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Response to ‘Classification of the cutaneous manifestations of COVID-19: a rapid prospective nationwide consensus study in Spain with 375 cases’: vesicular eruption in COVID-19 – to exclude varicella

DOI: 10.1111/bjd.19347

Dear Editor, We read with interest the classification of cutaneous manifestations in COVID-19 by Galván Casas et al.1 In particular, vesicular eruptions are characterized as monomorphic vesicles, involving the trunk, happening early in the course of the disease, and occasionally preceding other symptoms.1–3 However, investigations to exclude other causes of widespread vesicular eruption, in particular varicella, were absent.

In our clinical experience to date, we have had four patients with SARS-CoV-2 infection presenting with vesicular eruptions, which were subsequently confirmed to be true varicella with microbiological and serological investigations (Table 1). All four patients were young to middle-aged men with no previous history of varicella infection, vaccination or exposure, presenting with vesicular eruptions of variable durations. Each patient had some features not completely typical of varicella – two described no or mild pruritus, two did not report any prodromal symptoms, and two presented with monomorphic vesicular eruptions early in the course of varicella infection. They were all given systemic antiviral therapy with aciclovir or valaciclovir, with resolution.

In a patient presenting with a widespread vesicular eruption, differential diagnoses include infections, a drug-induced blistering process, and an autoimmune blistering disease. Among the infections, varicella, disseminated zoster, disseminated herpes, smallpox and rickettsialpox are possible causes.

Our experience with concomitant SARS-CoV-2 and varicella infection highlights the importance of excluding true varicella before ascribing vesicular eruptions to COVID-19. Atypical features may be present, especially in early or recurrent varicella. Moreover, we have also previously reported coinfection of varicella with another viral infection (herpes simplex virus) in an immunocompetent host.4 Hence, it is possible that cases of vesicular eruptions in COVID-19 may be arising from varicella infection.

As an accurate diagnosis of varicella has far-reaching clinical implications on the treatment, patient disposition and particular, vesicular eruptions are characterized as monomorphic vesicles, involving the trunk, happening early in the course of the disease, and occasionally preceding other symptoms.1–3 However, investigations to exclude other causes of widespread vesicular eruption, in particular varicella, were absent.

In our clinical experience to date, we have had four patients with SARS-CoV-2 infection presenting with vesicular eruptions, which were subsequently confirmed to be true varicella with microbiological and serological investigations (Table 1). All four patients were young to middle-aged men with no previous history of varicella infection, vaccination or exposure, presenting with vesicular eruptions of variable durations. Each patient had some features not completely typical of varicella – two described no or mild pruritus, two did not report any prodromal symptoms, and two presented with monomorphic vesicular eruptions early in the course of varicella infection. They were all given systemic antiviral therapy with aciclovir or valaciclovir, with resolution.

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As an accurate diagnosis of varicella has far-reaching clinical implications on the treatment, patient disposition and

Table 1 Demographic and clinical data of patients with concomitant varicella and COVID-19 infection

| Patient | 1 | 2 | 3 | 4 |
|---------|----|----|----|----|
| Sex     | Male | Male | Male | Male |
| Age (years) | 28 | 33 | 32 | 43 |
| Skin lesions | Diffuse monomorphic vesicular lesions | Diffuse monomorphic vesicular lesions | Diffuse papulovesicular lesions | Diffuse vesicular lesions |
| Skin symptoms | Itching | Mild itching | Itching | No itching |
| Localization | Head, neck, trunk | Neck, trunk | Head, trunk | Head, trunk |
| Time to onset of skin lesions from SARS-CoV-2 infection (days) | 18 | 21 | 17 | 19 |
| Systemic symptoms | Fever, headache | Fever, headache, myalgia | None | None |
| History of varicella infection or vaccination | None | None | None | None |
| History of varicella exposure | None | None | None | None |
| Investigation results | VZV PCR positive | VZV PCR positive | VZV IgG positive | VZV IgG positive |
| Treatment | Oral aciclovir | Oral valaciclovir | Oral valaciclovir | Oral valaciclovir |
| Course | Resolution | Resolution | Resolution | Resolution |

PCR, polymerase chain reaction; VZV, varicella zoster virus.
postexposure prophylaxis for contacts, varicella infection should be excluded in patients with COVID-19 presenting with vesicular eruptions.

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‘Vesicular eruption in COVID-19 – to exclude varicella’: reply from the authors

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Dear Editor, We agree with Drs Lim and Tey on the need to exclude varicella in vesicular eruptions in patients with COVID-19, as this diagnosis has important implications.

Once it is established that some patients with COVID-19 can have a vesicular eruption, there is a need to characterize this group of patients further. The association of some of these lesions with herpesvirus infections is very likely. One patient was excluded from our study with a diagnosis of varicella or disseminated herpes zoster. The list of case reports or case series is growing fast, and other authors have shown that patients with COVID-19 can have a vesicular eruption with presence of several herpesviruses. Their images show haemorrhagic bullae of different sizes and with a diameter >1 cm, larger than the eruption described in our paper, with many equal, 2–3-mm vesicles. As the paper by Drs Lim and Tey does not include pictures, we wonder whether this could be a sign suggesting herpessviruses infection (including varicella).

However, other reports have described a histological pattern of acantholysis and dyskeratosis with a suprabasal unilocular vesicle, different from varicella histology, indicating that at least some patients can have a disease that is not varicella. The diagnosis of these eruptions includes pseudoherpetic Grover disease, or they might be due to SARS-CoV-2 infection.

We suggest that further research should be done with consecutive patients, optimally including lymphocyte count, histology and/or Tranck smear, and SARS-CoV-2 and herpesvirus detection in the vesicles, to delineate better the possible diagnoses for patients who show a vesicular eruption associated with COVID-19.

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