Commentary on 'Psoriasis flare-up associated with second dose of Pfizer-BioNTech BNT16B2b2 COVID-19 mRNA vaccine'

Editor

We read with great interest the article titled 'Psoriasis flare-up associated with second dose of Pfizer-BioNTech BNT16B2b2 COVID-19 mRNA vaccine' by Krajewski *et al.*[1] At the beginning of the article, the authors stated that psoriasis flared up one day after the COVID-19 Pfizer-BioNTech BNT16B2b2 vaccine, but in the continuation of the article, they stated that the psoriasis flare-up started five days after the vaccine. It is important to clarify this period more clearly.

In general, the authors concluded that vaccination is a rare factor in triggering psoriasis exacerbations; however, they noted that the association of vaccination with new development or exacerbation of this skin disease has been reported. They noted that current reports of exacerbations are mostly due to vaccines such as influenza (H1N1), pneumococcal pneumonia and yellow fever. They also stated that there is no well-defined relationship between mRNA COVID-19 vaccines and psoriasis exacerbation, and their current case is the first case published on this subject. As the authors mentioned here, the number of publications on cutaneous reactions after COVID-19 vaccine is very limited. In an article published by McMahon *et al.*, which included 414 cutaneous reactions, it was reported that only two patients had exacerbation of psoriasis.[2]

As there was an intense concern for all people in the first periods when COVID-19 disease was seen intensely, the patient profiles seen in dermatology outpatient clinics have changed significantly.[3] The most important method of protection against the pandemic is to follow the rules such as mask and social distance. However, despite the past two years, the disease still remains a threat. It is a fact that the vaccines developed against the COVID-19 disease in the last year have enabled us to make significant progress in the fight against the disease. On the other hand, due to the fact that the side-effects of the vaccines developed in a short time are not fully known and new cases are emerging every day, our attention has turned to the side-effects of the vaccines. We would like to emphasize that more cases and studies will be published on this subject in the near future due to the intense use of mRNA vaccines recently and that exacerbations of psoriasis triggered by the COVID-19 vaccine are not as rare as previously thought. For example, in a recently published article, we reported three cases of exacerbation of generalized pustular psoriasis, palmoplantar psoriasis and psoriasis vulgaris after mRNA vaccine only in the centre where we work.[4] The publication of these three cases that we have reported shows that we should be more careful about vaccines.

We think that vaccination of the elderly and people in the risk group should be contented with recently, when new variants of COVID-19 that transmit rapidly and last for a shorter period of time have come to the fore.

Conflict of interest

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Authors' contribution statement

Dursun Turkmen is involved in supervision; conceptualization; visualization; and writing-original draft. Nihal Altunisik is involved in supervision; conceptualization; and visualization.

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Research data are not shared.

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Autoimmune bullous dermatoses associated with COVID-19 outbreak in Russian patients: a single case series

Editor

Autoimmune bullous diseases (AIBDs) are life-threatening disorders resulting in either intraepidermal or subepidermal blisters requiring long-term immunosuppressive therapies.[1] Coronavirus disease 2019 (COVID-19) is an infectious disease caused by severe acute respiratory syndrome (SARS) associated with SARS-CoV-2.[2]

Table 1 Characteristic features of patients with AIBDs associated with COVID-19 outbreak

Patient's No.	Acronym	Age	Gender	Duration of AIBDs (years)	Supportive dose of CSs (mg/day)	Adjuvant therapy	Duration of supportive therapy (years)	AIBDs severity BPDAI/PDAI	AIBDs type	Concomitant disorders	SARS-CoV-2				Lethal outcome Yes/no
											AIBDs relapses during COVID-19 outbreak		PCR test	Brescia-COVID Respiratory Severity Scale	
											Yes/no	Time of disseminated lesions onset			
1	V	50	M	3	10	No	3	Mild	PV	No	No	NA	Positive	2	No
2	T	49	M	11	10	Azathioprine	11	Moderate	PV	No	No	NA	Positive	2	No
3	B	53	M	3	10	Azathioprine	2.5	Moderate	PV	Chronic gastritis	No	NA	Positive	1	No
4	D	77	F	13	10	Azathioprine	13	Severe	PF	Hypertension† Chronic gastritis	No	NA	Positive	3	Yes
5	T	40	M	1.5	NA	No	NA	Severe	PF	No	Yes	Third week from the AIBD debut	Positive	1	No
6	B	65	F	1	NA	Azathioprine	NA	Severe	PV	Hypertension† Paroxysmal supraventricular tachycardia	Yes	Third week from the AIBD debut	Positive	3	Yes
7	T	80	F	4	10	Azathioprine	2	Mild	BP	Hypertension†	No	NA	Positive	1	No
8	P	43	F	3	10	Azathioprine	3	Severe	PV	No	No	NA	Positive	2	No
9	L	60	F	3	8	No	3	Mild	PV	Diabetes mellitus	No	NA	Positive	1	No

NA, not applicable.
†Hypertension stage 2, grade 2.

More than 3813 AIBD cases associated with COVID-19 outbreak have been reported in the literature.[3,4]

We observed nine patients aged ≥40 (mean: 57 years) with AIBDs during COVID-19 pandemic. To assess AIBDs severity, we used PDAI and BPDAI scales.[5,6] To assess COVID-19 severity, we used Brescia-COVID Respiratory Severity Scale.[7] PCR test for COVID-19 was positive in all the patients. Four patients had mild, three moderate, and two severe COVID-19 severity score[7] (Table 1).

The diagnosis of AIBDs was confirmed histologically and immunohistochemically according to European guidelines (Fig. 1e, f).[5] Three patients had a mild, two moderate (case #3; Fig. 1a, b, c, d) and four severe AIBDs. Six patients suffered from pemphigus vulgaris (PV), two had pemphigus foliaceus (PF) and one had bullous pemphigoid (BP). Five of nine patients had concomitant disorders: chronic gastritis, hypertension, paroxysmal supraventricular tachycardia and diabetes mellitus. The duration of AIBDs ranged from 1 to 13 years. There were no further AIBDs relapses in COVID-19 patients ($n = 7$) who had ongoing systemic immunosuppressive therapy at the dose of 10 mg/day. Two of patients with severe COVID-19 and without supportive systemic glucocorticoids (CS) developed severe AIBD and died (Table 1).

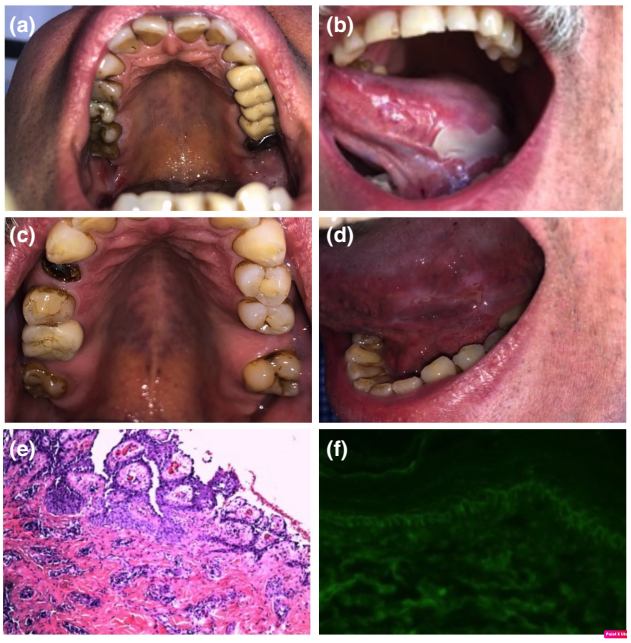

Figure 1 (a, b, c, d, e, f). Male patient (case #3, 53 years old) with PV: (a, b) before the treatment: erosions arising from the blisters affecting the oral mucosa; (c, d) after the treatment: regression of the erosions; (e) skin biopsy (H&E, original magnification ×200): suprabasilar blister with acantholysis, lymphohistiocytic infiltration in the upper dermis; (f) direct immunofluorescence microscopy: intercellular deposits of IgG.

Dermatological manifestations, such as AIBDs, identified in COVID-19 patients in several countries.[3] The hospitalisation rates and mortality because of COVID-19 complications were 12.2 and 7.1 in BP and 7.5 and 1.5 in pemphigus patients per 1000 person-years, respectively.[4]

In a recent systematic review, Kasperkiewicz M et al. analysed 732 AIBDs cases. Those patients who received systemic immunomodulatory therapy were not at increased risk of severe COVID-19 course. Considering the 1.5–3.6% mortality associated with COVID-19 in the population, the mortality in elderly patients with AIBDs and comorbidities such as diabetes mellitus, hypertension and atrial fibrillation was 0.4%.[3] Whereas, AIBDs patients with immunosuppressive therapy were not at increased risk of severe or fatal outcome.[4] We examined nine COVID-19 patients with previously diagnosed AIBDs and the mean age of 57 years (Table 1). Patients who did not receive immunosuppressive therapy during COVID-19 outbreak had severe AIBDs debut and relapses with mortality corresponding to that in the literature.[3]

Although old age and certain comorbidities, such as hypertension and diabetes, represent a well-described risk factors for complicated COVID-19, the role of immunosuppression remains controversial. Analysis suggests that patients with AIBDs receiving immunomodulatory therapies are basically not at increased risk of severe or fatal COVID-19.[8] According to Kridin K et al. 2021, BP patients had higher COVID-19-associated mortality.[4] However, authors showed that maintaining CS and immunosuppressive adjuvant agents during the pandemic in AIBDs patients was associated with favourable outcomes.[4]

There is a limited information concerning the impact of SARS-CoV-2 on the AIBDs course. AIBDs relapses during COVID-19 pandemic could be associated with IFN-1-mediated activation of CD4+ and CD8+ cytotoxic T-lymphocytes and proinflammatory cytokines release.[9] Patients with AIBDs who received a maintenance dose of CS (10 mg/day) over 3 years showed no AIBDs relapses, whereas those without systemic CS therapy developed severe AIBDs during COVID-19 outbreak. These two patients also had a severe COVID-19 course. However, no clear and comprehensive data have been provided on the management of ongoing immunosuppressive therapies in these patients.[10] To avoid mismanagement patients with AIBDs, they should be monitored regularly for symptoms of COVID-19. Unjustified withdrawal of CS can cause AIBDs exacerbation, especially in severe disease.[8]

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Conflict of interest

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Data available within the article or its supplementary materials.

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A rare case of reactive granulomatous dermatitis during COVID-19: a possible role of cephalosporine and potential mechanisms

Editor

Patients with COVID-19 present with a wide variety of cutaneous manifestations.[1] However, granulomatous lesions arising during or after COVID-19 infection are rare[2] and particularly reactive granulomatous dermatitis (RGD)[3] has not been reported. Here, we report a case of COVID-19 with a diffuse dermal infiltrate of epithelioid histiocytes possibly triggered by drug that resolved shortly.

A 61-year-old man with type 2 diabetes, hypertension and chronic renal failure requiring haemodialysis presented with headache, dry cough, and fever (38.5°C) for 2 days and SARS-CoV-2 polymerase chain reaction (PCR) test was positive. Computed tomography scan of the chest showed ground-glass opacities and bilateral lung involvement. Significant laboratory findings were as follows: white blood cell count, 7900/mm^3; lymphocyte count, 800/mm^3, platelet count, 128 000/mm^3; and C-reactive protein, 8.75 mg/dL. He was started on dexamethasone 6.6 mg, heparin 10 000 U and favipiravir 1200 mg. Ceftriaxone 1000 mg was introduced empirically. The course of medications, clinical events, and therapies is shown in Fig. 1. On day 19, he developed neutropenic fever (39°C), elevated transaminase levels and an absolute neutrophil count decreased to 0 cells/mm^3. He was treated with granulocyte colony-stimulating factor (G-CSF) (300 μg/day for 3 days) and cefepime for 2 days, which was replaced by meropenem, as a maculopapular-erythematous to violaceous rash developed on the trunk and extremities (Fig. 2a and b). Histopathology showed a diffuse dermal infiltrate composed of lymphocytes and epithelioid histiocytes expressing CD163 (Fig. 2c, d and f). The majority of the infiltrates were CD3$^+$T cells admixed with abundant CD163$^+$ epithelioid histiocytes. Multinucleate giant cells were not present in most specimens. Bone marrow biopsy showed multiple non-necrotizing granulomas composed of CD163$^+$ epithelioid cells (Fig. 2e). After cessation of ceftriaxone, cefepime, and G-CSF,[4] the skin lesions rapidly and completely resolved over the following 2 weeks. Lymphocyte transformation test showed positive reactions to both ceftriaxone (Stimulation Index, 7.32) and cefepime (2.82). There was no recurrence during the 3-month follow-up period.

Our patient's clinical course was noteworthy. First, his granulomatous lesions resolved rapidly over 2 weeks after drug cessation. Second, our patient's history of SARS-CoV-2 infection was likely a predisposing factor for the development of granulomatous lesions. No previous studies have detailed the unique constellation of clinical features observed in our patient. Given the atypical clinical presentations, it is appropriate to use the unifying umbrella term, RGD.[3] An association between RGD and COVID-19 has not been previously reported, but it is not surprising, considering the involvement of CD14$^+$16$^+$ proinflammatory monocytes producing IL-6 in COVID-19. The detrimental role of CD14$^+$16$^+$ proinflammatory monocytes in the pathogenesis of COVID-19 is only beginning to be understood: the temporal population shift from CD14$^+$16$^-$ classical monocytes to CD14$^+$16$^+$ intermediate or proinflammatory monocytes expressing CD163 in COVID-19 patients are associated with progression to severe disease.[5–7] This shift may share numerous features

