sanitaria Provinciale Catanzaro, Italy
[3]Department of Rheumatology, Southport and Ormskirk Hospital NHS Trust, Southport, United Kingdom
[4]Central and North West London NHS Trust, England

Dear Editor,

Polymyalgia rheumatica (PMR) has been reported as an adverse event following immunisation (AEFI) with COVID-19 vaccines [1, 2]. In April 2022, we published in Reumatologia a narrative review, stating that reports of PMR following COVID-19 vaccination were rare AEFI. Among these, atypical presentation (so-called "PMR-like sytndromes") were not uncommon. A shared understanding of the relationship between COVID-19 vaccination and PMR/PMR-like syndromes was to follow [3].

New PMR cases following COVID-19 vaccines have been published over the past 15 months (from May 2022 to July 2023), primarily as case reports. In some of these reports, clinical and laboratory findings mimicked PMR (PMR-like syndromes) [4–7]. In particular, in an Italian multicentric observational study, 6/46 patients diagnosed with PMR as AEFI were aged below 50 years [7].

Although PMR has also been reported after influenza B infection, and its pathogenesis may involve environmental triggers [8], the recently published literature confirmed the possibility that COVID-19 vaccination may be a potential trigger of PMR onset or PMR relapse [9–12]. An international online survey of COVID-19 vaccination in 5691 patients with systemic rheumatic diseases (PMR among these) highlighted the fact that a prior serious reaction to non-COVID-19 vaccines and the female sex were significant risk factors for relapse (odds ratio = 2.50 and 2.71, respectively) [12]. However, the use of self-reported data collected online in a volunteer sample (such as in this study) have been previously discussed as a factor favouring a misclassification in patients with PMR as AEFI [13].

The pathophysiologic mechanisms that link COVID-19 vaccines to PMR/PMR-like syndromes are still speculative. Recently, some investigators have confirmed the little importance of an autoimmune/autoinflammatory syndrome induced by adjuvants (ASIA syndrome). This is because novel mRNA vaccines are considered sufficiently immunogenic to induce an immunisation [7]. However, more research is needed on the role of adjuvant function of lipid nanoparticles containing ionizable lipids (iLNPs), which can transfer preserved mRNA to the cell cytoplasm [14]. What is certain is that the onset of PMR/PMR-like syndromes after exposure to adjuvant is very uncommon. For instance, among the nearly 500 cases listed in the ASIA Syndrome International registry, only four case of PMR/PMR-like syndromes were reported [15].

Similarly, the putative role of Toll-like receptor 7 and 9 (TLR-7 and TLR-9) in inducing PMR following COVID-19 vaccination is still speculative [16].

In conclusion, we all agree on the need of larger epidemiological studies to quantify the true incidence of PMR following COVID-19 vaccination, and that different methodological approaches should be used to explore the mechanisms linking COVID-19 vaccines to PMR development. But, as of now, we have a fragmented view of the entire subject.

The authors declare no conflict of interest.

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Address for correspondence:
Ciro Manzo, Health District No. 59, viale dei Pini 1, 80065, Sant' Agnello, Naples, Italy, e-mail: manzoreumatologo@libero.it
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