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

Polymyalgia rheumatica following COVID-19 vaccination: A case-series of ten patients

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Polymyalgia rheumatica (PMR) is a common disease, affecting people over age 50 years. It is characterized by inflammatory pain and stiffness of the shoulders and pelvic girdle. The disease can be associated with giant cell arteritis (GCA). It usually responds to low-dose glucocorticoids (GCs). The pathogenesis remains unclear, but environmental triggers, such as viral infections, are suspected [1].

PMR was reported after influenzae B infection and more recently after SARS-CoV-2 infection [2]. Regarding the risk of PMR after vaccination, a few cases were reported during the first 3 months after influenzae vaccination [1]. In the context of the COVID-19 pandemic and massive vaccination of the population, the question of the COVID-19 vaccine as a potential trigger can be raised. Here, we report a case-series of ten patients with PMR after COVID-19 vaccination.

The median age of the patients (70% women) was 74.5 years (range 65–89). The clinical and imaging features of all patients are described in Table 1. Seven patients had new-onset PMR and three had relapsing disease after respectively one, two and 11 years of free-drug remission. All patients fulfilled the 2012 ACR/EULAR criteria for PMR[3]. PMR-mimicking diseases such as rheumatoid arthritis or pyrophosphate calcium disease were ruled out. All patients had inflammatory pain and stiffness of the shoulders and pelvic girdle. The median symptom duration was 10.5 weeks (range 3–24). COVID-19 vaccines were BNT162b2 (Pfizer/BioNTech) for nine patients and mRNA-1273 (Moderna) for the remaining patient. The median delay between vaccination and the first PMR symptoms was 10 days (range 5–15). For all patients, PCR results of nasal swabs were negative for SARS-CoV-2. Seven patients underwent ultrasonography of the hip and shoulder and all showed typical features of PMR. All paztients underwent ^{18}F-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography, showing ^{18}F-FDG uptake in PMR-related sites (shoulders, hips, trochanteric and ischiatic bursitis, symphysis, sternoclavicular joints, interspinous bursitis). The median C-reactive protein level was 26 mg/l (range 3–224). GC therapy was initiated in nine patients and was associated with methotrexate ($n = 3$) or tocilizumab ($n = 1$) and led to an improvement in all. One patient was only treated by local steroid injection.

This case-series highlights that PMR can follow vaccination against COVID-19. This potential link between vaccination and new onset or relapse of PMR/giant cell arteritis was previously described with influenza vaccine [1]. The role of the adjuvant was suspected to induce inflammatory cytokine production such as interleukin-6 or tumor necrosis factor-α, leading to a flare of the disease [1]. For PMR after COVID-19 vaccination, only few cases were previously reported [4–6]. Recently, Cadiou et al. reported, after 7 to 14 days after first dose of vaccination, two patients with new onset of PMR and GCA, and one PMR patient relapsing with a final diagnosis of GCA [4]. COVID-19 mRNA vaccines had no adjuvant, but they can themselves stimulate innate immunity with activation of Toll-like receptors (TLRs), notably TLR-7 and TLR-9 [7]. TLR-7 and TLR-9 are overexpressed in mononuclear cells of patients with active PMR [8], which could explain the occurrence of PMR after mRNA vaccination. As previously reported [1], the clinical presentation of PMR after vaccination was similar to that without identified triggers. In our case series, the prognosis did not seem to be modified, with good response to the usual therapies.

In the context of worldwide vaccination against COVID-19, physicians must be aware of the possibility of the onset or relapse of PMR, notably in the first 2 weeks after vaccination. This short delay between the first PMR symptoms and vaccination strengthens the probable role of the vaccines in the occurrence of incident PMR. The start for vaccination for individuals over 75 years with comorbidities or living in nursing home started in France in January 2021. The intensification of COVID-19 vaccination for all individuals over 55 years occurred in France until May 15th of 2021. During this period (May to October 2021), 12 patients were diagnosed PMR including our nine vaccinated patients. Regarding the same period of May to October from previous years, PMR were diagnosed in 3 (2020 with confinement) and 6 (2018 and 2019) patients suggesting an increasing incidence of PMR. Despite this possible link, we cannot exclude that these patients would have developed PMR also without vaccination. In view of the spread of COVID-19 pandemic, the interest of the vaccination remains superior to the risk of PMR or GCA.

We report here series of patients with incident PMR occurring within 2 weeks after mRNA COVID-19 vaccination. Our findings suggest a possible vaccine causality and, in the context of the ongoing international COVID-19 vaccination campaign, encourage a search for recent vaccination in patients with incident PMR.

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Table 1
Characteristics of patients with polymyalgia rheumatica (PMR) after COVID-19 vaccination.

Patient number	Age/sex	Type of PMR onset	Painful joint sites	US features of PMR	Sites with increased ^{18}F-FDG uptake	Type of vaccine	Time from vaccination and symptom onset (days)	CRP level, mg/l	Treatment	Outcome
1	74/F	Relapse	Shoulder, pelvic girdle, neck	LB, SAB	Shoulders, hips, ischiatic tuberosities	Pfizer/ BioNTech	10 after 1st dose	3	GCs 0.3 mg/kg/day + TCZ IV 8 mg/kg/month	improvement
2	70/F	New onset	Shoulder and pelvic girdle	LB, SAB, GH and hip	Shoulders, hips, interspinous, ischiatic tuberosities, sternoclavicular joints	Pfizer/ BioNTech	15 after 2nd dose	224	GCs 0.3 mg/kg/day	improvement
3	74/F	New onset	Shoulder, pelvic girdle, neck, wrists	LB, SAB, GH and hip	Shoulders, hips, interspinous, ischiatic tuberosities, sternoclavicular joints, symphysis, wrists	Pfizer/ BioNTech	14 after 2nd dose	34	GCs 0.3 mg/kg/day + MTX 0.3 mg/kg/week	improvement
4	77/F	New onset	Shoulder, pelvic girdle, neck, wrists	ND	Shoulders, hips, interspinous, ischiatic tuberosities, sternoclavicular joints, wrists	Pfizer/ BioNTech	10 after 2nd dose	32	GCs 0.3 mg/kg/day	improvement
5	65/M	New onset	Shoulder, pelvic girdle, neck, wrists, knees	LB, SAB, GH and hip, wrists	Shoulders, hips, interspinous, ischiatic tuberosities, wrists	Moderna	10 after 2nd dose	34	GCs 0.3 mg/kg/day + MTX 0.3 mg/kg/week	improvement
6	78/F	New onset	Shoulder, pelvic girdle, wrists	ND	Shoulders, hips, interspinous, ischiatic tuberosities, sternoclavicular joints, symphysis, wrists	Pfizer/ BioNTech	15 after 2nd dose	100	GCs 0.3 mg/kg/day	improvement
7	73/F	New onset	Shoulder, pelvic girdle, wrists	LB, SAB, wrists	Shoulders, hips, ischiatic tuberosities, sternoclavicular joints, symphysis, wrists	Pfizer/ BioNTech	10 after 1st dose	114	GCs 0.3 mg/kg/day	improvement
8	75/F	New onset	Shoulder, pelvic girdle, neck	ND	Shoulders, hips, ischiatic tuberosities, interspinous, sternoclavicular joints, symphysis, wrists	Pfizer/ BioNTech	5 after 2nd dose	20	GCs 0.3 mg/kg/day	improvement
9	77/M	Relapse	Shoulder, pelvic girdle	LB, SAB, wrists	Shoulders, hips, interspinous,	Pfizer/ BioNTech	8 after 3rd dose	18	GCs 5 mg/day + MTX 0.3 mg/kg/week	improvement
10	89/M	Relapse	Shoulder, pelvic girdle	LB, SAB,	Shoulders, hips, ischiatic tuberosities, interspinous, symphysis,	Pfizer/ BioNTech	10 after 1st dose	9	Local steroid injection of shoulders	improvement

F: female; M: male; LB: long biceps; SAB: subacromial bursitis; GH: glenohumeral; ND: not done; ^{18}F-FDG: ^{18}F-fluorodeoxyglucose; GCs: glucocorticoids; MTX: methotrexate; TCZ: tocilizumab; IV: intravenous; US: ultrasonography; CRP: C-reactive protein.

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Disclosure of interest

The authors declare that they have no competing interest.

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