Table 1 Number of newly diagnosed melanomas and proportions of different histological characteristics, in the three COVID-19 epidemic phases, IDI-IRCCS, Rome, Italy, 1 January–6 June 2020

Year 2020	Melanomas	*In situ*	Nodular	Ulcerated	Superficial spreading with nodule
	N	*N* (%)	*N* (%)†	*N* (%)†	*N* (%)†
Prelockdown	158	39 (24.7)	5 (4.2)	7 (5.9)	6 (5.0)
Lockdown	34	10 (29.4)	2 (8.3)	2 (8.3)	0 (0)
Postlockdown	45	11 (24.4)	6 (17.6)	8 (23.5)	5 (14.7)
P value†		*0.856*	*0.015*	*0.011*	*0.032*

†The denominator of these percentages does not include *in situ* melanomas. ‡From Fisher exact tests.

Table 2 Breslow thickness of newly diagnosed melanomas in the three COVID-19 epidemic phases, IDI-IRCCS, Rome, Italy, 1 January–6 June 2020. Overall estimates, and stratification by sex and by age group

Year 2020	Thickness (mm)	By sex		By age group (years)		
	Overall	Females	Males	<50	50–64	65+
Prelockdown	0.88	0.79	0.96	0.66	0.89	1.06
Lockdown	0.66	0.66	0.66	0.40	0.38	1.33
Postlockdown	1.96	1.44	2.70	1.39	1.82	2.93
P value†	*0.001*	*0.325*	*<0.001*	*0.274*	*0.014*	*0.007*

†From non-parametric Kruskal–Wallis one-way ANOVA on ranks.

CI, 0.50–1.26) prelockdown and 1.96 (95% CI, 1.16–2.76) postlockdown. Table 2 shows the Breslow thickness stratified by sex and by age group: significant increases are observed for men (from 0.96 to 2.70) but not for women (0.79 to 1.44), and in patients 50 years old or older. The proportion of postlockdown *in situ* MMs (24.4%) is practically superimposable on the prelockdown one (24.7%), which is very close to the observed values for 2018 (23.8%) and 2019 (26.4%) on over 800 MMs per year. The reduced mean Breslow thickness of lesions seen during the lockdown (0.66 mm) and the increased proportion of *in situ* MMs (29.4%) indicate that more 'health-conscious' people were more likely to defy the lockdown limitations than people who might have been underestimating the severity of their lesions. Our data support the study hypothesis that during the COVID-19 lockdown period, diagnoses of MMs may have been delayed. Other studies should shed light on whether this is an isolated or more widespread phenomenon. Though it is way too early to gauge the consequences of such diagnostic delay, should this issue be neglected, dermatologists and their patients may pay a higher price later with increased morbidity, mortality and financial burden.

Conflict of interest

Not declared by any author.

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COVID-19-related cutaneous manifestations associated with multiple drug sensitization as shown by lymphocyte transformation test

Editor

Patients with novel coronavirus disease 2019 (COVID-19) can present with a wide variety of cutaneous manifestations.[1,2]

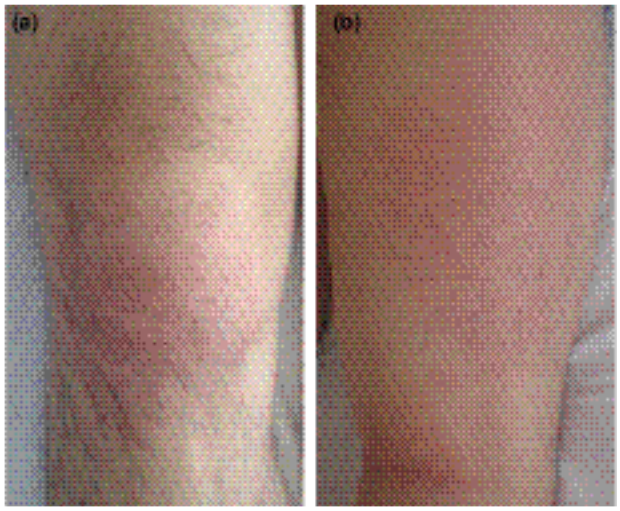

Figure 1 The patient developed symmetrically distributed erythematous macules on the flexural thigh.

Drug-induced eruptions, however, are often indistinguishable from the COVID-19-related rash. Because many patients (~20%) with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection have been shown to develop cutaneous manifestations,[3] the rash may have been reported as COVID-19-related rash without excluding the possibility of drug eruptions. Here, we report a case suspected of COVID-19-related rash, in which lymphocyte transformation tests (LTTs) to the culprit drugs were positive.

A 44-year-old man presented with fever (38.5°C). He denied cough, sore throat or shortness of breath, and had no history of drug eruptions. On the 17th day of symptoms, he developed erythematous macules and petechiae on his both legs; erythematous macules suddenly appeared in the knee, flexural thigh and popliteal fossae (Fig. 1). Significant laboratory findings are as follows: white blood cell count, 5300/mm^3; lymphocyte count, 715/mm^3; platelets, 118 000/mm^3; and C-reactive protein (CRP), 4.95 mg/dL. CT images displayed ground-glass opacification patterns and bilateral lung involvement. His COVID-19 reverse transcription–polymerase chain reaction test result was positive. About 6 days before the eruption appeared, he had received loxoprofen sodium hydrate, acetaminophen and favipiravir. He recalled that he had used loxoprofen and acetaminophen in the past but only on few occasions. Loxoprofen was withdrawn, and despite the use of acetaminophen and favipiravir, the eruption spontaneously involuted over 4 days without a trace (Fig. 2). LTTs were performed and showed positive reactions to all drugs used. He was discharged 7 days later and has no long-term sequelae.

The main difficulty in assigning a pathogenic role to SARS-CoV-2 infection in any cutaneous manifestation is that there were no or few standard laboratory methods to distinguish between virally induced rash and drug-induced rash. The identification of the causative drug appears to rely on the time interval between the beginning of drug use and onset of rash.[4] In our patient, loxoprofen was the most likely causative drug for cutaneous manifestations. In view of our observation that positive LTT reactions were detected not only to loxoprofen but also to

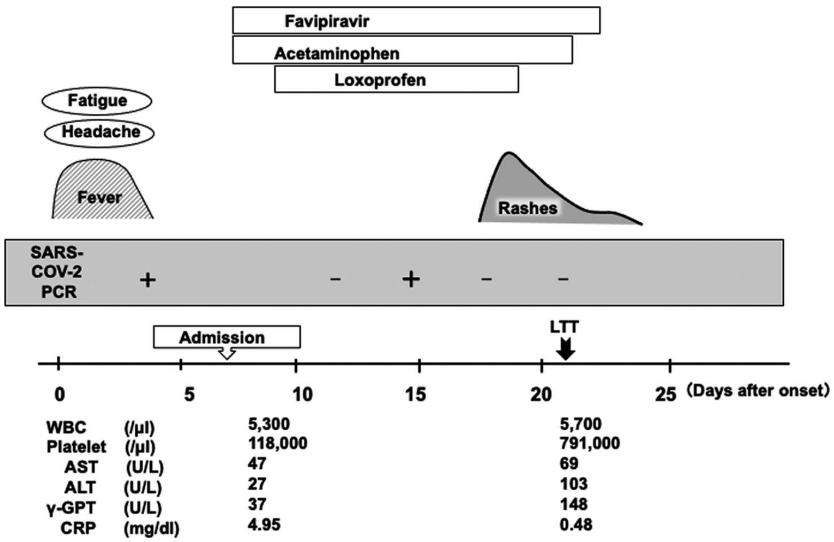

Figure 2 Clinical course of drug-induced rash in a patient with SARS-CoV-2 infection and relationship between WBC, platelet count, AST, ALT, γ-GTP and CRP levels, and SARS-CoV-2 RNA positivity.

other two drugs (Stimulation Index to each drug, 2.03–2.10), it is likely that our patient was sensitized to all the drugs. Such 'multiple drug hypersensitivity' can be most efficiently proven by LTTs.[5] Interestingly, such 'multiple drug hypersensitivity' was often observed associated with *mycoplasma pneumoniae* infection.[6] No previous reports, however, described the occurrence of multiple drug hypersensitivity in patients with SARS-CoV-2 infection. A straightforward interpretation is that our patient could be immunologically sensitized to multiple medications probably due to preceding or underlying SARS-CoV-2 infection, although it remains unknown whether SARS-CoV-2 infection could serve to enhance the activation of drug-specific T cells with cross-reactive reactivity.[7] Nevertheless, we cannot totally exclude the possibility that multiple drug sensitization proven solely by LTTs may be a mere epiphenomenon of the underlying SARS-CoV-2 infection.

In conclusion, we recommend that LTT tests be utilized in any patient with cutaneous manifestations of SARS-CoV-2 to exclude the possibility of drug sensitization. Multiple drug hypersensitivity is apparently under-reported because the diagnosis of SARS-CoV-2-induced rash is usually made without performing LTTs. If cutaneous symptoms were viewed as a mere manifestation of SARS-CoV-2 infection with no further search to identify drug hypersensitivity, then the disease would remain regarded as SARS-CoV-2-induced rash. Indeed, the presentation of our patient was consistent with symmetrical drug-related intertriginous and flexural exanthema (SDRIFE).[8] Although SDRIFE-like skin lesions have been reported as a cutaneous manifestation of COVID-19,[9] a drug aetiology could have caused SDRIFE-like skin lesions in patients with SARS-CoV-2 infection.

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Conflict of interest

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[Correction added on 14 October 2020, after first online publication: ORCID of authors 'H.Takakura' and 'T.Shiohara' have been added to this version.]

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Scabies outbreak during home confinement due to the SARS-CoV-2 pandemic

Editor

In response to the rapid spread of COVID-19 at the start of the pandemic, governments introduced severe measures of home confinement and isolation of the population in an effort to prevent their health systems from collapsing. On March 14, with more than 4000 confirmed cases,[1] Spain began its nationwide lockdown which has extended for almost three months.

In recent weeks, numerous articles have reported a wide range of skin symptoms of COVID-19,[2] but there are other dermatological conditions that may have been aggravated during this global pandemic. Scabies is a highly contagious skin infestation caused by the mite *Sarcoptes scabiei* (*variety hominis*). In developed countries, scabies is usually observed sporadically or as institutional outbreaks in hospitals, nursing homes, prisons, long-term care facilities or in displaced persons and asylum seekers.[3,4] However, we have observed a significant increase of scabies cases in our region during the confinement period (March, April and May 2020) compared to the average for the same period during the previous five years (64 vs. 18.6 patients).