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EPIDERMOLYSIS BULLOSA ACQUISITA-LIKE CUTANEOUS REACTION REPORTED AFTER THE 2ND DOSE OF PFIZER-BIONTECH COVID-19 VACCINATION: A CASE REPORT

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Abstract

Although they are poorly investigated, cutaneous reactions to messenger RNA (mRNA)-based COVID-19 vaccinations have been documented. In this case report, we presented a case of cutaneous EBA-like response following the second shot of the Pfizer COVID vaccine in a 58-year-old woman with no previous chronic health conditions. The clinical picture showed skin rash with mild itching, burning sensation, and mild redness over her hands and face. On the 2nd day, large, tense blisters were developed. There were multiple eroded flaccid bullae with crusts; some were healed with hypopigmentation over the upper parts of the dorsal surface of the hands and feet. The histopathological report showed sub-epidermal cleft, re- epithelization, characteristic fibrinoid necrosis at the blister base, and no inflammatory cells. The patient's condition has improved on the administration of Prednisolone within eight weeks.

Keywords: *Epidermolysis Bullosa Acquisita; COVID-19, Vaccination, Pfizer BioNTech.*

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INTRODUCTION:

The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic is a potent reminder of infectious diseases' propensity to sicken, kill, and disrupt even the most technologically powerful nations. The prompt declaration of the outbreak and the early publishing of the viral sequence allowed the development of a vaccine solution to begin within weeks after China's initial reporting of the epidemic to the World Health Organization (WHO) on the 31st of December, 2019 [1].

Recovery from a viral illness is dependent on a combination of antibodies in biological fluids that neutralize viral particles and the killer activity of lymphocytes that track out and destroy virus-infected cells in many cases. However, there are viral illnesses whose repair is mostly, if not entirely, dependent on the antibody response and others where the destructive action of killer cells is critical. What is going on with COVID-19 is unclear, but multiple data points to antibodies against the Spike protein, namely its receptor-binding domain, as being the key protective factor [2].

The Food and Drug Administration (FDA) approved an Emergency Use Authorization (EUA) on the 11th of December, 2020 for the Pfizer-BioNTech COVID-19 vaccine to prohibit COVID-19, administered in two doses separated by 21 days. The Advisory Committee on Immunization Practices (ACIP) adopted a comprehensive recommendation for using the Pfizer-BioNTech COVID-19 vaccine on the 12th of December, 2020 [3].

As of the 23rd of December, 2020, a total of 1,893,360 first doses of Pfizer- BioNTech COVID-19 vaccine had been administered in the United States, with reports of 4,393 (0.2 percent) adverse events occurring after receiving Pfizer

BioNTech COVID-19 vaccine being submitted to the Vaccine Adverse Event Reporting System (VAERS). Among them, 175 case reports were selected as likely cases of severe allergic response, including anaphylaxis, and were subjected to additional investigation [4].

Epidermolysis bullosa acquisita (EBA) is a rare autoimmune blistering disease that results in vesicle and bullae formation on the skin and erosions on the mucous membranes [5]. EBA is recognized by a deterioration of tolerance and the subsequent production of autoantibodies against collagen VII [6]. Collagen VII is the primary component of anchoring fibrils in the hemidesmosomes present in the skin's sublamina densa and mucous membranes [7, 8].

Elliott described hereditary dystrophic epidermolysis bullosa in 1904 and proposed the name "epidermolysis bullosa acquisita" as a descriptive clinical diagnosis for individuals with adult-onset and symptoms like those of hereditary dystrophic epidermolysis bullosa [9]. **Roenigk *et al.*** were the first to identify EBA from other bullous illnesses based on different clinical and histological findings, proposing the first diagnostic criteria for EBA in 1971 [10]. Following that, in the 1970s and 1980s, the clinical, histological, immuno-histological, and serological aspects of EBA were classified [11].

Until this date, this is the first case to be described with EBA like cutaneous reaction as an adverse effect for the Pfizer BioNTech COVID-19 vaccine.

Case Presentation Case History

A 58-year-old retired healthy woman with no previous chronic medical diseases was admitted to the emergency department with a report of skin rash. She denied taking any medications before being vaccinated. The patient is physically active and has a healthy lifestyle; she is not a smoker and does not intake alcohol. She loves walking and frequent sun exposure. No previous Allergy or Photosensitivity was reported. No family history of autoimmune diseases or malignancy was reported.

On the 28th of March 2021, between 2-3 PM, she received her 2nd dose of the Pfizer BioNTech COVID-19 vaccine. At 8:30 PM of the same day, she had mild itchiness, burning sensation, and mild redness over her hands and face.

On the 2nd day, large, tense blisters appeared (the patient described them as big blisters). She did not report any dysphagia, abdominal pain, joint pain, muscle ache, fever, or flu symptoms.

Examination and Laboratory Investigations

Her Fitzpatrick skin type is type III. Skin examination showed erosions and crusts over her cheeks. Upper and lower extremities examination revealed multiple eroded flaccid bullae with crusts; some were healed with hypopigmentation over the upper parts of the dorsal surface of the hands and feet. No scar formation, milia, or skin wheals were detected. On mouth examination, we found bilateral buccal erosions. These erosions and crusts did not involve the scalp, palms, soles, genitalia, mucous membranes, folds, and nails.

We have performed differential CBC, liver function

test, renal profile, and they were all normal. We also performed a 3-mm skin punch biopsy from a flaccid blister over the right leg and sent for H&E staining (Hematoxylin and eosin stain), requested one week after initial presentation **(Figure 1).** As there were no new lesions, direct immunofluorescence was not performed (all lesions beyond 24-48 hours)**.**

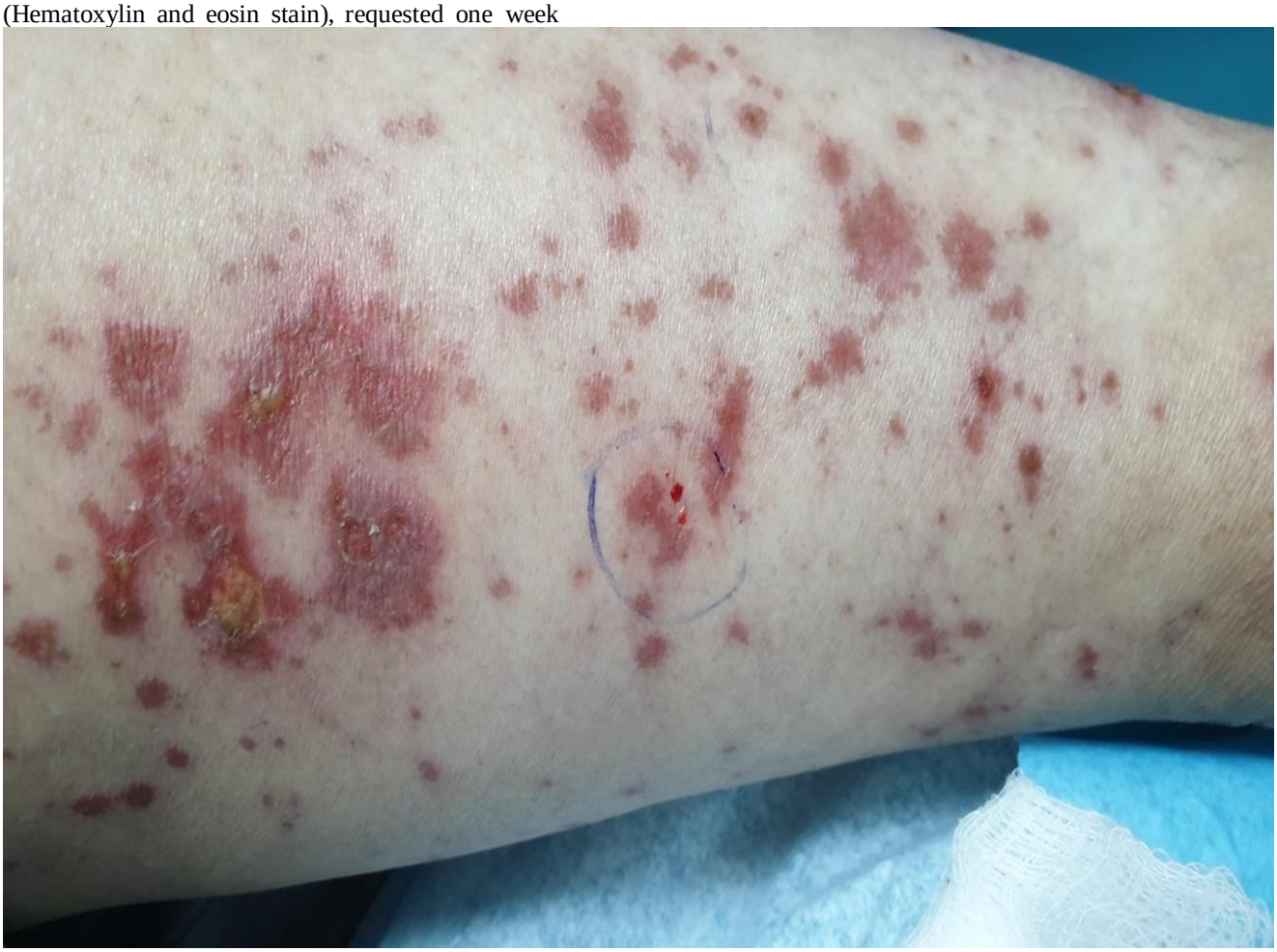


Figure 1. Site of skin biopsy marked in the right leg.

Histopathological Report

The histopathological report showed sub-epidermal cleft, re-epithelization, characteristic fibrinoid necrosis at the blister base, and no inflammatory cells **(Figure 2).** Clinical presentation and H&E Findings are similar to those seen in EBA. There are four primary clinical types of EBA: classical, inflammatory, cicatricial pemphigoid–like, and Brunsting-Perry pemphigoid–like forms, each with an IgG and an IgA-EBA form. Patients frequently describe blister development after a few hours after localized skin damage. A bullous lesion can occur as a result of relatively minor trauma or skin irritation [12].

Histopathological examination alone is not adequate to diagnose EBA-like cutaneous reaction. Direct immunofluorescence staining is important to distinguish EBA from other blistering diseases, especially bullous pemphigoid and porphyria cutanea tarda (PCT). However, immunofluorescence staining is only useful with fresh blisters.

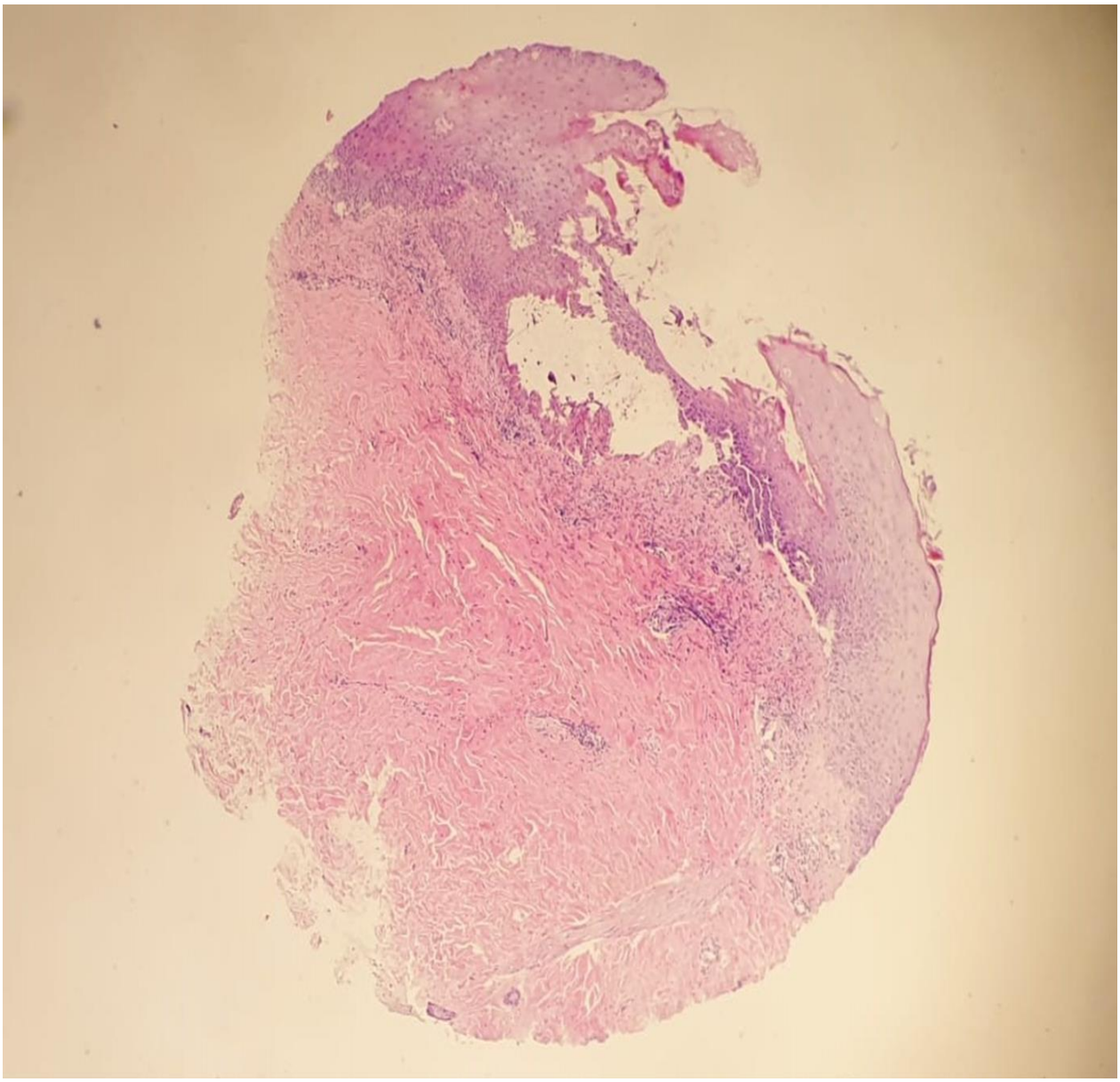


Figure 2. Low power view of a blister with H&E showing sub-epidermal cleft, re-epithelization, characteristic fibrinoid necrosis at the base of the blister, and no inflammatory cells.

A week before visiting the Clinic, she was seen by a senior dermatology consultant and started a course of a systemic steroid (Prednisolone 80 mg with tapering) without performing a skin biopsy. Then, she came for a follow-up visit after one week to the clinic.

Upon the follow-up, she did not develop any new lesions; however, the lesions still not dried and with mild impetiginization. The physician planned for a skin biopsy on the 11th of April, and a written Consent was signed **(Figure 3).**

The physician prescribed moderate potency topical corticosteroids with topical antibiotics and systemic steroids (Prednisolone, 30 mg) once per day, omeprazole 20 mg once per day, and Vitamin D supplement. The patient was advised to avoid sun exposure and use a sun protection method. She was also warned about rubbing her skin, washing her skin with hot water, or using harsh soaps.

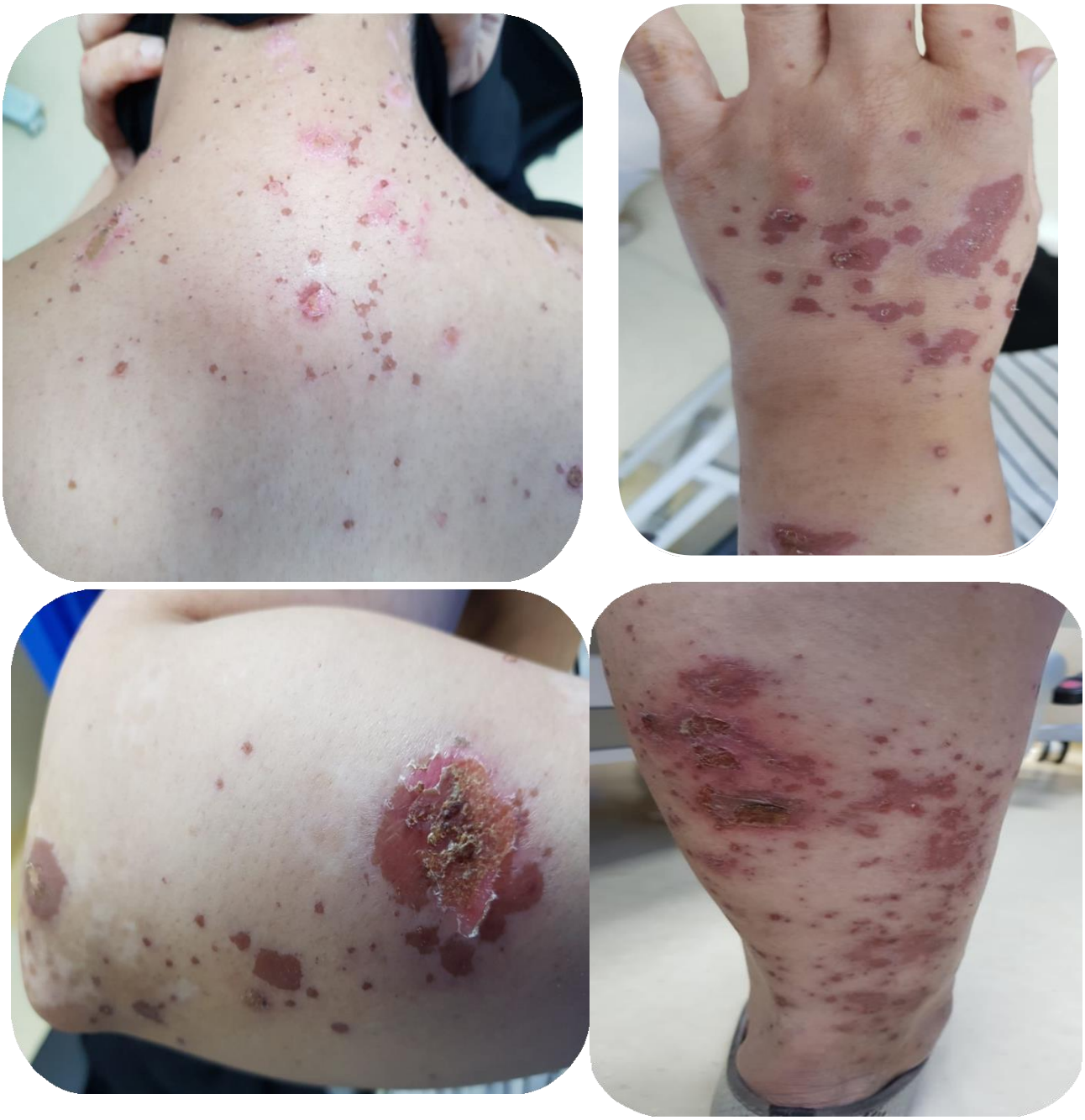
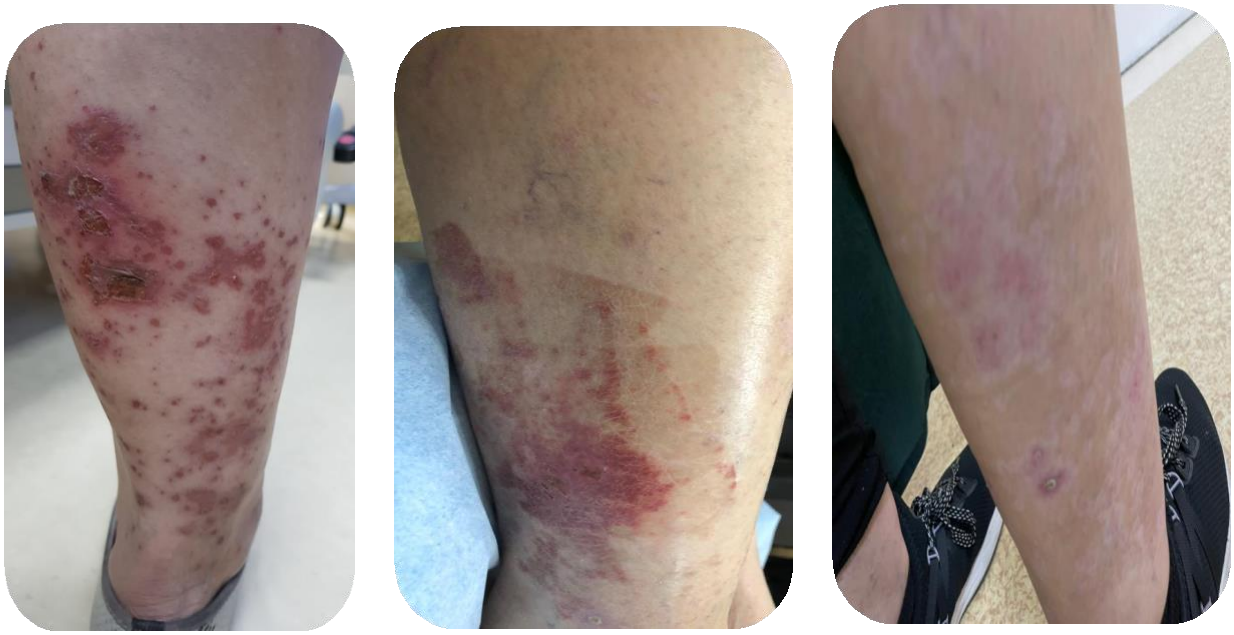


Figure 4. Clinical pictures of blisters and skin erosions on the day of biopsy (the 10th of April).

In **Figure 4,** there are multiple flaccid vesicles and bullae with some crusts, erosions over background of pink erythema, and post-inflammatory hypo-pigmented patches. The lesions showed a better prognosis after nearly three weeks and eight weeks of administration of Prednisolone, as presented in **figure 5.** All of the attached clinical pictures are after receiving the prescribed treatment, as there are no clear, tense blisters shown as the patient-reported. Additionally, the initial clinical pictures in the emergency department were not pictured **(Figure 6, 7).**

The possible clinical differential diagnoses are cutaneous hypersensitivity reaction following COVID-19 vaccination, EBA, PCT, bullous pemphigoid, pemphigus, pityriasis lichenoides et varioliformis, and linear IgA bullous dermatosis.



At day 7 **After 24 days** **After 55 days**

Figure 5. Pictures are showing the progression of skin lesions on Prednisolone administration.

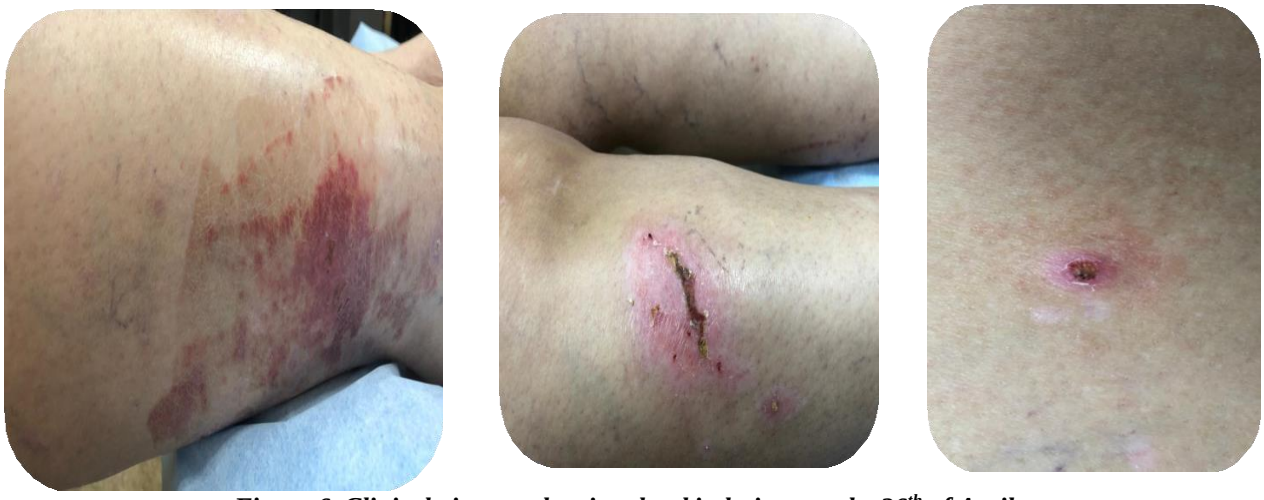


Figure 6. Clinical pictures showing the skin lesions on the 26th of April.

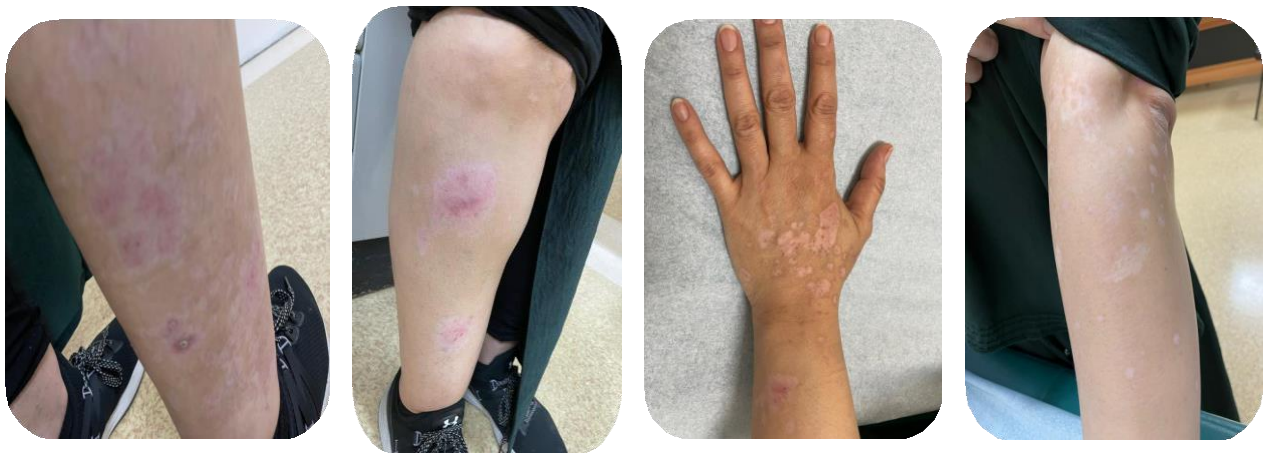


Figure 7. Clinical pictures presenting the follow-up of the patient's skin lesion on 27th May.

DISCUSSION:

Vaccination stimulates the immune system, and unwanted adverse effects are common. Discomfort at the injection site, headache, muscle, and joint pain, and an overall sense of being sick are all common adverse effects. However, cutaneous reactions are rarely seen [13].

With the emergency permission of the vaccines came several questions regarding the safety of the vaccinations. In the case above, we described EBA-like cutaneous reaction in a 58-year-old woman after being vaccinated with the Pfizer COVID vaccine. With over 80 million individuals vaccinated to date, this is a very unusual adverse effect. Although no fatalities have been reported thus far, one incidence of severe acute ITP, exacerbated by a fatal cerebral hemorrhage, was detected three days after immunization with the Pfizer COVID vaccine. The best available evidence from all phases of the vaccine clinical trials and persons inoculated to date indicate that the relationship was most likely unrelated, but further research is needed because this is a novel vaccine [14, 15].

Many possible clinical differential diagnoses were considered, including cutaneous hypersensitivity reaction following COVID-19 vaccination, PCT, bullous pemphigoid, pemphigus, pityriasis lichenoides, and varioliformis and linear IgA bullous dermatosis. However, EBA was more likely given the clinical presentation of our case and the histopathological picture that presents sub-epidermal cleft, re- epithelization, characteristic fibrinoid necrosis at the blister base, and no inflammatory cells.

A thorough evaluation of its safety must carefully accompany the use of a novel vaccination. This is especially significant because vaccination is not a medicine for sick individuals who are dying but rather a medication given to healthy individuals to reduce the likelihood of becoming ill [16].

CONCLUSION:

We presented a case of an EBA-like cutaneous reaction following the second shot of the Pfizer COVID vaccine. The clinical picture revealed skin rash with mild itching, burning sensation, and mild redness over her hands and face. On the 2nd day, large, tense blisters appeared. There were multiple eroded flaccid bullae with crusts; some were healed with hypopigmentation over the upper parts of the dorsal surface of the hands and feet. The histopathological report showed sub-epidermal cleft, re- epithelization, characteristic fibrinoid necrosis at the blister base, and no inflammatory cells. More extensive investigations are necessary to interpret these findings and gain a better comprehension of the pathophysiology.

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