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The significance of exanthems in COVID-19 patients hospitalized at a tertiary care centre

Dear Editor,

Cutaneous manifestations have been associated with COVID-19 infection, and their significance in hospitalized patients remains unclear.[1–3] This study catalogues the exanthems observed in hospitalized COVID-19 patients to determine prevalence and inform clinicians in devising diagnostic and management strategies.

A retrospective review of 1216 adults hospitalized with laboratory-confirmed SARS-CoV-2 infection from 12 March 2020 to 31 May 2020 at a single institution was conducted. Keyword search of patient records combined with manual chart review by at least two dermatologists, with a third dermatologist for adjudication, identified patients with cutaneous manifestations based on chart documentation (Fig. 1).

Exanthems occurred in 39 patients (3.2%) and were categorized clinically as morbilliform eruptions ($n = 37/39$; 94.9%) and urticarial eruptions ($n = 2/39$; 5.1%) based on chart documentation and visual morphology (Table 1). Reviewers were aided by photographs for 26 patients (66.7%) and inpatient dermatology consultations for 16 patients (41.0%). A minority of patients ($n = 7/39$; 17.9%) had exanthems occurring within 14 days of COVID-19 symptom onset and thereby could be considered a possible viral reaction. The remaining 32 patients developed a rash more than 14 days after initial COVID-19 symptom onset. 21 patients ($n = 21/32$; 65.6%) developed a rash within 14 days of a clear causative medication exposure, suggesting a drug reaction aetiology. Dermatology reviewers identified likely culprit drugs in these patients, most commonly beta-lactam antibiotics ($n = 17/21$; 81.0%). Within the remaining 11 patients ($n = 11/32$; 28.2%), five patients were favoured to have a drug reaction within 28 days of culprit drug exposure based on clear documentation from chart review. The remaining six patients had insufficient data to adequately confirm the aetiology of their late-onset rash, though drug exposure was suspected based on the timeline.

Exanthems can present a diagnostic conundrum in distinguishing medication hypersensitivity versus viral infection as likely aetiologies. Exanthems due to viral infections typically present within 14 days of viral symptom onset.[4] Skin rashes in COVID-19 are believed to present around the same time as other symptoms, typically during the first few days of fever and respiratory symptoms.[1] In this cohort, only a minority of exanthems ($n = 7/39$; 17.9%) developed within 14 days of COVID-19 symptom onset to be considered for a viral rash. One of these seven patients was evaluated by dermatology and confirmed to have a drug hypersensitivity reaction by skin biopsy. The remaining six patients, 0.49% of all patients overall, could be potentially compatible with a viral aetiology for their exanthem based on timing of symptom onset.

Drug eruptions can result within 14 days of initial administration of the culprit drug but may also be delayed further by up to several weeks.[5] The majority ($n = 21/39$; 53.8%) of exanthems in this cohort developed within 14 days of clear exposure to a common culprit drug and also after the 14-day window of COVID-19 symptom onset and resolved with cessation of drug use, supporting a medication-induced aetiology. In general, cutaneous drug reactions are estimated to develop in approximately 2% of patients,[6] increasing to 8% with exposure to certain antibiotic groups.[5] This is similar to the incidence of 3.2% ($n = 39/1216$) found within this study.

In this study population of 1216 patients admitted with COVID-19, rashes from SARS-CoV-2 were exceedingly uncommon. These findings suggest that rashes previously ascribed to SARS-CoV-2 may have alternate explanations and highlight the importance of routinely considering medication exposures in the evaluation of generalized rashes occurring in hospitalized patients. Clinicians encountering exanthems in hospitalized patients with COVID-19 should maintain their usual standard of care for drug rashes[7] in providing symptomatic treatment if necessary and considering withdrawal of the offending agent if a prolonged course of exposure is anticipated.

Conflict of interest

The authors have no conflicts of interest to declare.
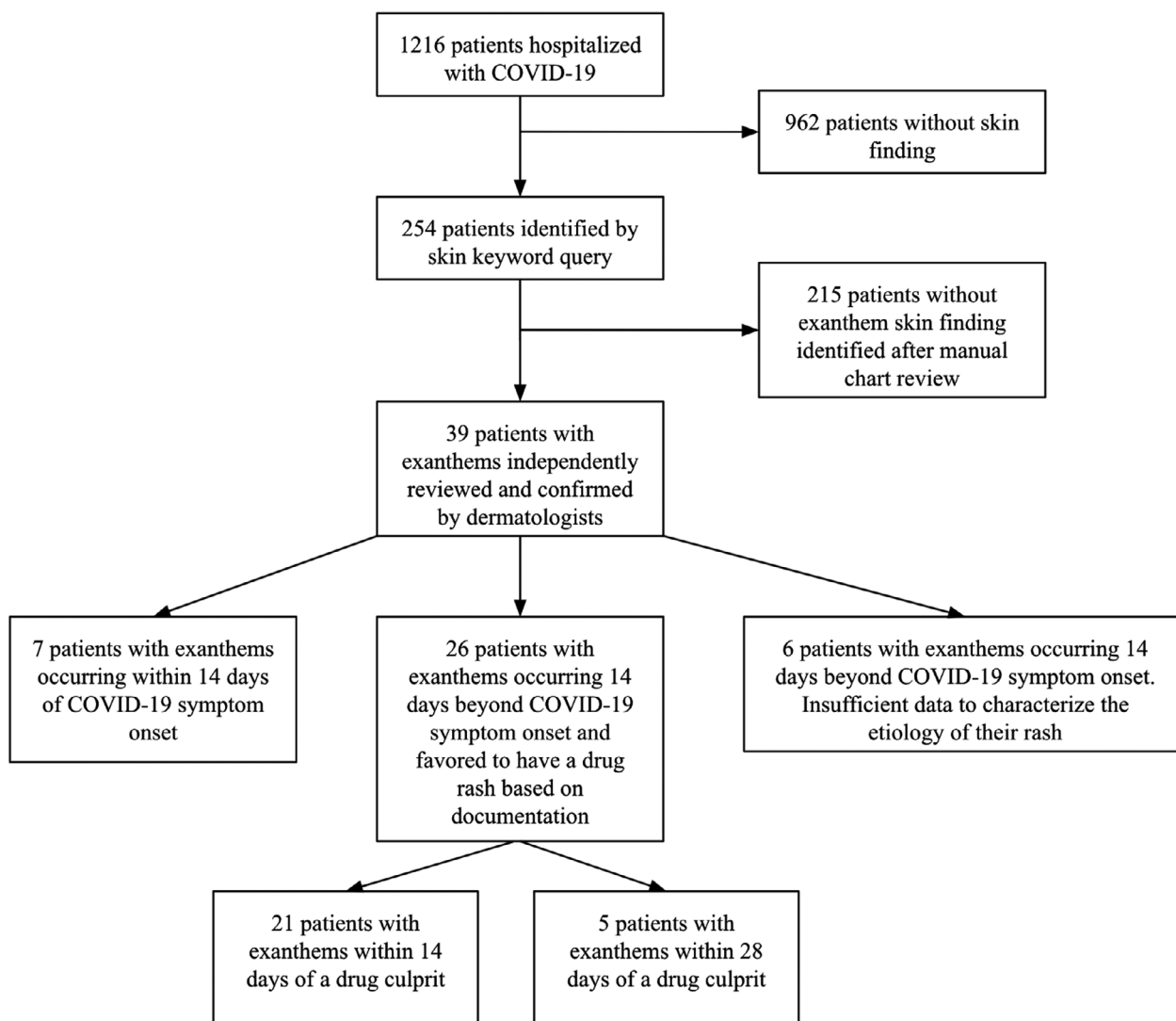
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Figure 1 Flow chart of patient selection for exanthem and findings. Exanthem skin findings are characterized in relation to COVID-19 symptom onset and likely culprit medication exposure to differentiate potential viral versus medication-induced aetiology

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Table 1 Description of patient exanthema findings

Characteristic	Patients with morbilliform eruptions (*n* = 37)	Patients with urticarial eruptions (*n* = 2)
Demographics		
Age in years (mean ± SD)	58.8 ± 15.1	71.3 ± 12.1
Gender		
Male	25 (67.6%)	1 (50.0%)
Female	12 (32.4%)	1 (50.0%)
Hospitalization:		
Length of stay in days (mean ± SD)	34.2 ± 18.8	28.5 ± 16.3
Intensive care unit admission	34 (91.9%)	1 (50.0%)
Death	3 (8.1%)	–
Culprit drugs		
Day of rash onset since admission (mean ± SD)	12.0 ± 9.5	0.0 ± 7.1
Day of rash onset since COVID symptom onset (mean ± SD)	24.7 ± 12.6	7.5 ± 10.7
Rash onset within 14 days of COVID-19 symptom onset	6 (16.2%)	1 (50.0%)
Having any possible culprit drugs identified	36 (97.3%)	1 (50.0%)
Having any likely† culprit drugs identified	28 (75.7%)	1 (50.0%)
Having likely culprit drug exposure from 0 to 7 days of rash onset	17	1
Having likely culprit drug exposure from 8 to 14 days of rash onset	9	–
Having likely culprit drug exposure from 15 to 28 days of rash onset	1	–
Day of rash onset since exposure to likely drug culprits (mean ± SD)	7.8 ± 5.9	0.0 ± 0.0
Most common likely culprit drugs identified		
Cefepime	16	–
Ceftriaxone	8	1
Meropenem	3	–
Vancomycin	4	–
Azithromycin	1	–

Abbreviations: SD, standard deviation.
†Likely culprit drugs were distinguished by reviewers based on epidemiologic incidence of induction of cutaneous adverse reactions.

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Evolution of notified sexually transmitted infections in Barcelona during the first wave of the COVID-19 pandemic

Dear Editor,

With the arrival of COVID-19, STI units decreased their activity or even closed and individuals avoided healthcare facilities. These factors conditioned the diagnosis of severe conditions,[1] including STI. The main objective of this study was to analyse the number of newly notified STI cases and HIV postexposure prophylaxis (PEP) in Barcelona during the COVID-19 pandemic.

A retrospective study including all cases of gonorrhoea, primary and secondary syphilis, lymphogranuloma venereum (LGV) and new HIV diagnoses reported to the Public Health Agency of Barcelona (ASPB), from January 2019 to September 2020, was carried out. The number of PEP prescribed in three university hospitals in Barcelona (Hospital del Mar, Hospital Vall d'Hebron and Hospital Sant Pau), during the same period, was also included as an indicator of unprotected sexual practices during the lockdown.

The evolution of cases for each STI was evaluated with multiple linear regression analysis with time as a covariate. Fisher's exact test was used to compare the numbers of diagnoses. The study protocol was approved by the institutional review board (2020/9420).

The demographic characteristics of the included patients are shown in Table 1. Cases of gonorrhoea decreased globally in a