

Case Report

Secondary Polymyalgia Rheumatica Following SARS-CoV-2 Infection

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An 81-year-old Japanese man with a medical history of diabetes mellitus and hypertension was diagnosed with the novel coronavirus disease 2019 (COVID-19). The patient developed pain in the bilateral shoulders and hips 3 days after the disease onset and presented to our outpatient clinic after 1 month. Referring to diagnostic criteria, we diagnosed him with polymyalgia rheumatica (PMR). We initiated prednisolone at 15 mg per day and his symptoms improved immediately. The clinical course of the patient indicated that the SARS-CoV-2 infection triggered the onset of autoimmune disease, PMR in this case.

Key words: COVID-19, SARS-CoV-2, polymyalgia rheumatica, autoimmune diseases, human leukocyte antigen

The novel coronavirus disease 2019 (COVID-19) caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread globally since early 2020 [1] and caused an unprecedented pandemic. COVID-19 and other emerging infectious diseases have yielded new insight into the association between viral infection and development of autoimmune diseases [2]. According to a global, retrospective, propensity score-matched cohort study, individuals after SARS-CoV-2 infection exhibited significantly higher risks of various autoimmune diseases, including rheumatoid arthritis (adjusted hazard ratio [aHR]: 2.98), ankylosing spondylitis (aHR: 3.21), systemic lupus erythematosus (aHR: 2.99), dermatomyositis (aHR: 1.96), and so forth [3].

Polymyalgia rheumatica (PMR) is an acute-onset chronic inflammatory disease, and is categorized as one of the representative autoimmune diseases. Although the disease primarily affects the elderly, causing pain

and stiffness in the proximal muscles of extremities [4], its etiology remains to be elucidated. The risk of developing PMR has been shown to be increased after COVID-19 (aHR: 2.90; 95% CI: 2.36-3.57) [3]. However, there are few reports in the literature describing patients who develop PMR after COVID-19 [4-7]. We herein present the case of an elderly Japanese patient who developed PMR shortly after SARS-CoV-2 infection.

Case Description

An 81-year-old Japanese man with a history of diabetes mellitus and hypertension, who had received SARS-CoV-2 vaccines five times previously, was diagnosed with COVID-19 and treated with molnupiravir. Although his acute COVID-19 symptoms subsided immediately, the patient developed pain and stiffness at the bilateral shoulders and hips 3 days after disease onset. The musculoskeletal manifestations persisted for

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1 month and the patient presented to our internal medicine outpatient clinic. At presentation he reported experiencing difficulty raising his upper limbs and standing up from bed, along with morning hand stiffness lasting over 1 h. He was hospitalized at our hospital for further investigation and treatment. His SARS-CoV-2 viral load was not examined on admission.

Upon hospital admission, the patient was well-oriented, and his vital signs were as follows: blood pressure, 115/91 mmHg; heart rate, 80 beats/min; oxygen saturation, 98% (room air); and body temperature, 36.6°C. A physical examination revealed pain in the proximal muscles of the bilateral upper limbs during spontaneous movement. No findings suggesting arthralgia of the fingers were observed. Neither tenderness at the superficial temporal artery nor jaw claudication was detected. Laboratory findings — including an increased white blood cell count (13,850/ μ l), an elevated erythrocyte sedimentation rate (71 mm/h) and an elevated C-reactive protein level (9.3 mg/dl)— suggested an inflammatory status (Table 1). Tests for rheumatoid factor, anti-cyclic citrullinated peptide antibody, and anti-nuclear antibody were all negative. Human leukocyte antigen (HLA) was later confirmed to be HLA-A24, -B52, -DR15. Blood and urine bacterial cultures were negative. Systemic (chest to pelvic) contrast-enhanced computed tomography (CT) scanning revealed no large vessel vasculitis or other remarkable

findings. However, joint ultrasonography showed thickening and fluid collection around the long head of the biceps (Fig. 1).

His manifestations satisfied the classification criteria scoring algorithm for PMR (7 points) advocated by the American College of Rheumatology and the European League Against Rheumatism (ACR/EULAR) [8]. Under a diagnosis of PMR, we administered prednisolone at 15 mg per day on the 8th day of hospitalization. Shortly after initiating therapy, his symptoms improved and he was discharged on the 18th day of hospitalization.

Discussion

We presented the case of an elderly Japanese man who developed PMR following COVID-19. The clinical manifestations of the patient were typical for PMR and fully met the ACR/EULAR criteria of the disease. Although the exact causal relationship between COVID-19 and PMR has not been sufficiently clarified, it is plausible that the preceding SARS-CoV-2 infection might have triggered the onset of secondary PMR. There are two distinctive points to be noted in the present case. First, the interval between the onset of COVID-19 and PMR was exceptionally short, *i.e.*, a mere 3 days. The second point pertains to the HLA genotyping of the patient, HLA-B52, as this genotype has recently been associated with PMR onset.

Table 1 Laboratory data on admission

Complete blood count		Biochemistry		Serology	
White blood cell	13,850 / μ l	Total protein	7.4 g/dl	C reactive protein	9.3 mg/dl
Neutrophil	86.2 %	Albumin	3.0 g/dl	Thyrotropin	1.628 μ U/ml
Lymphocyte	7.9 %	Total bilirubin	0.7 mg/dl	Free T4	0.99 μ g/dl
Monocyte	5.1 %	Aspartate aminotransferase	15 U/l	Rheumatoid factor	(—)
Eosinophil	0.4 %	Alanine aminotransferase	22 U/l	ACPA	(—)
Basophil	0.4 %	Alkaline phosphatase	83 U/l	ANA	(—)
Red blood cell	4,720,000 / μ l	Gamma-glutamyl transpeptidase	46 U/l		
Hemoglobin	14.1 g/dl	Lactate dehydrogenase	123 U/l	Urine	
Hematocrit	42.7 %	Urea nitrogen	22.4 mg/dl		
Platelet	367,000 / μ l	Creatinine	1.05 mg/dl	Specific gravity	1.025
		Uric acid	4.1 mg/dl	pH	5.5
		Sodium	134.6 mmol/l	protein	(—)
		Potassium	4.9 mmol/l	Glucose	(1+)
Prothrombin time (PT)	88.8 %	Chlorine	99.9 mmol/l	ketoic body	(—)
PT-INR	1.08	Creatine phosphokinase	13 U/l		
APTT	25.7 sec	Glucose	285 mg/dl		
		Hemoglobin A1c	7.2 %		

APTT, Activated partial thromboplastin time; ACPA, anti-cyclic citrullinated peptide antibody; ANA, anti-nuclear antibody

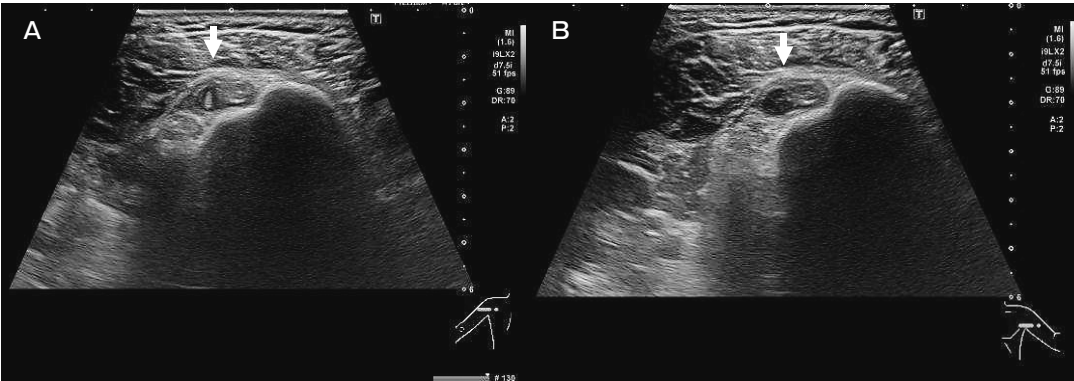


Fig. 1 Ultrasonographic findings around biceps brachii (A,B)

Table 2 Clinical characteristics of patients developing polymyalgia rheumatica (PMR) following COVID-19

No.	Year	Age	Sex	Country	Past medical history	Latency*	GCA	HLA	Outcome	Reference
1	2022	61	Female	Egypt	DM, HT, DL, GD	15 days	Yes	unknown	Visual loss	[5]
2	2022	73	Male	United States	RA	6 weeks	No	unknown	Favorable	[6]
3	2022	89	Male	United States	none	6 weeks	No	unknown	Favorable	[6]
4	2023	68	Female	United States	gout	2 weeks	Yes	unknown	Favorable	[10]
5	2024	75	Female	Mexico	none	2 weeks	No	unknown	Favorable	[7]
6	2024	81	Male	Japan	DM	3 days	No	A24, B52, DR15	Favorable	The present case

GCA, giant cell arteritis; DM, diabetes mellitus; HT, hypertension; DL, dyslipidemia; GD, Graves disease; RA, rheumatoid arthritis
*Latency from the onset of COVID-19 to the development of PMR

There is a significant volume of research on COVID-19, including studies on its potential effects on the immune system [3,9]. For example, a retrospective cohort study involving over 3.8 million participants in Taiwan revealed the risk of developing various autoimmune diseases after COVID-19 [3]. Indeed, the COVID-19 cohort in this Taiwanese study exhibited a nearly three-fold increased risk of developing PMR. However, such a database study cannot corroborate a causal relationship, and detailed case reports are required.

Accordingly, we searched the MEDLINE database for reports containing both the terms “polymyalgia rheumatica” and “COVID-19”. As of 1st June 2024, we had detected 66 such articles. Among them, we identified 5 reports describing cases of PMR that were complicated by COVID-19, as summarized in Table 2 [5-7,10]. The first case involved a 61-year-old woman in Egypt who developed PMR 2 months after the onset of COVID-19 [5]. Two other cases were men from the United States who developed PMR 6 weeks after SARS-CoV-2 infection [6]. Another case involved a 68-year-old woman in the United States who developed PMR

2 weeks after a diagnosis of COVID-19 [10]. The final case was a 75-year-old woman in Mexico who developed PMR 2 weeks after the SARS-CoV-2 infection [7]. Two out of five patients also developed giant cell arteritis, and one of these two eventually lost their vision completely despite undergoing treatment with 1 g per day of methylprednisolone for 3 days. Further accumulation of clinical data will be needed in order to fully elucidate the clinical characteristics of patients at risk of developing PMR after COVID-19.

The underlying etiology of PMR remains unknown, but several hypotheses exist. Specific genotypes, such as HLA-DRB1*0401 and HLA-DR B1*0404, may be associated with the onset of PMR in general [11]. Results of HLA typing were not given in the previous reports of COVID-19-associated PMR cases, but in our present case they were HLA-A24, -B52, and -DR15. A retrospective Japanese study reported that patients who had unclassified elderly onset large vessel vasculitis with PMR had higher HLA-B52 positivity (85.7%) compared to those without PMR (28.6%), indicating that HLA-B52 may be related to PMR complicated by large vessel

vasculitis [12]. In addition, it has been reported that PMR can be triggered by viral infections [13]. Thus, we conjecture that HLA-B52 may have played a role in the development of PMR after SARS-CoV-2 infection in the present case. Moreover, in consideration of the cases described above, it seems possible that COVID-19 may tend to develop in individuals with a certain HLA genotype as a consequence of viral-induced immunomodulation.

In summary, we have described the case of an elderly patient who developed PMR following SARS-CoV-2 infection. We summarized the clinical characteristics of this case and the previous cases of PMR after SARS-CoV-2 in order to search for common features. Although the detailed relationship between these two disease entities remains to be elucidated, this case highlights the possibility that COVID-19 may give rise to the development of PMR.

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