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DR CARLOS MUÑOZ-SANTOS (Orcid ID : 0000-0003-3721-8030)
DR CRISTINA GALVAN CASAS (Orcid ID : 0000-0002-9662-9537)
DR CARLOS GONZÁLEZ-CRUZ (Orcid ID : 0000-0003-0117-8858)
DR RICARDO RUIZ-VILLAVERDE (Orcid ID : 0000-0002-0381-6174)
DR ORIANNA YILSY MARCANTONIO SANTA CRUZ (Orcid ID : 0000-0001-5281-8750)
DR DIEGO FERNANDEZ-NIETO (Orcid ID : 0000-0003-4461-1770)
DR JORGE ROMANI (Orcid ID : 0000-0002-6134-5155)
DR PEDRO RODRIGUEZ-JIMÉNEZ (Orcid ID : 0000-0002-7061-3027)
DR INGRID HILTUN (Orcid ID : 0000-0001-7377-1533)
DR ISABEL POLIMON OLABARRIETA (Orcid ID : 0000-0003-1659-7254)

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**Cutaneous reactions after SARS-COV-2 vaccination: A cross-sectional Spanish nationwide study of 405 cases**

**Running head:** Cutaneous reactions after SARS-COV-2 vaccination

A. Català,[1]* C. Muñoz-Santos,[2]* C. Galván-Casas,[3]* M. Roncero Riesco,[4] D. Revilla Nebreda,[4] A. Solá-Truyols,[5] P. Giavedoni,[1] M. Llamas-Velasco,[6] C. González-Cruz,[7] X. Cubiró,[8] R. Ruíz-Villaverde,[9] S. Gómez-Armayones,[1] M.P. Gil Mateo,[10] D. Pesqué,[11] O. Marcantonio,[11] D. Fernández-Nieto,[1], J. Romaní,[13] N. Iglesias Pena,[14] L. Carnero Gonzalez,[15] J. Tercedor-Sanchez,[16] G. Carretero,[17] T. Masat-Ticó,[18] P. Rodríguez-Jiménez,[6] A.M. Gimenez-Arnau,[11] M. Utrera-Busquets,[19] E. Vargas Laguna,[20] A.G. Angulo Menéndez,[21] E. San Juan Lasser,[22] M. Iglesias-Sancho,[23] L. Alonso Naranjo,[24] I. Hiltun,[25] E. Cutillas Marco,[26] I. Polimon Olabarrieta,[3] S. Marinero Escobedo,[3] X. García-Navarro,[27] M.J. Calderón Gutiérrez,[28] G. Baeza-Hernández,[29] L. Bou Camps,[30] T. Toledo-Pastrana[31] and A. Guilabert[2]

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[1] Servicio de Dermatología. Hospital Clínic. Barcelona, Spain

[2] Servicio de Dermatología. Hospital General de Granollers. Barcelona, Spain

[3] Servicio de Dermatología. Hospital Universitario de Móstoles. Madrid, Spain

[4]Servicio de Dermatología. Complejo Asistencial Universitario de Salamanca. Salamanca, Spain.

[5] Servicio de Dermatología. Hospital Universitario Son Llatzer. Mallorca, Spain.

[6] Servicio de Dermatología. Hospital Universitario de La Princesa. Madrid, Spain.

[7] Servicio de Dermatología. Hospital Universitari Vall D'Hebron. Barcelona, Spain.

[8] Servicio de Dermatología. Hospital de la Santa Creu i Sant Pau. Barcelona, Spain.

[9] Servicio de Dermatología. Hospital Universitario San Cecilio. Granada, Spain.

[10] Servicio de Dermatología. Hospital General de La Palma. Santa Cruz de Tenerife, Spain.

[11] Servicio de Dermatología. Hospital del Mar. IMIM. Universitat Autònoma.Barcelona, Spain.

[12] Servicio de Dermatología. Hospital Ramón y Cajal. Madrid, Spain.

[13] Servicio de Dermatología. Parc Taulí Hospital Universitari. Sabadell, Barcelona, Spain.

[14] Servicio de Dermatología. Hospital Universitario Lucus Augusti. Lugo, Spain.

[15] Servicio de Dermatología. Hospital Universitario Araba. Vitoria, Spain.

[16] Servicio de Dermatología. Hospital Virgen de las Nieves. Granada, Spain.

[17] Servicio de Dermatología.Hospital Universitario Gran Canaria Doctor Negrín. Las Palmas Gran Canaria, Spain.

[18] CAP Cardedeu. Institut Català de la Salut. Barcelona, Spain.

[19] Servicio de Dermatología. Hospital Comarcal Infanta Elena. Huelva, Spain.

[20] Servicio de Dermatología. Hospital Universitario Severo Ochoa. Madrid, Spain.

[21] Servicio de Dermatología. Serveis Medics Penedés Vilanova i la Geltrú. Barcelona, Spain.

[22] Consulta privada. Dra Eliana San Juan Lasser. Madrid, Spain.

[23] Servicio de Dermatología. Hospital Universitari Sagrat Cor. Barcelona, Spain.

[24] Servicio de Dermatología. Hospital Universitario de Toledo. Toledo, Spain.

[25] Servicio de Dermatología. Complejo Hospitalario de Navarra. Navarra, Spain.

[26] Servicio de Dermatología. Hospital General Universitario Reina Sofia. Murcia, Spain

[27] Servicio de Dermatología. Consorci Sanitari Alt Penedès-Garraf. Barcelona, Spain.

[28] Consulta Privada Mª José Calderón. Bilbao, Spain.

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[29] Servicio de Dermatología. Hospital Universitario de Fuenlabrada. Madrid, Spain.

[30]Consulta Dr. Lola Bou. Barcelona, Spain.

[31]Hospital Quirónsalud Infanta Luisa. Sevilla, Spain.

* Contributed equally as first authors.

**Corresponding author:** Carlos Muñoz-Santos

**Email:** carlosmunozsantos@gmail.com

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**What is already known about this topic?**

- COVID-19 vaccines were associated with cutaneous adverse events, especially local injection-site reactions, in clinical trials.
- Previous descriptions of cutaneous reactions beyond the injection site were case reports or mostly reported by non-dermatologists and lacked clinical images.

**What does this study add?**

- We describe and classify a large, representative sample of patients with unexplained skin manifestations after COVID-19 vaccination, using consensus to define associated morphological patterns.
- We describe six morphological reaction patterns and herpes virus reactivations and their association with demographic factors and the medical record and provide illustrations to allow for easy recognition.

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**SUMMARY**

**Background:** Cutaneous reactions after SARS-CoV-2 vaccines are poorly characterized.

**Objectives**: The primary objective was to describe and classify cutaneous reactions after SARS-CoV-2 vaccination.

**Methods:** A nationwide Spanish cross-sectional study was conducted. We included patients with cutaneous reactions within 21 days after any dose of the approved vaccines at the time of the study. After a face-to-face visit with a dermatologist, information on cutaneous reactions was collected through an online professional survey and clinical photographs were sent by email. Investigators searched for consensus on clinical patterns and classification.

**Results:** From February 16 to May 15, 2021, we collected 405 reactions after vaccination with the BNT162b2 (Pfizer-BioNTech, 40.2%), mRNA-1273 (Moderna, 36.3%) and AZD1222 (AstraZeneca, 23.5%) vaccines. The mean patient age was 50.7 years and 80.2% were female. Cutaneous reactions were classified as: injection-site (COVID-ARM, 32.1%), urticaria (14.6%), morbilliform (8.9%), papulovesicular (6.4%), pityriasis rosea-like (4.9%) and purpuric (4%) reactions. Varicella zoster and herpes simplex virus reactivations accounted for 13.8% of reactions. The COVID-ARM was almost exclusive to women (95.4%). The most reported reaction in each vaccine group were COVID-ARM (mRNA-1273, Moderna, 61.9%), varicella zoster virus reactivation (BNT162b2, Pfizer-BioNTech, 17.2%), and urticaria (AZD1222, AstraZeneca, 21.1%). Most reactions to the mRNA-1273 (Moderna) vaccine were described in women (90.5%). Eighty reactions (21%) were classified as severe/very severe and 81% required treatment.

**Conclusions:** Cutaneous reactions after SARS-CoV-2 vaccination are heterogeneous. Most are mild-to-moderate and self-limiting, although severe/very severe reactions are reported. Knowledge of these reactions during mass vaccination may help healthcare professionals and reassure patients.

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## INTRODUCTION

The search for an effective vaccine has been unceasing since December 31 2019, when the first cases of SARS-COV-2 were reported in China[1]. As of June 4, 2021, COVID-NMA, an international WHO-supported research initiative that live-maps and reviews SARS-CoV-2 trials, had compiled 256 vaccine trials (https://covid-nma.com/vaccines/mapping/).

Vaccine development may take more than 15 years.[3] SARS-CoV-2 vaccines have had an accelerated timeline and were approved in record time,[3] showing good safety and immunogenicity profiles in randomized controlled trials (RCT). [4-7] Currently, the European Medicines Agency (EMA) has authorized four vaccines: BNT162b2 (Pfizer-BioNTech), mRNA-1273 (Moderna), AZD1222 (AstraZeneca) and Ad26.COV2.S (Janssen).

SARS-CoV-2 is associated with a wide spectrum of skin manifestations.[8-11] Some may appear after immunization with vaccines expressing the SARS-CoV-2 spike (S) protein. The Spanish Agency for Medicines and Health Products (AEMPS) pharmacovigilance report found that, as of April 25,

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2021, of 14,290,507 vaccine doses administered in Spain (70% BNT162b2, 24% AZD1222, 6% mRNA-1273), 1,468 non-specified cutaneous adverse events (0.01 %) had been notified.[12] Cutaneous adverse events reported in clinical and post-authorization trials include local injection-site reactions and local or generalized reactions beyond the injection-site. Local injection-site reactions, both immediate or delayed (≥ 4 days after vaccination), were the most frequent manifestation[4,5,6,13,14,15, 16]. Apart from anaphylactic rashes[16], less-frequent cutaneous reactions have been described in case reports and small case series: urticaria, maculopapular or morbilliform rash, pityriasis rosea-like rash, chilblain-like lesions, facial dermal filler reactions, reactivation of varicella zoster virus (VZV), lichen planus, erythema multiforme, and non-specific hypersensitivity eruptions.[4,5,7,13,15,18-27] An American registry-based study analysed 414 cases after mRNA vaccination.[28] Most reactions were reported by non-dermatologists and a small number of clinical images were shown.

Since the beginning of mass vaccination in Spain, dermatologists have treated skin rashes in vaccinees. The reactions were poorly characterized and some observers considered them more frequent than previously reported and mimicking some reactions described after SARS-COV-2 infection.[8-11]

The primary objective of our study was to characterize and classify the clinical features of cutaneous reactions after SARS-CoV-2 vaccination. Secondary objectives were to identify the timing of reactions, associations with other dermatologic or allergic conditions and possible relationships with diagnoses of SARS-CoV-2 or SARS-CoV-2 -associated cutaneous reactions.

## MATERIAL AND METHODS

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We conducted a nationwide, multicentre, cross-sectional observational study. The study was endorsed by the Spanish Academy of Dermatology and all Spanish dermatologists were invited to participate.

The planned recruitment period lasted 3 months (February 16 to May 15, 2021). Inclusion criteria were people of all ages vaccinated against SARS-CoV-2 with any skin manifestation within 21 days after any dose of a vaccine approved by the EMA and AEMPS. Exclusion criteria were explainable causes other than SARS-CoV-2 vaccination and injection-site reactions lasting ≤ 3 days, as this reaction was very common in SARS-CoV-2 vaccine RCT.[4-7]

Data were collected and managed using an electronic case report form (e-CRF) and a questionnaire administered using an on-line professional survey (LimeSurvey GmbH, Hamburg, Germany). Data treatment complied with the European Commission General Data Protection Regulation and Information Security regulations. After a face-to-face visit, patient data was recorded and clinical pictures, if available, were sent by e-mail. Data were encrypted, patient and investigator anonymity were assured, and no external servers were used. Case entry was restricted to dermatologists, to provide a more accurate description and classification of the morphology of the lesions. As in a previous study of SARS-CoV-2 skin manifestations,[8] reporting dermatologists pre-classified skin rashes in a predefined cutaneous reaction pattern, with an option for free clinical description. Only the three principal investigators had access to the clinical image dataset and independently reviewed the photographs and clinical data and sought consensus on the cutaneous patterns. If clinical images were not available, the case was considered as missing data, unless the clinical pattern described was unequivocal. If consensus was not initially reached but histopathology was available, the case was classified according to an agreed clinicopathological correlation. If consensus was not reached and histopathology was not available or not diagnostic, the reporting dermatologist was consulted, and if clinical consensus was not reached, the case was not classified.

Variables collected through the e-CRF included a) patient characteristics: geographic area, age, sex, history of allergy, atopic dermatitis, urticaria and/or cutaneous reactions to other vaccines before SARS-CoV-2 diagnosis, previous SARS-CoV-2-associated cutaneous manifestations and new drugs prescribed in the 5 weeks before the reaction. Vaccine reaction data included type of

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vaccine, dose at the time of the cutaneous reaction, and days between doses. Cutaneous reaction data included day of onset, duration, injection-site involvement (local or generalized beyond the injection-site), location, clinical pattern of the reaction (pre-defined or free description), cutaneous and systemic symptoms, treatment, photographs, and histopathologic findings, if available.

The severity of reactions was classified as: grade 1 or mild (local macular or papular erythematous rash without associated systemic symptoms); grade 2 or moderate (the same as grade 1 plus systemic symptoms); grade 3 or severe (generalized erythematous macular or papular or vesicular rash); and grade 4 or very severe (generalized erythrodermic or exfoliative or ulcerative or bullous rash).

The study was authorized by the Ethics Committees of the three principal investigation centres and the regional drug regulatory agency for post-authorization of observational studies (Generalitat de Catalunya, registry number: 9015-363592/2021). All patients gave written informed consent to participate and explicit consent to publish images.

The sample size could not be determined *a priori* because of the uncertain number of reported reactions and participating dermatologists. We planned three months of recruitment to include the AstraZeneca vaccine (approved in Spain after the RNA-based vaccines) and to cover populations other than healthcare workers and older people. The analysis included description of the data and distribution tests ($\chi 2$-test for qualitative variables and ANOVA for quantitative variables). Patients with missing data for a specific mandatory parameter were excluded. $P < 0.05$ was considered statistically significant in the univariate analyses. The analysis was made using SPSS software (v 22.0).

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**RESULTS**

We collected 419 cases of cutaneous reactions from 31 public hospitals and private clinics. Fourteen cases not meeting the inclusion criteria and/or with missing data were excluded. The final sample included 405 reactions in 391 patients after BNT162b2 (n= 163, 40.2%), mRNA-1273 (n=147, 36.3%) and AZD1222 (n=95, 23.5%) vaccination. Due to delayed authorization, only one reaction after Janssen vaccination was reported, which was finally excluded from the analysis. A flow chart of patient inclusion is shown in **Figure 1**. Skin biopsies were performed in 50 cases (12.3%).

**Table 1** shows baseline patient characteristics. All patients were White, with a mean age of 50.7 (SD:17.6) years and 80.2% were female. Of the mRNA vaccines, 165 reactions (53.2%) appeared after the first dose and 145 (46.8%) after the second. We could not evaluate the AZD1222 vaccine as second doses were not administered during the study period. Fourteen patients with first dose reactions (14/165, 8.5%) after mRNA vaccines developed a second dose reaction, of whom seven had the same reaction and seven had different reactions.

Reactions were located at the injection site in 131 cases (32.3%) and beyond the injection site in 274 (67.7%) (138 local and 136 generalized). The mean onset time was 5.1 days (SD: 4.4) after vaccination and the mean duration was 12.2 days (SD: 13.1).

Clinical images were available in 293 reactions (72.3%). Six major clinical morphologic reaction patterns were described in 287 reactions (70.9%). Other miscellaneous cutaneous reactions were

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reported after vaccination. Photographic examples and the main features of each pattern are shown in **Figure 2, Table 2, and the Supplementary material**. The six major patterns described were (in order of frequency):

1. **Local injection-site reactions (commonly known as "*COVID-ARM*")** (n=130, 32.1%). Erythematous patches or swollen plaque at the injection site, of which 53.8% were delayed (≥4 days after vaccination).
2. **Urticarial and/or angioedema** (n= 59, 14.6%). Hives mostly distributed in the trunk or generalized and usually appearing > 24 hours post-vaccination (93.2%).
3. **Morbilliform** (n=36, 8.9%). An erythematous, maculopapular rash reminiscent of measles, mostly generalized affecting the trunk and limbs.
4. **Papulovesicular or pseudo-vesicular** (n=26, 6.4%). Small papules/vesicles with surrounding erythema, without herpetiform arrangement.
5. **Pityriasis rosea-like** (n=20, 4.9%)**.** Erythematous, scaly oval-shaped plaques in a "Christmas tree" distribution on the trunk.
6. **Purpuric rashes** (n=16, 4.0%)**.** Mostly located in the limbs. Four reactions were consistent with small-vessel vasculitis according to the histopathology.

Cutaneous findings not included in this classification were grouped as:

1. **Flare/reactivation of latent pre-existing cutaneous infection or condition**: VZV, (n=41, 10.1%), herpes simplex virus (HSV, n= 15, 3.7%), psoriasis (n=6) and lichen planus (n =3).
2. **New-onset condition**: n=31, 7.6%, listed in **Table 3**
3. **Non-classifiable**: n= 22, 5.5%.

The most frequently reported reactions were injection-site reactions in women (124/325, 38.1%) and VZV reactivation in men (16/80, 20%). Systemic symptoms associated with the skin rash were present in 207 patients (51.1%), particularly in those with the COVID-arm pattern (64.6%) with low-fever/fever being the most frequent symptom in this group (45.3%). The earliest pattern that appeared was the morbilliform pattern (mean 4 days), the last was VZV reactivation (mean 6.9 days) and the longest-lasting was pityriasis rosea-like (mean 25.2 days).

Thirty-one patients (7.7%) were taking new drugs at the time of the cutaneous reaction, of which acetaminophen was the most frequent (9/31; 29%).

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Forty-five patients (11.1%) had been diagnosed with mild or asymptomatic SARS-CoV-2 infection. Seven (15.5%) had cutaneous reactions after both infection and vaccination. Cutaneous reactions after vaccination and their severity in this group are shown in the **Supplementary Table**. There were no significant differences in the severity of cutaneous reactions between this group and patients with no prior SARS-CoV-2 infection (22.1% vs 21% of severe/very severe reactions).

Dermatologic findings and systemic symptoms according to type of vaccine are shown in **Table 3**. There were more reactions in men with the BNT162b2 (n=49, 30.1%) vaccine than with the mRNA-1273 (n=14, 9.5%) and AZD1222 (n=17, 17.9%) vaccines. Nearly all patients with a reaction to the Moderna vaccine were women (90.5%). The most frequently reported patterns in each vaccine group were VZV infection (BNT162b2, 17.2%), COVID-ARM (mRNA-1273, 61.9%) and urticaria (AZD1222 21.1%).

One-hundred and sixty-six reactions (41%) were classified as grade 1 (mild), 154 (38%) as grade 2 (moderate), 80 (19.8%) as grade 3 (severe) and 5 (1.2%) as grade 4 (very severe). Very severe reactions included one case each of morbilliform rash progressing to erythroderma, bullous pemphigoid, acute generalized exanthematous pustulosis, vasculitis and urticaria. Fifty-eight patients (14.3%) took sick leave, mostly due to herpes zoster (15/58, 25.9%) and urticaria (10/58, 17.2%). Severe/very-severe cases were reported more frequently with the BNT162b2 (25.2% and 2.4%) and AZD1222 (25.3% and 1.0%) vaccines. No patient died. Treatment was required in 328 cases (81%) and is detailed in **Table 2**.

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**DISCUSSION**

We described dermatologic reactions after vaccination with three SARS-CoV-2 vaccines (two mRNA and one adenovirus-vectored) and classified them into six well-defined morphologic reactions patterns and new-onset or reactivation of dermatosis.

Initial reports mostly described local injection-site reactions and, subsequently, other miscellaneous skin reactions, after mRNA vaccination[4,5,7,13,15,18-27]. Recently, McMahon et al[28] published a large registry-based study (mostly with the mRNA-1273 vaccine) in healthcare workers and older people, describing injection-site reactions but also urticarial and morbilliform rashes.

Unlike McMahon et al, our data entry, description and assignment of clinical patterns were made by dermatologists and were mostly supported by photographs. Case collection throughout Spain and the three-month recruitment period permitted a more representative sample beyond healthcare workers and older people.

Reactions were more frequent in women (80.2%), which may reflect a real difference or reporting bias, although women are known to have greater reactogenicity to vaccines[29] and 60% of vaccinated people in Spain were women.[12] Therefore, womens' immune systems may be more reactive to SARS-CoV-2 proteins, which would result in lower susceptibility to the disease and greater reactogenicity to vaccines.

Few cases had had previous atopic dermatitis (6.9%) or urticaria (6.4%). In the general population, the prevalence of atopic dermatitis is around 10%[30,31] and the lifetime prevalence of acute urticaria is approximately 20%,[32] so it cannot be concluded that previous atopy or acute urticaria predisposes to SARS-CoV-2 vaccine cutaneous reactions. However, 18.6% of patients

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with acute urticarial reactions to vaccines in our study had a history of urticaria. Case-control studies are needed to clarify this association. Only 7.7% of cases were receiving new drugs (mainly acetaminophen) at the time of the reaction, and therefore this factor was unlikely to be related to cutaneous reactions.

There was a previous diagnosis of SARS-CoV-2 in 11.1% of cases, similar to the seroprevalence in Spain at the time of writing (9.9%).[33] The severity of cutaneous reactions in this group did not differ from the rest of the sample. Thus, prior SARS-CoV-2 infection does not seem to predispose to cutaneous reactions or more severe reactions, after vaccination.

The COVID-ARM, the most reported pattern was described after vaccination with all three vaccines, particularly mRNA-1273 (70.0%), and almost exclusively in women (95.4%). This pattern had the closest association with systemic symptoms (64.6%).
Two-thirds of reported reactions were beyond the injection-site. Each morphologic pattern seems to correspond to a different spectrum of delayed hypersensitivity reaction, with most of the few skin biopsies that were performed showing nonspecific changes consistent with this reaction. In contrast to previous series,[28] some reactions were scarce (chilblain-like/pernio) or unrepresented (erythromelalgia), while other reactions were more frequently reported (pityriasis rosea-like, VZV reactivations and papulovesicular rashes). The morbilliform and purpuric patterns were reported mostly after BNT162b2 and AZD1222 vaccination and were associated with more severe reactions. VZV reactivation was more frequent after BNT162b2 vaccination and in men. UK spontaneous adverse event reports are the main information source on AZD1222 vaccine cutaneous reactions[34] which, in our series, were mainly acute urticaria (21.1%), injection-site reactions (16.8%) and morbilliform rash (11.6%). Due to the precautionary suspension of the vaccine in the initial target population, we could not study the second dose.

We found a large number of herpes reactivations (VZV and HSV, 13.8%). For VZV, the number (n=41, 10.1%), severity (36.6% took sick leave) and the percentage in healthy people aged < 50 years (29.2%) are particularly striking.[35,36] There were fewer HSV than VZV reactivations, probably because HSV patients do not usually seek medical care. We also found pityriasis rosea-

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like eruptions, which might be due to human herpes virus 6 and 7 reactivation. These herpetic reactivations were also described after SARS-CoV-2 infection and other vaccinations.[8, 9, 37, 38] Taken together, this data strengthens a causal link between herpes virus reactivation and the SARS-CoV-2 vaccine. A plausible mechanism is that a strong specific immune response against SARS-CoV-2 or the S protein from vaccines may distract the cell-mediated control of another, latent virus.

New-onset or worsening of inflammatory conditions were also reported, including psoriasis, lichen planus and bullous pemphigoid. These conditions were previously described after SARS-CoV-2[20,28] and other vaccinations.[39,41-43] As previously stated[43], vaccines may exacerbate skin manifestations in patients with immune-mediated skin diseases, but further investigation is necessary.

The patterns found in this and previous studies[28] are heterogeneous and similar to those described in association with SARS-CoV-2 infection.[8,9] One case repeated the same papulovesicular rash after SARS-CoV-2 infection and vaccination. Therefore, the host immune response to the infection, and not direct viral damage, may cause these skin manifestations. However, a delayed hypersensitivity reaction against vaccine excipients cannot be ruled out.

Although most reactions were classified as mild/moderate, 21% were considered severe/very severe. This degree of severity was not reported in the study by McMahon et al.[28] This percentage is most likely overrepresented (reporting bias) but should not be ignored, as some reactions may be life-threatening.

The study has some limitations: a) the design does not permit causal associations or the measurement of risks or incidence. We could not compare the incidence or severity of cutaneous reactions by vaccine type, since vaccine distribution depended on availability during the study period; b) the data collection period was short, which might limit study of the comprehensive data and evolution, especially after the second doses and AZD1222 vaccination; c) only 12.3% of cases were biopsied and histopathology might have prevented misclassification; d) there was a

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possible reporting bias towards previously-reported or more serious reactions; e) SARS-CoV-2 infection after vaccination cannot be excluded as a plausible cause of cutaneous reactions; f) the lack of ethnic diversity in our sample does not permit generalization of the results.

In conclusion, we described and classified cutaneous reactions reported after SARS-CoV-2 vaccination in a large Spanish case series. Most reactions were mild-moderate and self-limiting, but some were severe/very-severe and required treatment. Better knowledge of these reactions may aid physicians during mass vaccination and reassure patients seeking advice.

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**Figure legends.**

**Figure 1**. Flow chart of the inclusion and exclusion of reported reactions in the study.

**Figure 2**. Multi-panel figure summarizing the main features of the six reaction patterns.

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**Table 1.** Baseline characteristics of patients.

| | | |
|---|---|---|
| **Number of patients** | | 391 |
| **Number of reactions** | | 405 |
| **Number of patients with reported reactions after both doses** | | 14 |
| **Age, mean (SD), years** | | 50.7 (17.6) |
| **Age, range** | | 20-95 |
| **Sex, No. (%)** | Female | 325 (80.2) |
| | Male | 80 (19.8) |
| **Medical history, N. (%)** | Atopic dermatitis | 28 (6.9) |
| | Allergic asthma | 24 (5.9) |
| | Allergic rhinitis | 42 (10.4) |
| | Urticaria | 26 (6.4) |
| **History of allergy to drugs or excipients, N. (%)** | Yes | 47 (11.6) |
| | No | 358 (88.4) |
| | Any antibiotic | 23 (5.7) |
| | Acetylsalicylic acid and/or NSAIDs | 16 (4.0) |
| | Iodine | 4 (1.0) |
| **History of cutaneous reactions to other vaccines, N. (%)** | | 9 (2.2) |
| **Previous diagnosis of SARS-CoV-2 infection, N (%)*** | Yes | 45 (11.1) |
| | No | 360 (88.9) |
| | Clinical suspicion only | 2 (4.4) |
| | PCR+ | 33 (73.3) |
| | Antibody + | 11 (24.4) |
| | Rapid antigen test + | 3 (6.8) |
| **Cutaneous manifestations after SARS-CoV-2 infection, Number/total number within category** | Yes | 7/45 |
| | Maculopapular rash | 3/7 |
| | Urticaria | 2/7 |
| | Morbilliform rash | 1/7 |
| | Pseudovesicular rash | 1/7 |

*Some patients were diagnosed by ≥ 1 method

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**Table 2.** Characteristics of patients with cutaneous reaction after SARS-CoV-2 vaccine

| Characteristics | | **Covid-Arm** | **HSV reactivation** | **VZV reactivation** | **Papular vesicular** | **Pityriasis rosea-like** | **Morbilliform** | **Urticaria and/or Angioedema** | **Purpuric** | **P-value** |
|---|---|---|---|---|---|---|---|---|---|---|
| No. of cases (%) | | 130 (32.1) | 15 (3.7) | 41 (10.1) | 26 (6.4) | 20 (4.9) | 36 (8.9) | 59 (14.6) | 16 (4.0 | |
| Age, (years), mean +/- SD | | 48.8 +/-15.7 | 44.0 +/-14.6 | 60.6 +/- 17.4 | 43.5 +/-15.4 | 39.7 +/- 15.3 | 50.4 +/- 20.8 | 47.9 +/-15.5 | 55.9 +/- 20.5 | <0.001 |
| Sex, No. (%) | Female | 124 (95.4) | 12 (80.0) | 25 (61.0) | 22 (84.6) | 15 (75.0) | 27 (75.0) | 46 (78.0) | 11 (68.8) | <0.001 |
| | Male | 6 (4.6) | 3 (20.0) | 16 (39.0) | 4 (15.4) | 5 (25.0) | 9 (25.0) | 13 (22.0) | 5 (31.2) | |
| Medical history | Atopic dermatitis | 12 (9.2) | 0 (0.0) | 1 (2.4) | 1 (3.8) | 2 (10.0) | 4 (11.1) | 6 (10.2) | 1 (6.3) | 0.714 |
| | Allergic asthma | 6 (4.6) | 2 (13.3) | 1 (2.4) | 4 (15.4) | 0 (0.0) | 5 (13.9) | 1 (1.7) | 0 (0.0) | 0.030 |
| | Allergic rhinitis | 13 (10.0) | 2 (13.3) | 2 (4.9) | 2 (7.7) | 5 (25.0) | 8 (22.2) | 5 (8.5) | 1 (6.3) | 0.147 |
| | Urticaria | 6 (4.6) | 0 (0.0) | 2 (4.9) | 1 (3.8) | 2 (10.0) | 2 (5.6) | 11 (18.6) | 0 (0.0) | 0.053 |
| History of allergy to drugs or excipients | | 19 (14.6) | 0 (0.0) | 2 (4.9) | 1 (3.8) | 0 (0.0) | 8 (22.2) | 5 (8.5) | 4 (25.0) | 0.023 |
| History of cutaneous reactions to other vaccines | | 5 (3.8) | 0 (0.0) | 0 (0.0) | 1 (3.8) | 0 (0.0) | 0 (0.0) | 1 (1.7) | 0 (0.0) | 0.835 |
| Vaccine | BNT162b2 (Pfizer) | 23 (17.7) | 5 (33.3) | 28 (68.3) | 11 (42.3) | 11 (55.0) | 19 (52.8) | 24 (40.7) | 7 (43.8) | <0.001 |
| | mRNA-1273 (Moderna) | 91 (70.0) | 4 (26.7) | 6 (14.6) | 7 (26.9) | 5 (25.0) | 6 (16.7) | 15 (25.4) | 0 (0.0) | |
| | AZD1222 (AstraZeneca) | 16 (12.3) | 6 (40.0) | 7 (17.1) | 8 (30.8) | 4 (20.0) | 11 (30.5) | 20 (33.9) | 9 (56.2) | |
| Vaccination dose at the time of cutaneous reaction | First | 85 (65.4) | 9 (60.0) | 26 (63.4) | 18 (69.2) | 12 (60.0) | 25 (69.4) | 35 (59.3) | 11 (68.8) | 0.969 |
| | Second | 45 (34.6) | 6 (40.0) | 15 (36.6) | 8 (30.8) | 8 (40.0) | 11 (30.6) | 24 (40.7) | 5 (31.2) | |
| Time to onset after vaccination, (days) mean | | 4.9 +/- 3.7 | 4.6 +/- 4.0 | 6.9 +/- 6.4 | 6.4 +/- 5.2 | 6.3 +/- 3.6 | 4.0 +/-3.9 | 4.9 +/- 3.4 | 7.6 +/-5.4 | 0.002 |

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| | | | | | | | | | | |
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| +/- SD | | | | | | | | | | |
| Duration of the reaction, days, mean (SD)* | | 7.4 +/- 4.1 | 9.3 +/- 5.9 | 12.1 +/- 6.8 | 19.3 +/-17.2 | 25.2 +/- 14.5 | 10.3 +/- 12.0 | 7.5 +/- 10.0 | 15.7 +/- 11.9 | <0.001 |
| Photograph availability, n (%) | | 83 (63.8) | 10 (66.6) | 30 (73.2) | 26 (100) | 19 (95) | 29 (80.5) | 35 (59.3) | 15 (94) | <0.001 |
| Associated skin symptoms | Yes | 118 (90.8) | 14 (93.3) | 38 (92.7) | 24 (92.3) | 11 (55.0) | 30 (83.3) | 54 (91.5) | 9 (56.2) | <0.001 |
| | No | 12 (9.2) | 1 (6.7) | 3 (7.3) | 2 (7.7) | 9 (45.0) | 5 (13.9) | 5 (8.5) | 7 (43.8) | |
| | Itch | 74 (56.9) | 3 (20.0) | 14 (34.1) | 23 (88.5) | 10 (50.0) | 28 (77.8) | 49 (83.1) | 5 (31.2) | <0.001 |
| | Pain | 62 (47.7) | 4 (26.7) | 34 (82.9) | 2 (7.7) | 0 (0.0) | 0 (0.0) | 6 (10.2) | 4 (25.0) | <0.001 |
| | Stinging | 25 (19.2) | 8 (53.3) | 14 (34.1) | 2 (7.7) | 0 (0.0) | 6 (16.7) | 8 (13.6) | 0 (0.0) | <0.001 |
| | Burning | 19 (14.6) | 1 (6.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | <0.001 |
| | Dysesthesia | 0 (0.0) | 0 (0.0) | 1 (2.4) | 0 (0.0) | 0 (0.0) | 1 (2.8) | 1 (1.7) | 0 (0.0) | 0.354 |
| | Painful lymph node | 8 (6.2) | 1 (6.7) | 4 (9.8) | 0 (0.0) | 0 (0.0) | 1 (2.8) | 0 (0.0) | 0 (0.0) | 0.175 |
| Systemic symptoms | Yes | 84 (64.6) | 8 (53.3) | 20 (48.8) | 11 (30.6) | 8 (40.0) | 16 (44.4) | 29 (49.2) | 5 (31.2) | 0.046 |
| | No | 46 (35.4) | 7 (46.7) | 21 (51.2) | 15 (69.4) | 12 (60.0) | 20 (55.6) | 30 (50.8) | 11 (68.8) | |
| | Cough | 1 (0.8) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 3 (5.1) | 0 (0.0) | 0.377 |
| | Dyspnoea | 1 (0.8) | 0 (0.0) | 0 (0.0) | 1 (3.8) | 0 (0.0) | 1 (2.8) | 2 (3.4) | 0 (0.0) | 0.520 |
| | Low fever (37.1 - 38ºC) | 31 (23.8) | 1 (6.7) | 10 (24.4) | 5 (17.9) | 4 (20.0) | 5 (13.9) | 8 (13.6) | 1 (6.3) | 0.416 |
| | Fever (> 38ºC) | 28 (21.5) | 4 (26.7) | 1 (2.4) | 1 (3.8) | 0 (0.0) | 5 (13.9) | 6 (10.2) | 0 (0.0) | 0.002 |
| | Myalgia | 37 (28.5) | 4 (26.7) | 2 (4.9) | 4 (15.4) | 3 (15.0) | 8 (22.2) | 10 (16.9) | 2 (12.5) | 0.060 |
| | Asthenia | 38 (29.2) | 5 (33.3) | 8 (19.5) | 5 (17.9) | 1 (5.0) | 11 (30.6) | 15 (25.4) | 5 (31.2) | 0.342 |
| | Headache | 29 (22.3) | 3 (20.0) | 6 (14.6) | 3 (11.5) | 3 (15.0) | 8 (22.2) | 13 (22.0) | 3 (18.8) | 0.891 |
| | Nausea/Vomiting/Diarr | 17 (13.1) | 1 (6.7) | 0 (0.0) | 1 (3.8) | 1 (5.0) | 4 (11.1) | 6 (10.2) | 1 (6.3) | 0.236 |

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| | hoea | | | | | | | | | |
| | Anosmia/Ageusia | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (3.8) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0.224 |
| Severity of cutaneous reaction | Mild – Grade 1 | 66 (50.8) | 9 (60.0) | 13 (31.7) | 10 (38.5) | 5 (25.0) | 10 (27.8) | 21 (35.6) | 9 (56.3) | <0.001 |
| | Moderate – Grade 2 | 64 (49.2) | 6 (40.0) | 23 (56.1) | 7 (26.9) | 2 (10.0) | 8 (22.2) | 17 (28.8) | 4 (25.0) | |
| | Severe – Grade 3 | 0 (0.0) | 0 (0.0) | 5 (12.2) | 9 (34.6) | 13 (65.0) | 17 (47.2) | 20 (33.9) | 2 (12.5) | |
| | Very severe – Grade 4 | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (2.8) | 1 (1.7) | 1 (6.2) | |
| Medical sick leave | Yes | 10 (7.7) | 1 (6.7) | 15 (36.6) | 3 (11.5) | 0 (0.0) | 8 (22.2) | 10 (16.9) | 5 (31.2) | <0.001 |
| | No | 120 (92.3) | 14 (93.3) | 26 (63.4) | 23 (88.5) | 20 (100.0) | 28 (77.8) | 49 (83.1) | 11 (68.8) | |
| Treatment of cutaneous reactions | Yes | 93 (71.5) | 12 (80.0) | 40 (97.6) | 22 (84.6) | 13 (65.0) | 30 (83.3) | 57 (96.6) | 8 (50.0) | <0.001 |
| | No | 37 (28.5) | 3 (20.0) | 1 (2.4) | 4 (15.4) | 7 (35.0) | 6 (16.7) | 2 (3.4) | 8 (50.0) | |
| | Topical corticosteroids | 48 (36.9) | 1 (6.7) | 1 (2.4) | 12 (46.2) | 9 (45.0) | 12 (33.3) | 16 (27.1) | 4 (25.0) | <0.001 |
| | Systemic corticosteroids | 3 (2.3) | 0 (0.0) | 0 (0.0) | 6 (23.1) | 1 (5.0) | 9 (25.0) | 15 (25.4) | 5 (31.2) | <0.001 |
| | Topical antibiotics | 5 (3.8) | 1 (6.7) | 7 (17.1) | 5 (17.9) | 1 (5.0) | 1 (2.8) | 3 (5.1) | 0 (0.0) | 0.024 |
| | Oral antibiotics | 4 (3.1) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (5.0) | 1 (2.8) | 0 (0.0) | 0 (0.0) | 0.601 |
| | Paracetamol | 42 (32.3) | 0 (0.0) | 6 (14.6) | 2 (7.7) | 1 (5.0) | 3 (8.3) | 3 (5.1) | 1 (6.3) | <0.001 |
| | NSAIDs | 12 (9.2) | 0 (0.0) | 7 (17.1) | 1 (3.8) | 0 (0.0) | 1 (2.8) | 1 (1.7) | 0 (0.0) | 0.057 |
| | Oral antihistamines | 33 (25.4) | 0 (0.0) | 3 (7.3) | 17 (65.4) | 7 (35.0) | 22 (61.1) | 53 (89.8) | 2 (12.5) | <0.001 |
| | Adrenaline | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 1 (1.7) | 0 (0.0) | 0.621 |
| | Systemic antiviral | 0 (0.0) | 10 (66.7) | 38 (92.7) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | 0 (0.0) | <0.001 |
| New drugs (last 5 weeks) before the onset of cutaneous reaction | | 9 (6.9) | 0 (0.0) | 4 (9.8) | 3 (11.5) | 1 (5.0) | 3 (8.3) | 4 (6.8) | 4 (25.0) | 0.370 |
| Prior diagnosis of SARS-CoV-2 infection | | 19 (14.6) | 2 (13.3) | 3 (7.3) | 1 (3.8) | 2 (10.0) | 5 (13.9) | 6 (10.2) | 1 (6.3) | 0.808 |

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Data are presented as numbers and column percentages, unless otherwise stated. *P*-values are from $\chi^2$-tests for qualitative variables and ANOVA for quantitative variables.

*Missing data for 12 patients; the percentages are calculated using the available d

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**Table 3.** Characteristics of patients with cutaneous reactions according to vaccine.

| **Characteristics** | | **BNT162b2 (Pfizer-BioNTech)** | **mRNA-1273 (Moderna)** | **AZD1222 (AstraZeneca)** | P-value |
|---|---|---|---|---|---|
| No. of cases (%) | | 163 (40.2) | 147 (36.3) | 95 (23.5) | |
| Age, (years), mean +/- SD | | 55.3 +/- 20.7 | 46.1 +/- 13.8 | 50.0 +/- 15.2 | <0.001 |
| Sex, No. (%) | Female | 114 (69.9) | 133 (90.5) | 78 (82.1) | <0.001 |
| | Male | 49 (30.1) | 14 (9.5) | 17 (17.9) | |
| Medical history | Atopic dermatitis | 9 (5.5) | 9 (6.1) | 10 (10.5) | 0.278 |
| | Allergic asthma | 11 (6.7) | 10 (6.8) | 3 (3.2) | 0.426 |
| | Allergic rhinitis | 19 (11.6) | 14 (9.5) | 9 (9.5) | 0.784 |
| | Urticaria | 9 (5.5) | 11 (7.5) | 6 (6.3) | 0.780 |
| History of allergy to drugs or excipients | Yes | 20 (12.2) | 18 (12.2) | 9 (9.5) | 0.760 |
| | No | 143 (87.8) | 129 (87.8) | 86 (90.5) | |
| History of cutaneous reactions to other vaccines | Yes | 5 (3.1) | 4 (2.7) | 0 (0.0) | 0.261 |
| | No | 158 (96.9) | 143 (97.3) | 95 (100.0) | |
| Cutaneous reaction | COVID-ARM | 23 (14.1) | 91 (61.9) | 16 (16.8) | <0.001 |
| | HSV reactivation | 5 (3.1) | 4 (2.7) | 6 (6.3) | 0.301 |
| | VZV reactivation | 28 (17.2) | 6 (4.1) | 7 (7.4) | <0.001 |
| | Papulovesicular | 11 (6.7) | 7 (4.8) | 8 (8.4) | 0.371 |
| | Pityriasis rosea-like | 11 (6.7) | 5 (3.4) | 4 (4.2) | 0.419 |
| | Morbilliform | 19 (11.7) | 6 (4.1) | 11 (11.6) | 0.037 |
| | Urticaria and/or Angioedema | 24 (14.7) | 15 (10.2) | 20 (21.1) | 0.065 |
| | Purpuric | 7 (4.3) | 0 (0.0) | 9 (9.5) | 0.001 |
| | Other* | 35 (21.5) | 13 (8.8) | 14 (14.7) | 0.008 |
| Vaccination dose at the time of cutaneous reaction | First | 82 (50.3) | 83 (56.5) | 95 (100.0) | <0.001 |
| | Second | 81 (49.7) | 64 (43.5) | 0 (0.0) | |

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| | | | | | |
|---|---|---|---|---|---|
| Systemic symptoms | No | 104 (63.8) | 54 (36.7) | 40 (42.1) | |
| | Cough | 2 (1.2) | 3 (2.0) | 0 (0.0) | 0.374 |
| | Dyspnoea | 3 (1.8) | 4 (2.7) | 0 (0.0) | 0.309 |
| | Low fever (37.1 - 38ºC) | 21 (12.9) | 33 (22.4) | 16 (16.8) | 0.084 |
| | Fever (> 38ºC) | 6 (3.8) | 30 (20.4) | 16 (16.8) | <0.001 |
| | Myalgia | 20 (12.3) | 37 (25.2) | 22 (23.2) | 0.010 |
| | Asthenia | 27 (16.6) | 44 (29.9) | 32 (33.7) | 0.003 |
| | Headache | 17 (10.4) | 34 (23.1) | 25 (26.3) | 0.002 |
| | Nausea/Vomiting/Diarrhoea | 8 (4.9) | 18 (12.2) | 10 (10.5) | 0.062 |
| | Anosmia/Ageusia | 0 (0.0) | 1 (0.7) | 0 (0.0) | 0.598 |
| Severity of cutaneous reaction | Mild – Grade 1 | 66 (40.5) | 64 (43.5) | 36 (37.9) | 0.002 |
| | Moderate – Grade 2 | 52 (31.9) | 68 (46.3) | 34 (35.8) | |
| | Severe – Grade 3 | 41 (25.2) | 15 (10.2) | 24 (25.3) | |
| | Very severe – Grade 4 | 4 (2.4) | 0 (0.0) | 1 (1.0) | |
| Medical sick leave | Yes | 30 (18.4) | 10 (6.8) | 18 (18.9) | 0.005 |
| | No | 133 (81.6) | 137 (93.2) | 77 (81.1) | |

Data are presented as numbers and column percentages, unless otherwise stated. *P*-values are from $\chi^2$-tests for qualitative variables and ANOVA for quantitative variable * Other include: A) **Flare/reactivation of latent pre-existing cutaneous infection or condition**: VZV, (n=41, 10.1%), herpes simplex virus (HSV, n= 15, 3.7%), psoriasis (n=6) and lichen planus (n =3). B) **New-onset condition**: psoriasis (n=3), eczema (n=7), chilblain-like/pernio (n=3), acute generalized exanthematous pustulosis (n=2), Raynaud's (n=2), bullous pemphigoid (n=2), erythema multiforme (n=2), generalized morphoea (n=1), cutaneous B lymphoma (n=1), livedo reticularis (n=1), symmetrical drug-related intertriginous and flexural exanthema (SDRIFE)-like eruption (n=1), erythema nodosum (n=1), reaction to facial dermal fillers (n=1), scrotal tongue (n=1), xantonichia (n=1), staphylococcal skin infection (n=1), ankle oedema secondary to deep vein thrombosis (n=1). C) **Non-classifiable**.

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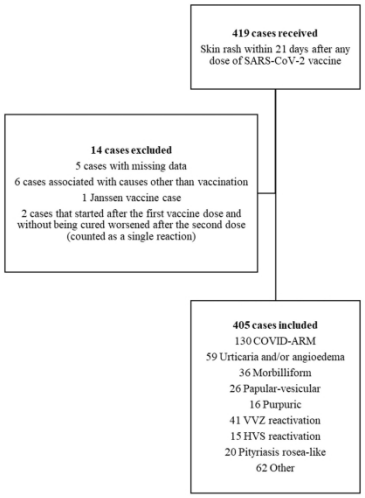
Accepted Article

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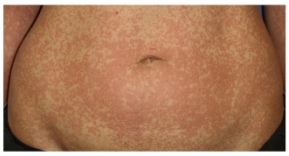
Accepted Article

**Covid Arm (32.1%)**
Inmediate (46.2%) or delayed (53.8%)
100% Mild or moderate
70% mRNA-1273 vaccine (Moderna)
36.9% topical steroids

**Urticarial (14.6%)**
>24 h after vaccination (93.2%). Mean duration: 7.5 days
35.6% Severe/very severe
No differences between vaccines
89.8% oral antihistamines



**Morbiliform (8.9%)**
Earliest time to onset (4.0 days). Mean duration: 10.3 days
50% Severe /very severe
52.8% BNT162b2 vaccine and 30.5% AZD1222 vaccine
25% : oral steroids

**Papulo vesicular (6.4%)**
Time to onset: 6.4 days. Mean duration: 19.3 days
65.4% Mild or moderate
No differences between vaccines
23.1% oral steroids

**P. Rosea-like (4.9%)**
Time to onset: 6.3 days. Mean duration: 25.2 days
Younger age (Mean 39.7 years +/-SD 15.3)
No differences between vaccines

**Purpuric (4.0%)**
50% of biopsied cases: small-vessel vasculitis
43.8% BNT162b2 vaccine and 56.2% AZD1222 vaccine
31.2% oral steroids

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# CUTANEOUS REACTIONS AFTER SARS-COV-2 VACCINATION: A CROSS-SECTIONAL SPANISH NATIONWIDE STUDY OF 405 CASES

ALBA CATALÀ, CARLOS MUÑOZ-SANTOS, CRISTINA GALVÁN-CASAS, MÓNICA RONCERO RIESCO, DAVID REVILLA NEBREDA, AMADOR SOLÁ-TRUYOLS, PRISCILA GIAVEDONI, MAR LLAMAS VELASCO, CARLOS GONZÁLEZ-CRUZ, XAVIER CUBIRÓ, RICARDO RUÍZ-VILLAVERDE, SARA GÓMEZ ARMAYONES, MARÍA DEL PINO GIL MATEO, DAVID PESQUÉ, ORIANNA MARCANTONIO, DIEGO FERNÁNDEZ-NIETO, JORGE ROMANÍ, NICOLÁS IGLESIAS PENA, LUCÍA CARNERO GONZALEZ, JESÚS TERCEDOR, GREGORIO CARRETERO, TERESA MASAT, PEDRO RODRÍGUEZ JIMÉNEZ, ANA MARÍA GIMENEZ-ARNAU, MARTA UTRERA BUSQUETS, ELENA VARGAS LAGUNA, ANA G. ANGULO MENÉNDEZ, ELIANA SAN JUAN, MARIBEL IGLESIAS SANCHO, LAURA ALONSO NARANJO, INGRID HILTUN, EUGENIA CUTILLAS MARCO, ISABEL POLIMON OLABARRIETA, SILVIA MARINERO ESCOBEDO, XAVIER GARCÍA NAVARRO, MARÍA JOSÉ CALDERÓN GUTIÉRREZ, GLORIA BAEZA HERNÁNDEZ, LOLA BOU CAMPOS, TOMÁS TOLEDO PASTRANA. ANTONIO GUILABERT.

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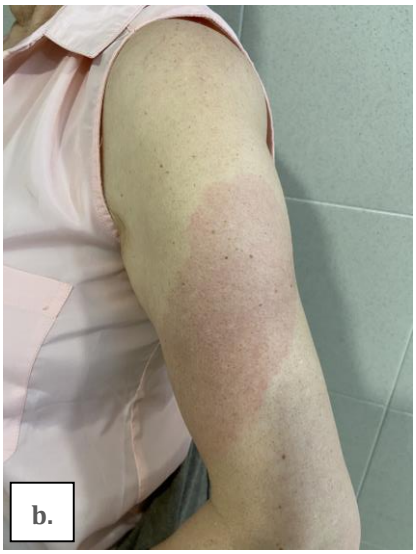
# SUPPLEMENTARY MATERIAL: PHOTOGRAPHIC ATLAS

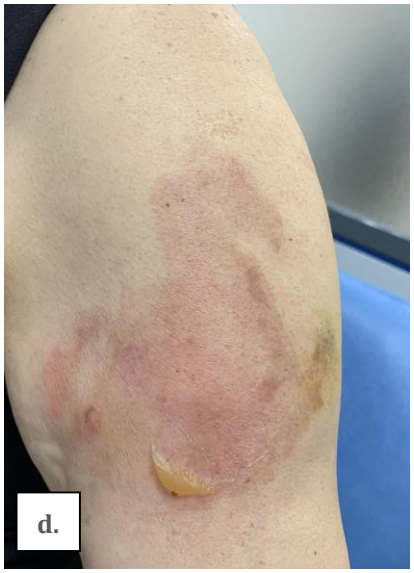
## Covid-Arm

a. 64-year-old woman. Covid-arm. Onset 2 days after AZD1222 first dose. Resolved in 12 days. No treatment.

b. 62-year-old woman. Delayed covid-arm. Onset 9 days after mRNA-127vaccine first dose. Resolved in 7 days. Treatment: NSAIDs and cold packs. Published by the present authors in https://doi.org/10.1016/j.ad.2021.05.011



c. 71-year-old woman. Delayed covid-arm. Onset 7 days after mRNA-127 first dose vaccine. Resolved in 7 days. Treatment: topical corticosteroids.




d. 61-year-old woman. Bullous covid-arm. Onset 1 day after AZD1222 first dose . Resolved in 15 days. Treatment: paracetamol.

e. 51-year-old woman. Covid-arm. Onset 1 day after mRNA-127 first dose vaccine. Resolved in 5 days. Treatment: paracetamol.

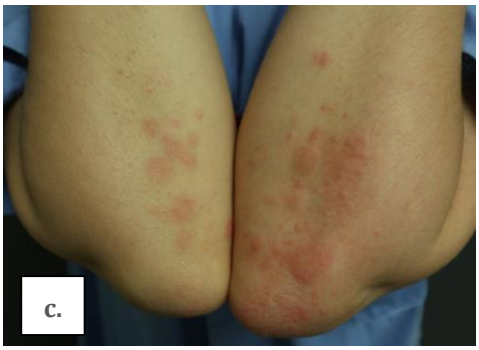
# SUPPLEMENTARY MATERIAL: PHOTOGRAPHIC ATLAS

## Urticaria and/or Angioedema

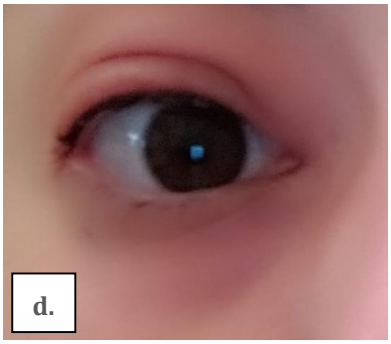
a. 66-year-old woman. Acute urticaria. Onset 24h after AZD1222 first dose. Resolved in 7 days. Treatment: oral antihistamines.

b. 27-year-old man. Acute urticaria. Onset 6 days after AZD1222 first dose vaccine. Treatment: oral antihistamines and topical corticosteroids.

c. 28-year-old woman. Acute urticaria. Onset 6 days after mRNA-127 second dose. Treatment: oral antihistamines.




d. 38-year-old woman. Acute angioedema. Onset 2 days after BNT162b2 second dose. Resolved in 24h. Treatment: endovenous antihistamines.



e. 34-year-old man. Acute urticaria. Onset 3 days after BNT162b2 second dose. Resolved in 35 days. Treatment: oral antihistamines and oral corticosteroids.

# SUPPLEMENTARY MATERIAL: PHOTOGRAPHIC ATLAS

## Morbilliform

a. 44-year-old woman, Allergic to NSAIDs. No previous drugs. Morbilliform rash. Onset <24h after BNT162b2 first dose. Low-grade fever, headache, and asthenia. Resolved in 5 days .Treatment: oral antihistamines, plus oral and topical corticosteroids.

b. 71-year-old man. Dyslipidaemia and prostate hyperplasia. No previous drugs. Morbilliform rash. Onset 7 days after BNT162b2 first dose. Resolved in 7 days. Treatment: oral antihistamines and oral corticosteroids.

c. 87-year-old woman Previous drugs: metamizole. Morbilliform rash. Onset 5 days after BNT162b2 first dose. Resolved in 20 days. Treatment: oral antihistamines.

d. 61-year-old woman. Allergic to egg protein. No previous drugs. Morbilliform rash. Onset 3 days after AZD1222 first dose. Low-grade fever, myalgia and diarrhea. Resolved in 10 days. Treatment: oral antihistamines and topical corticosteroids.

e. 49-year-old woman. Allergic to metamizole. No previous drugs. Morbilliform rash. Onset <24h after mRNA-127 second dose. Resolved in 7 days. Treatment: oral antihistamines and topical corticosteroids.

# SUPPLEMENTARY MATERIAL: PHOTOGRAPHIC ATLAS

## Papulovesicular

a. 42-year-old woman. No previous drugs. Papulovesicular rash. Onset 10 days after mRNA-127 second dose. Low-grade fever. Resolved in 7 days. Tratment: oral antihistamines, topical corticosteroids and topical antibiotics. Same rash when she had COVID-19.

b. 21-year-old woman. No previous drugs. Papulovesicular rash. Onset 15 days after BNT162b2 first dose. Low-grade fever, myalgia and diarrhea. Resolved in 10 days. Treatment: oral antihistamines. Skin biopsy: lymphocytic vasculitis.

c. 35-year-old woman. No previous drugs. Papulovesicular rash. Onset 6 days after BNT162b2 first dose. Low-grade fever, myalgia and diarrhea. Resolved in 6 days. No treatment.

d. 63-year-old woman. No previous drugs. Papulovesicular rash. Onset 8 days after mRNA-127 first dose. Fever, myalgia and headache. Resolved in 60 days. Treatment: oral and topical corticosteroids.

# SUPPLEMENTARY MATERIAL: PHOTOGRAPHIC ATLAS

## Pityriasis rosea-like

a. 35-year-old man. Pityriasis rosea eruption. Onset 11 days after mRNA-127 first dose. Resolved in 7 days. Treatment: oral antihistamines and oral antibiotics. Skin biopsy: pityriasis rosea.

b. 77-year-old woman. Medical history: Chronic B lymphoid leukemia. No previous drugs. Pityriasis rosea eruption. Onset 3 days after BNT162b2 first dose. Resolved in 8 days. Treatment: oral antihistamines..

c. 41-year-old woman. No previous drugs. Pityriasis rosea eruption. Onset 9 days after BNT162b2 first dose. Resolved in 40 days. Treatment: topical Corticosteroids. Skin biopsy: pityriasis rosea.

d. 30-year-old man. Previously treated with acetaminophen. Pityriasis rosea eruption. Onset 2 days after BNT162b2 second dose. Resolved in 21 days. No treatment.

# SUPPLEMENTARY MATERIAL: PHOTOGRAPHIC ATLAS

## Purpuric

a. 64-year-old woman. No previous drugs. Purpuric eruption. Onset 7 days after AZD1222 first dose. Fever, asthenia and diarrhea. Resolved in24 days. Treatment: oral corticosteroids.

b. 71-year-old woman. Allergic to codeine. Previous drugs: tapentadol. Purpuric eruption. Onset 7 days after BNT162b2 first dose. Resolved in 50 days. Treatment: oral corticosteroids.

c. 88-year-old man: Medical history: heart failure and cardiac arrhythmia on anticoagulants. Previous drugs: gabapentin. Purpuric eruption. Onset 5 days after BNT162b2 second dose. Resolved in 15 days. Treatment: oral and topical corticosteroids. Skin bipsy: toxicoderma.

d. 64-year-old woman. No previous drugs. Purpuric eruption. Onset 14 days after AZD1222 first dose. Resolved in 15 days. No treatment. Skin biopsy: leukocytoclastic vasculitis.

# SUPPLEMENTARY MATERIAL: PHOTOGRAPHIC ATLAS

## Varicella zoster virus reactivation

a. 89-year-old man. Thoracic herpes zoster. Onset 12 days after first dose BNT162b2 vaccine. It resolved after 30 days with oral antiviral and NSAIDs.

b. 48-year-old man. Facial herpes zoster. Onset 5 days after BNT162b2 first dose. Resolved in 10 days. Treatment: oral antiviral.

c. 93-year-old man. Lumbar herpes zoster. Onset 1 day after BNT162b2 second dose. Resolved in 10 days. Treatment: endovenous antiviral and topical antibiotics.

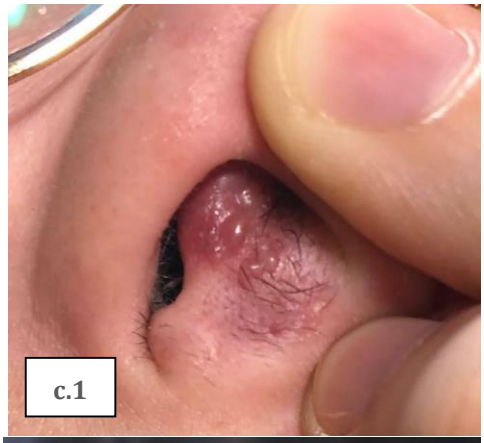
d. 22-year-old woman. Facial herpes zoster. Onset 15 days after AZD1222 first dose. Resolved in 20 days. Treatment: oral antiviral.

# SUPPLEMENTARY MATERIAL: PHOTOGRAPHIC ATLAS

## Herpes simplex virus reactivation

a. 58-year-old woman. Lip HVS reactivation. Onset 7 days after mRNA-127 first dose. Fever. Resolved in 5 days. Treatment: topical antiviral.

b. 35-year-old man. Chin HVS reactivation. Onset: 2 days after mRNA-127 second dose. Resolved in 7 days. No treatment.

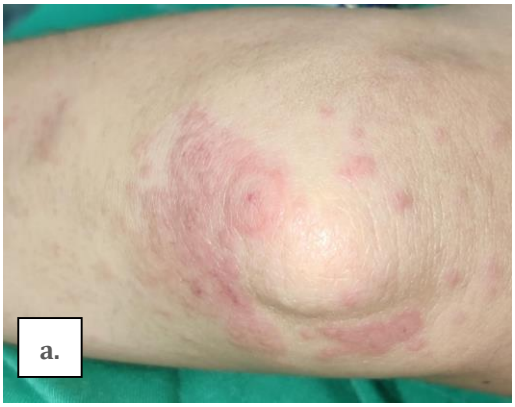


c. 22-year-old woman. Intranasal and oral HVS reactivavation. Onset 4 days after AZD1222 first dose. Fever, myalgia, asthenia, diarrhea, and headache. Resolved in 8 days. Tratment: oral antiviral.

d. 29-year-old woman. Lip HVS reactivation. Onset 2 days after mRNA-127 first . Resolved in 10 days. No treatment.

# SUPPLEMENTARY MATERIAL: PHOTOGRAPHIC ATLAS

## Other eruptions




a. 39-year-old woman. No previous drugs. Erythema multiforme –like eruption. Onset 2 days after mRNA-127 first dose. Resolved in 15 days. Treatment topical corticosteroids.

b. 52-year-old woman. No previous drugs. Raynaud–like eruption. Onset 6 days after AZD1222 first dose. Resolved in 30 days. Treatment: manidipine.

c. 72-year-old man. Medical history: Chronic plaque psoriasis (no palmo plantar) treated with adalimumab. Psoriasis outbreak on palms and soles. Onset 3 days after BNT162b2 second dose. Resolved in 21 days. Treatment: topical and oral corticosteroids.

d. 58-year-old man. No previous drugs. Generalized pustular rash. Onset 3 days after BNT162b2 second dose. Resolved in 10 days. Treatment: topical corticosteroids and topical antibiotics. Skin biopsy: acute generalized exanthematous pustulosis.

# SUPPLEMENTARY MATERIAL: PHOTOGRAPHIC ATLAS

e. 91-year-old man. No previous drugs. Bullous pemphigoid. Onset 24h after BNT162b2 second dose. Resolved in 35 days. Treatment: topical and oral corticosteroids. Skin biopsy: Bullous pemphigoid.

f. 67-year-old woman. No previous drugs. Symmetrical drug-related intertriginous and flexural exanthema (SDRIFE). Onset 24h after AZD1222 first dose. Fever. Resolved in 1 day. Treatment: topical and oral corticosteroids and antihistamines.

**Supplementary Table.** Cutaneous reactions and their severity after SARS-CoV-2 vaccines in people who had previous SARS-CoV-2 infection.

| **Variable** | | **Values** |
|---|---|---|
| **Past diagnosis of SARS-CoV-2 infection, No.** | | 45 |
| Degree of skin reaction **No. (%)** | Mild – Grade 1 | 10 (22.2) |
| | Moderate – Grade 2 | 25 (55.6) |
| | Severe – Grade 3 | 8 (17.8) |
| | Very severe – Grade 4 | 2 (4.4) |
| Cutaneous reaction **No. (%)** | COVID-ARM | 19 (42.2) |
| | HVS reactivation | 2 (4.4) |
| | VVZ reactivation | 3 (6.7) |
| | Papular-vesicular | 1 (2.2) |
| | Pityriasis rosea-like | 2 (4.4) |
| | Morbilliform | 5 (11.1) |
| | Urticaria and/or Angioedema | 6 (13.4) |
| | Purpuric | 1 (2.2) |
| | Other | 6 (13.4) |