Allopurinol, a first-line drug used for treating gout, is one of the most common drugs associated with SJS/TEN. Piroxicam is an enolic derivative of the oxicam class of non-steroidal anti-inflammatory drugs (NSAIDs), and is usually associated with an increased risk of SJS/TEN. Nevertheless, the concurrent use of piroxicam might increase the risk of allopurinol-induced SJS/TEN [5]. Herein, the patient, who had a history of allopurinol-induced SJS two years ago, developed TEN on exposure to piroxicam. Therefore, in line with previous studies, we suggest that patients with a history of allopurinol-associated drug hypersensitivity reactions should be cautiously prescribed piroxicam. ■

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1. Porebski G, Pecaric-Petkovic T, Groux-Keller M, Bosak M, Kawabata TT, Pichler WJ. *In vitro* drug causality assessment in Stevens-Johnson syndrome - alternatives for lymphocyte transformation test. *Clin Exp Allergy* 2013; 43: 1027-37.

2. Landry Q, Zhang S, Ferrando L, Bourrain JL, Demoly P, Chiriac AM. Multiple drug hypersensitivity syndrome in a large database. *J Allergy Clin Immunol Pract* 2020; 8: 258-66.e1.

3. Picard D, Vellar M, Janela B, Roussel A, Joly P, Musette P. Recurrence of drug-induced reactions in DRESS patients. *J Eur Acad Dermatol Venereol* 2015; 29: 801-4.

4. Pichler WJ, Srinoulprasert Y, Yun J, Hausmann O. Multiple drug hypersensitivity. *Int Arch Allergy Immunol* 2017; 172: 129-38.

5. Syu FK, Pan HY, Chuang PC, Huang YS, Cheng CY, Cheng FJ. Incidence of Stevens-Johnson syndrome following combination drug use of allopurinol, carbamazepine and phenytoin in Taiwan: a case-control study. *J Dermatol* 2018; 45: 1080-7.

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Late-onset cutaneous eruption in hospitalized COVID-19 patients

In the recent months of the COVID-19 pandemic, many clinical manifestations have been described [1,2]. We describe eight COVID-19 positive patients who, after having a negative nasopharyngeal swab (NPS), developed a macular exanthem with a distinct pattern. All the information regarding the patients and the timing of the rash are summarized in *supplementary table 1*.

We observed six males and two females (mean age: 65.5+/-3.1), hospitalized for COVID-19 infection; five patients were admitted to the ICU. All patients tested positive by NPS before/during their hospitalization. After establishing a negative NPS, in all patients, a cutaneous eruption was observed. The mean latency period between the onset of COVID-19 signs and symptoms and the onset of the rash was 25 days (range: 18-40 days); for this reason, it was considered a late-onset rash (*supplementary table 2*). Despite being treated with many drugs, no new drugs were introduced before the onset of the rash nor were drugs changed as a result of the rash.

Five out of eight patients already had systemic steroid therapy and in two of them, this was implemented; all the patients started systemic antihistamine (anti-H1) and topical steroid therapy. The skin findings were similar in all patients: erythematous macules and patches with jagged margins, that usually localized to the trunk, laterally and symmetrically, with involvement of neck, axillae, and groin folds, but always sparing the palmoplantar areas, face and mucosae (*figure 1*). Patients experienced mild pruritis. Lesions resolved with mild scaling.

Despite the huge number of COVID-19 studied cases, reports of dermatological diseases have been scarce. A skin rash has been reported in two out of 1,099 and three out of 1,590 patients presenting with COVID-19 disease in China [1, 2]. In Italy, Recalcati [3] reported cutaneous manifestations in 18 out of 88 COVID-19 patients, describing three main patterns: erythematous rash, urticaria, and chickenpox-like lesions. Marzano *et al*. [4] reported a varicella-like exanthem in the first 15 days of COVID-19 disease. Mahé *et al*. [5] reported a case with an erythematous rash on antecubital fossae, trunk and axillary folds. This rash appeared reminiscent of symmetric drug-related intertriginous and flexural exanthema (SDRIFE). Amatore *et al*. [6] described a rash characterized by erythematous and oedematous, annular plaques involving the trunk and arms, sparing the face and mucous membranes.

Galván Casas *et al.* [7] described 375 Spanish cases of rash related to suspected or confirmed COVID-19 and classified them into five patterns: pseudo-chilblain, vesicular eruptions, urticarial lesions, maculopapular eruptions and livedo or necrosis.

Herrero-Moyano *et al*. [8] were the first to report a series of patients with late-onset maculopapular rash, and hypothesized that this could be linked to the cytokine storm of the hyperinflammatory phase caused by the virus or drugs,

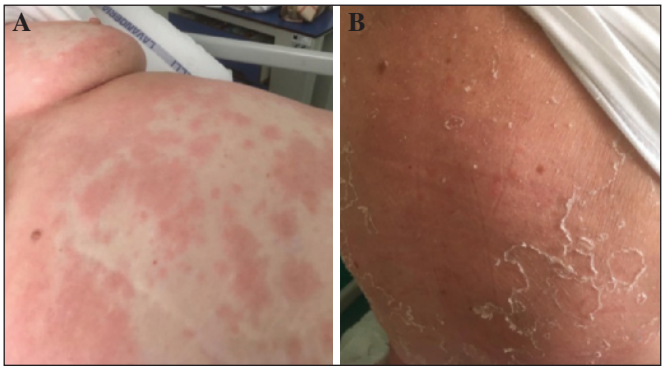

Figure 1. A) Erythematous macules and confluent patches with jagged margins, localized on the trunk and the folds (Patient 6). **B**) Mild desquamation on the back (Patient 6).

however, they reported difficulty in distinguishing between a viral and drug origin of the rashes. Skroza *et al*. [9] described a late-onset erythematous macular rash in a previous COVID-19 patient with two negative NPS. This was interpreted as a "plausible adverse drug reaction". From a clinical point of view, late-onset rashes are reminiscent of laterothoracic exanthem, also known as "asymmetric periflexural exanthem of childhood" (APEC).

In our cases, as in the cases described by Herrero-Moyano *et al*. [8] and Skroza *et al*. [9], the rash can be defined and categorized as an atypical rash or, in any case, not belonging to the viral rashes related to "classic exanthems" commonly occurring in childhood [10]. Indeed, exanthems, defined as "atypical" for the different morphology and causal agents, may occur in adults.

Undoubtedly, in our patients, it is not possible to exclude that there was a multidrug effect associated with the virus, however, the trend of the rash (late onset) and the cutaneous sites (trunk and limbs with no palmoplantar nor mucosal involvement) are certainly peculiar. As for many atypical/paraviral exanthems, this late-onset rash may be considered as a response of the immune system to the infectious pathogen. In this context, the late appearance of a rash represents a further step towards understanding the clinical course of the disease. ■

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Supplementary data

Supplementary data (Table S1, S2) associated with this article can be found, in the online version, at doi:10.1684/ejd.2020.3855.

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1. Liang WH, Guan WJ, Li CC, *et al*. Clinical characteristics and outcomes of hospitalised patients with COVID-19 treated in Hubei (epicenter) and outside Hubei (non-epicenter): a nationwide analysis of China. *Eur Respir J* 2020; 55: 2000562.

2. Guan WJ, Ni ZY, Hu Y, *et al*. Clinical characteristics of coronavirus disease 2019 in China. *N Engl J Med* 2020; 382: 1708-20.

3. Recalcati S. Cutaneous manifestations in COVID-19: a first perspective. *J Eur Acad Dermatol Venereol* 2020; 34: e212-3.

4. Marzano AV, Genovese G, Fabbrocini G, *et al*. Varicella-like exanthem as a specific COVID-19-associated skin manifestation: multicenter case series of 22 patients. *J Am Acad Dermatol* 2020; 83: 280-5.

5. Mahé A, Birckel E, Krieger S, Merklen C, Bottlaender L. A distinctive skin rash associated with Coronavirus disease 2019? *J Eur Acad Dermatol Venereol* 2020; 34: e246-7.

6. Amatore F, Macagno N, Mailhe M, *et al*. SARS-CoV-2 infection presenting as a febrile rash. *J Eur Acad Dermatol Venereol* 2020; 34: e304-6.

7. Galván Casas C, Català A, Carretero Hernández G, *et al*. Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases. *Br J Dermatol* 2020; 183: 71-7.

8. Herrero-Moyano M, Capusan TM, Andreu-Barasoain M, *et al*. A clinicopathological study of 8 patients with COVID-19 pneumonia and a late-onset exanthema. *J Eur Acad Dermatol Venereol* 2020; 10.1111/jdv.16631.

9. Skroza N, Bernardini N, Balduzzi V, *et al*. A late onset widespread skin rash in a previous Covid-19 infected patient: viral or multidrug effect? *J Eur Acad Dermatol Venereol* 2020; 10.1111/jdv.16633.

10. Drago F, Ciccarese G, Gasparini G, *et al*. Contemporary infectious exanthems: an update. *Future Microbiol* 2017; 12: 171-93.

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