Case 3. A 84-year-old male with BP in remission since 4 years after oral prednisone and azathioprine treatment was administered the first dose of the Moderna mRNA-1273 vaccine. After 2 weeks, he started showing mild blistering lesions on the trunk, which were deemed not to require systemic immunosuppressive treatment. 28 days later, the patient was given the second dose; a worsening of the lesions which became more widespread, involving also the oral cavity, took place. A treatment with oral prednisone was started.

Case 4. A 82-year-old female with BP in remission since 3 years after oral prednisone and mycophenolate mofetil treatment was given the first dose of the Pfizer mRNABNT162b2 vaccine. 3 days later, the patient experienced a moderate BP flare in the form of small blisters on the arms and legs. The patient lived in a nursing home where only teledermatological consultations were possible. Oral prednisone was prescribed, and the second dose was administered 21 days later. No further BP flares and no injection site reactions occurred.

Case 5. A 80-year-old male with a history of PV remitted before 1 year after oral prednisone and mycophenolate mofetil treatment experienced a flare 3 days after the first dose of the mRNABNT162b2 vaccine. He was seen in a teledermatological consultation because of severe blisters on the back, and he was treated with oral prednisone. After 21 days, the patient was able to complete the second dose of Pfizer mRNABNT162b2 vaccination. No further BP flares and no injection site reactions occurred.

Despite the ongoing treatment with immunosuppressants, all patients developed IgG antibodies against the SARS-CoV-2 S1-receptor binding domain (RBD) (>150 UI) 1 month after the second dose, which supports the assumption that the vaccination was effective in all cases presented.

These anecdotal data suggest that both mRNA vaccines may trigger relapses in AIBD patients. Vaccines are important in AIBDs patients, since the latter are characterized by a vulnerability against infections in the mucocutaneous barrier[5]: completion of vaccination is advisable, and patients should be treated for flares when needed. However, data on the effect on immunosuppressants on IgG antibodies titres in short and long term are needed. IgG S1-RBD persistence in AIBD patients is also a matter of concern; this should encourage dermatologists to monitor anti-COVID-19 immunity.

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None.

Author contribution
Giovanni Damiani: Conceptualization, Data curation, Formal analysis, Investigation, Project administration, Visualization, Writing – original draft, Writing – review and editing. **Alessia Pacifico:** Investigation, Methodology, Project administration, Software, Validation. Writing – review and editing. **Francesco Pelloni:** Investigation, Project administration, Validation, Writing – review and editing. **Matilde Iorizzo:** Conceptualization, Methodology, Project administration, Resources, Supervision, Writing – review and editing.

Data availability statement
Data available on request due to privacy/ethical restrictions.

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Ulcus vulvae acutum and SARS-CoV-2: an aetiological role?

Editor,

A 10-year-old girl presented with a sudden onset of fever and vulvar pain. Genital examination revealed vulvar oedema especially affecting the labia minora; on the inner face, deeply

penetrating ulcers were observed bilaterally, a larger one of about 3 cm in diameter on the left and two on the right of about 2 cm in diameter (kissing ulcers). They were well-circumscribed, centrally covered with a fibrinous membrane and with purple edges (Fig. 1).

A clinical diagnosis of ulcus vulvae acutum was made.

The patient had never had sexual intercourse, was not affected by any disease and was not taking drugs.

Complete blood count was normal; laboratory findings showed elevated levels of serum C-reactive protein.

Serology was negative for a wide spectrum of infectious diseases, namely syphilis, HSV 1-2, parvovirus B19, adenovirus and HIV; EBV serology and CMV serology was positive only for IgG. Bacterial cultures were negative including Mycoplasma and Trichomonas Vaginalis.

Severe acute respiratory syndrome coronavirus 2 SARS-CoV-2) serology was requested; anti-SARS-CoV-2 IgM was positive with IgG antibodies negative. A molecular nasopharyngeal swab for the virus was performed with a negative result.

Due to the severity of the clinical picture and for preventing bacterial superinfection, the patient was treated with topical and systemic antibiotics before the laboratory results became available. We empirically chose broad-spectrum molecules, i.e. gentamicin cream and oral amoxicillin. Because of the pain, she took ibuprofen for a total of 7 days.

Healing appeared within 2 weeks with scarring.

One month after healing, anti-SARS-CoV-2 IgG antibodies turned positive.

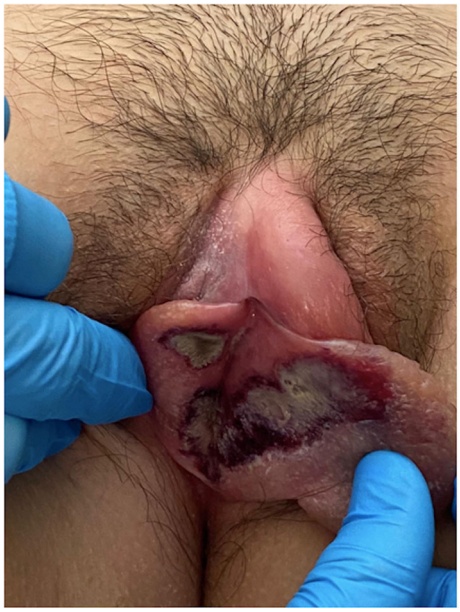

Figure 1 Clinical image of the vulva with the typical kissing ulcer.

Ulcus vulvae acutum was first described by Lipschutz in 1913 and was therefore also called *ulcus vulvae acutum Lipschutz* (UVAL).

It is an uncommon clinical entity characterized by sudden painful vulvar ulcerations, of non-venereal origin, occurring mostly in young and virgin girls. Ulceration is often preceded by flu-like symptoms like fever, fatigue, malaise or chills.[1]

Guidelines for diagnosis and therapy are lacking.

A recently published systematic review of the literature, based on comparative and meta-analyses of the case reports described so far, proposes a diagnostic algorithm for a standardized diagnosis of UVAL (Table 1).[2]

Our case fulfilled these diagnostic criteria.

The aetiopathogenesis of UVAL is still unclear. Several infective agents have been associated with the disease in particular EBV, CMV, mycoplasma pneumoniae, flu virus, toxoplasmosis, mumps, salmonella and PVB19.[2]

A hyperactivity of the immune system elicited by these infectious agents has been hypothesized as well as a type-III hypersensitivity reaction with vascular immune complex deposition, complement activation, micro-thrombosis and subsequent tissue necrosis.[3]

In our patient, the initial flu-like symptoms and the current epidemiological situation made it mandatory to perform the serology for SARS-CoV-2.

During coronavirus disease 2019 (COVID-19), numerous and polymorphous skin and, to a lesser extent, mucosal manifestations have been described with different degrees of severity. Sometimes, they can be observed in asymptomatic patients or in patients with very mild systemic symptoms of COVID-19, assuming therefore an important diagnostic value.[4]

Some very severe cutaneous signs of COVID 19 are attributable to an immune disreactivity triggered by the virus with complement activation and possible interaction with coagulation pathways.[5]

It is worthy of note that immune alteration and vascular damage are shared pathomechanisms for both UVAL- and COVID-19-associated skin manifestations.

Table 1 Diagnostic criteria of UVAL according to a recently published systematic review of the literature[2]

Algorithm for diagnosis of UVAL
Major criteria:
• Acute onset of one or more painful ulcerous lesions in the vulvar region
• Exclusion of infectious and other non-infectious causes for the ulcer
Minor criteria:
• Localization of ulcer at vestibule or labia minora
• No sexual intercourse ever (i.e. patient is a virgin) or within the last 3 months
• Flu-like symptoms
• Systemic infection within 2–4 weeks prior to onset of vulvar ulcer

Adapted from Sadoghi *et al.*[2]

The necrosis and peripheral purpuric appearance of vulvar ulcers could also recall one of the typical skin patterns described during COVID-19.[6]

The lack of definitive knowledge on the aetiology of UVAL, as well as the limited use of histology in confirming the imputability of a specific infectious agent, does not allow us to affirm with certainty that SARS-CoV-2 is the cause of UVAL in our patient. However, the timing of onset and the unique positive serology for SARS-CoV-2 may suggest an aetiological role of this virus.

During the COVID-19 pandemic, it seems advisable to include SARS-CoV-2 as a possible cause of UVAL and to focus attention on the possible association with UVAL and its rare male counterpart, the juvenile gangrenous vasculitis of the scrotum.

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Conflict of interest

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Development of severe pemphigus vulgaris following SARS-CoV-2 vaccination with BNT162b2

Dear Editor,

Pemphigus vulgaris (PV) is a rare and severe autoimmune disorder of skin and mucosa. In PV, the production of autoantibodies against desmosomal proteins of the skin, namely desmoglein (Dsg) 1 and Dsg3, leads to a clinical phenotype characterized by blistering and severe erosions. Several factors including genetic susceptibility, certain drugs and malignant disorders have been reported to trigger or exacerbate PV.[1] Here, we report the first case of a patient, who developed PV following COVID-19 vaccination with the mRNA vaccine BNT162b2 (Comirnaty®, Biontech/Pfizer).

A 40-year-old female patient of Asian ethnicity was referred to our department following the outbreak of painful, non-healing erosions of the oral mucosa, the trunk and the back (Fig. 1a–c). The patient's history revealed that first oral lesions occurred mid-January 5 days after the first administration of BNT162b2. Three days after the patient received the second vaccine dose, oral lesions worsened heavily; in addition, blisters and erosions occurred on the upper part of the body. Prior to vaccination, the patient was otherwise healthy, without any history of skin disease and without any medication. Due to the clinical presentation suspicious for pemphigus disease, we performed skin and blood sampling. The histology of lesional skin showed acantholysis within the lower epidermal layers, and the presence of a dense lymphocytic dermal infiltrate, accompanied by a rich presence of plasma cells (Fig. 1d). Direct immunofluorescence from perilesional skin revealed a prominent deposition of IgG in a honeycomb-like intercellular epidermal pattern (Fig. 1e). Finally, we detected high titres of autoantibodies against Dsg3 and Dsg1 in the patient's sera (974 and 124 RE/mL, respectively) (Euroimmun, Lübeck, Germany). With these findings, we confirmed the clinically suspected diagnosis of PV and initiated an immunosuppressive treatment with oral prednisone (1mg per kg body weight, eventually tapered) and azathioprine (100mg/day).[2] This approach ceased blistering and diminished autoantibody production. The patient is currently under regular clinical follow-ups in our clinic.

Single cases of manifestation of PV following vaccination have been reported after administration of vaccines against rabies, influenza, hepatitis B, diphtheria, typhoid, tetanus and anthrax (Table 1). The BNT162b2 vaccine is a lipid nanoparticle-formulated nucleoside-modified RNA (modRNA) encoding the SARS-CoV-2 full-length spike protein in its perfusion conformation. Following injection, common side effects like local redness,