Conflict of interest

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Treatment adherence in psoriatic patients during COVID-19 pandemic: Real-world data from a tertiary hospital in Greece

Dear Editor

COVID-19 pandemic raised questions both in dermatologists and in patients about the use of immunosuppressive medications. Although dermatologic societies recommend the continuing of psoriatic systemic therapies and biologics, little is known about treatment adherence in psoriatic patients during COVID-19 outbreak.[1] Medication self-management may feel burdensome to patients with psoriasis due to the nature of treatments and many of them face additional challenges as they may suffer from comorbidities. Under these already difficult conditions, COVID-19 disease puts extra pressure on individuals and may undermine adherence. Acknowledging treatment non-adherence as a consequence of conflicting goals may help to find the reasons for but, most important, solutions to non-adherence especially during public health crises. The objective of our study was to evaluate the adherence of psoriatic patients in traditional systemic treatment as well as biologics and identify possible influencing factors of drug interruption during COVID-19 pandemic.

This observational, single-institution study was conducted between 15 March 2020 and 30 April 2020 at the 1st Dermatology Department (Aristotle University of Thessaloniki, Greece). A total of 237 psoriatic patients were interviewed through phone calls about their adherence to medication (methotrexate, cyclosporine, apremilast, adalimumab, etanercept, brodalumab,

Table 1 Adherence rates, clinical and demographic data

	Number of cases (*n*)	Percentage (%)
Adherence		
Yes	181	76.4
No	56	23.6
Age group		
15–30	12	5.1
31–45	50	21.1
46–60	65	27.4
61–75	96	40.5
76–90	14	5.9
Type of treatment		
MTX	16	6.8
CyS	20	8.4
APREM	54	22.8
ADA	44	18.6
SECUK	38	16
USTEK	24	10.1
BROD	28	11.8
ETA	13	5.5
Type of comorbidities		
None	102	43
Psoriatic arthritis	7	2.9
Arterial hypertension	34	14.3
Diabetes mellitus	22	9.3
Cardiovascular disease	10	4.2
Depression	6	2.5
Dyslipidemia	18	7.6
Obesity	14	5.9
Other	24	10.1
Number of comorbidities		
None	102	43
1	50	21.1
2–3	41	17.3
>3	44	18.6
Total	237	100

ADA, adalimumab; APREM, apremilast; BROD, brodalumab; CyS, cyclosporine; ETA, etanercept; MTX, methotrexate; SEC, secukinumab; UST, ustekinumab.

Table 2 Association between age, treatment and comorbidities, and medication adherence in psoriatic patients

	P-value	O.R.	95% C.I.	
Age group				
15–30	Ref			
31–45	0.77	3.20	0.41	6.82
46–60	0.64	0.15	0.28	1.46
61–75	0.21	0.32	0.79	2.18
76–90	0.91	1.73	0.48	8.92
Type of treatment				
MTX	Ref			
CyS	0.41	0.46	0.07	2.87
APREM	0.69	0.71	0.13	3.83
ADA	0.08	4.19	0.84	2.84
SECUK	0.45	1.88	0.36	9.58
USTEK	0.22	2.83	0.54	14.76
BROD	0.67	0.71	0.15	3.37
ETA	0.48	1.77	0.36	8.65
Type of comorbidities				
None	Ref			
Psoriatic arthritis	0.78	2.44	0.16	3.78
Arterial hypertension	0.86	0.85	0.14	4.99
Diabetes mellitus	0.48	0.55	0.11	2.86
Cardiovascular disease	0.30	0.37	0.06	2.42
Depression	0.66	0.81	0.30	5.28
Dyslipidemia	0.23	0.17	0.09	3.03
Obesity	0.32	0.42	0.08	2.32
Other	0.83	0.82	0.14	4.97
Number of comorbidities				
None	Ref			
1	0.47	0.62	0.77	1.57
2–3	0.95	1.04	0.31	3.50
>3	0.03*	6.29	1.23	2.27

$P < 0.05$ is considered statistically significant and is indicated with *.
C.I., Confidence Interval; O.R., Odds Ratio.

ustekinumab, secukinumab) and reasons for non-adherence. Their answers were checked against electronic pharmacy refill and prescription records. Influencing factors regarding drug discontinuation such as age and comorbid conditions were also analysed.

Our study showed that most patients (76.4% vs. 23.6%) continued to take their medicines, as prescribed (Table 1). However, patients with more than three comorbidities were over six times more likely not to adhere to their treatment ($P = 0.03$; O.R. 6.29, 1.23–2.27 95% C.I.). Age, type of treatment or any particular type of comorbidity did not appear to influence the therapeutic routine of psoriatic patients during the COVID-19 outbreak (Table 2).

Despite the satisfactory safety profile of biologics and psoriatic systemic treatment, there is concern that such therapies could reduce resistance to infection. This concern is inevitably heightened during COVID-19 outbreak. Restrictive measures were essential, and the approach to psoriatic patients had to be adjusted; telecounselling was mandatory to offer patients support and not to deprive them of dermatologic care. In Greece, patients were able to receive their electronic prescriptions by e-mail or text messages. The high rates of adherence in our study could, therefore, be partially attributed to the seamless access patients had to their medical treatment.

The majority of our patients continued to receive their therapies as prescribed irrespective of the type of medication. In the international literature, adherence to biologics may reach 100% according to self-reports among psoriatic patients, while adherence to systemic agents ranges between 46–96%.[2–5] Moreover, contrary to popular perception that some demographic features are related to non-adherence, our findings are in line with several systematic reviews, where there is no consistent correlation between demographic traits, particularly age, and adherence in psoriatic patients.[6]

Drug discontinuation in our patients seemed to be driven exclusively by concerns about the potential for coronavirus infection. The most important risk factors that worsen the prognosis of COVID-19 disease are comorbidities that are also present in psoriatic patients.[1,7] Our results are agreed with relevant reports which suggest that the presence of comorbidities are linked to sustained drug survival. Several authors support the rationale that the more patients are accustomed to medication use for coexisting health issues, the higher and more long-lasting their adherence to additional treatments.[8] Our study suggests that necessity beliefs about therapy are a prerequisite for taking medicines and that the need for treatment appears to outweigh the fears about the medication.

Conclusively, we recommend embracing a non-judgmental approach that acknowledges difficulties in adherence, especially in situations of increased public health risks, and encouraging patients to discuss factors contributing to non-adherence. This approach may assist patients to determine conflicting goals and find possible solutions, support psychological welfare and improve adherence.

Conflicts of interest

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An unusual case of bullous haemorrhagic vasculitis in a COVID-19 patient

Dear Editor

A novel Coronavirus strain, named 'Severe Acute Respiratory Syndrome Coronavirus 2' (SARS-CoV-2) was recently identified as the etiological agent of the COronaVIrus Disease 2019 (COVID-19). Interestingly, a consistent number of COVID-19-associated skin manifestations seem to share a certain degree of vascular damage as common pathogenetic mechanism.[1] Vascular injury may be due to the direct damage of endothelial cells by the virus or may represents an epiphenomenon of a dysregulated host inflammatory responses triggered by the infection.[2] Here, we describe an unprecedented case of leukocytoclastic vasculitis presenting with a haemorrhagic bullous eruption in a patient affected by COVID-19.

A 79-year-old man with a history of hypertension, myocardial infarction and chronic obstructive pulmonary disease has been hospitalized for acute heart failure. The patient was tested for COVID-19 (RT-PCR on nasopharyngeal swab sample) and resulted negative. Medical treatment for heart failure was started and patient's conditions progressively improved. On day 15 of the hospitalization, he rapidly developed fever and dyspnea. Chest radiograph and CT scan revealed a radiologic pattern suggestive for COVID-19 pneumonia and nasopharyngeal swab RT-PCR confirmed SARS-CoV-2 infection. Treatment with hydroxychloroquine (400 mg bid), prophylactic anticoagulation (enoxaparin 4000 IU qd), empiric antibiotics (ceftaroline 600 mg bid) and intravenous corticosteroids (methylprednisolone 80 mg qd) was started. Concomitantly, oxygen therapy was initiated at 8 liters/minute (approximately 40% FiO_2) via a non-rebreathe mask. After ten days, the patient developed multiple non-itching vesiculobullous lesions on neck and dorsal areas of hands (Fig. 1a,b). Laboratory tests including whole blood count, biochemical and coagulation parameters were within normal limits. Antinuclear antibody, antineutrophil cytoplasmic antibody and cryoglobulins resulted negative and serum protein electrophoresis as well as complement levels were normal. Moreover, the patient tested negative for enzyme-linked immunosorbent assay (ELISA) for detecting BP180 and BP230 antibodies. A punch skin biopsy was performed. Histopathologic examination demonstrated irregular hyperplasia of the epidermis and abundant erythrocytes extravasation with formation of intraepithelial haemorrhagic bullae. The epidermis was partly necrotic with keratinocytes focally showing nuclear hyperchromasia and cytoplasmic eosinophilia (Fig. 1c). Within the superficial dermis, there were marked erythrocytes extravasation and severe neutrophilic infiltrate within the wall of small vessels and in their proximity with scant leukocytoclasia (acute vasculitis). Endothelial cells were activated showing nuclear enlargement and hyperchromasia (Fig. 1d). Eosinophils and lymphocytic infiltration were not observed. Fibrinoid vascular changes and thrombi were absent as well as no viral cytopathic changes were observed. The histopathologic findings demonstrated a typical picture of leukocytoclastic vasculitis. Unfortunately, in the following days patient's respiratory conditions deteriorated and, despite intensive care support, he died of respiratory insufficiency.

The case described is an unusual case of bullous haemorrhagic vasculitis in a COVID-19 patient. The macroscopic characteristics of the lesions were compatible with a localized bullous pemphigoid (BP) or a heparin-induced bullous haemorrhagic dermatosis (BHD).[3,4] In our patient, absence of eosinophilic infiltrates as well as negativity of ELISA for BP180/BP230 autoantibodies reasonably rule out the hypothesis of localized BP. The second diagnostic diagnosis was BHD. Nevertheless, focally necrotic epidermis and vasculitis observed in our case have never been reported in BHD and thus we excluded this diagnosis. Histopathologic features observed in our patient are characteristic of an evolving leukocytoclastic vasculitis (LCV).[5] Interestingly, capillary injury and/or neutrophilic infiltrates have been described in lung tissues from COVID-19 and, in one recent report, also in the skin.[6,7] Nonetheless, we can expect that the number of reports concerning COVID-19-related vasculitis is likely to increase since inflammatory vascular damage is emerging as one of the main pathogenic mechanisms of SARS-CoV-2 infection, including its cutaneous manifestations. However, only further studies, novel reports including clinical images and detailed histology as well as data from international dermatology registries will be able to confirm this hypothesis.

