Rose Colin (Orcid ID: 0000-0002-9864-1660)

Cutaneous lupus erythematosus-like reaction arising after COVID-19 vaccination

Keywords: COVID-19, vaccine reaction, cutaneous lupus erythematosus-like

Authors and affiliations:

Corresponding Author:
Colin Rose[1], BSc
Walter Reed National Military Medical Center, Department of Dermatology
8901 Wisconsin Ave.
Bethesda, MD 20889
Telephone: 301-295-4574
Fax: 301-295-9736
E-mail: rosecj@etsu.edu

Ryan Apgar, DO
Walter Reed National Military Medical Center, Department of Dermatology

Margaret Green, DO, MSc, FAAD
Walter Reed National Military Medical Center, Department of Dermatology

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Abstract

Multiple adverse cutaneous reactions have been described following vaccination against COVID-19. This case report describes a reaction to the Pfizer-BioNTech (BNT162b2) vaccine that histopathologically resembles cutaneous lupus erythematosus with vacuolar interface alteration, superficial to mid-dermal perivascular and periadnexal lymphocytic infiltrate with clusters of CD123 positive cells, and mildly increased dermal mucin.

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[1] Currently resides at 1712 Southwest Ave Apt 106, Johnson City, TN 37604

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Main Text

Introduction

Several adverse cutaneous reactions have been reported following both infection with SARS-CoV-2 (COVID-19) and vaccination against COVID-19. This case report describes an additional adverse cutaneous reaction pattern after administration of the Pfizer-BioNTech COVID-19 vaccine, which histopathologically resembles cutaneous lupus erythematosus

Case Report

A 33-year-old Fitzpatrick skin type V woman with no significant past medical history presented for evaluation of a rash that appeared within hours of the administration of the second dose of the BNT162b2 COVID-19 BioNTech-Pfizer vaccine. There was annular edema and erythema around the injection site that was associated with significant tenderness that resolved after two days. She subsequently developed a pruritic rash with a different morphology that began at the injection site but continued to spread over her arm and became more intensely pruritic over the next six weeks. Betamethasone dipropionate 0.05% ointment led to resolution, but the rash recurred within days of its discontinuation. She then developed similar-appearing lesions on the anterior and posterior trunk. Review of systems was unremarkable. There were erythematous and hyperpigmented, mildly edematous papules with no overlying scale, coalescing into flat-topped plaques on the left lateral arm, at the injection site (Figure 1). There was patchy hyperpigmentation in a similar distribution on her left upper back and central abdomen. A punch biopsy of the left lateral arm demonstrated vacuolar interface alteration with superficial and mid-dermal perivascular and periadnexal lymphocytes (Figures 2, 3, and 4). A special stain for colloidal iron showed mildly increased dermal mucin (Figure 5), and a special stain for periodic

acid-Schiff showed no significant increase in thickness of the basement membrane (not shown). An immunostain for CD123 demonstrated clusters of positive cells within the infiltrate (Figure 6). Eosinophils were not identified. Treatment with fluocinonide 0.05% ointment led to complete resolution after four weeks. Anti-nuclear antibodies were negative. The patient was re-evaluated nine months after the initial onset, and she remains symptom-free but has not received a COVID-19 booster due to concern for a flare of similar cutaneous symptoms.

Discussion

There is a wide variety of clinical and histopathologic reactions reported after administration of the various COVID-19 vaccinations, including several describing a lichenoid reaction pattern (Table 1).[1,2] The immunogenicity of the spike protein for both the COVID-19 virus and the vaccines is suspected to be responsible for the development of adverse cutaneous reactions.[3] To our knowledge, there have been no significant comparison studies that determine predisposition for a specific adverse cutaneous reaction based on the brand of vaccine administered. However, women seem disproportionately affected by adverse cutaneous reactions from the Pfizer-BioNTech, Moderna (mRNA-1273), and AstraZeneca (AZD1222) COVID-19 vaccines. In two separate studies, 90% of reactions to the Moderna vaccine were seen in women.[3,4] Additionally, women represented 69.9% and 82.1% of patients with adverse cutaneous reactions to Pfizer and AstraZeneca vaccines, respectively.[3] We theorize these statistics are related to women having increased rates of autoimmunity and drug reactions in general.[5]

There is reported overlap in the immune response that occurs during COVID-19 infection, after the RNA-based COVID-19 vaccines, and in the autoimmunity of systemic lupus erythematosus (SLE), including its cutaneous manifestations.[5,6] All produce an immune response with increased production of type I interferon (IFN) by plasmacytoid dendritic cells.[5] Interestingly,

people of African heritage have increased expression of type I IFN compared to other ethnicities, and this is thought to be the reason SLE occurs more frequently in this group of patients.[5] Because our patient is of African descent, she may have increased expression of type I IFN at baseline, supported by the presence of CD123-positive plasmacytoid dendritic cells in the biopsy, and this may have led to the adverse cutaneous reaction she experienced. More population-based studies are necessary to determine if adverse cutaneous reactions with this pattern are indeed more frequent in different ethnic groups or if the reaction is secondary to viral proteins alone. This case adds to the broad range of cutaneous reactions secondary to COVID-19 vaccination. Because this patient did not develop any life-threatening symptoms and was effectively managed with topical corticosteroids, this type of reaction should not prevent patients from completing the vaccine series or from receiving recommended boosters.

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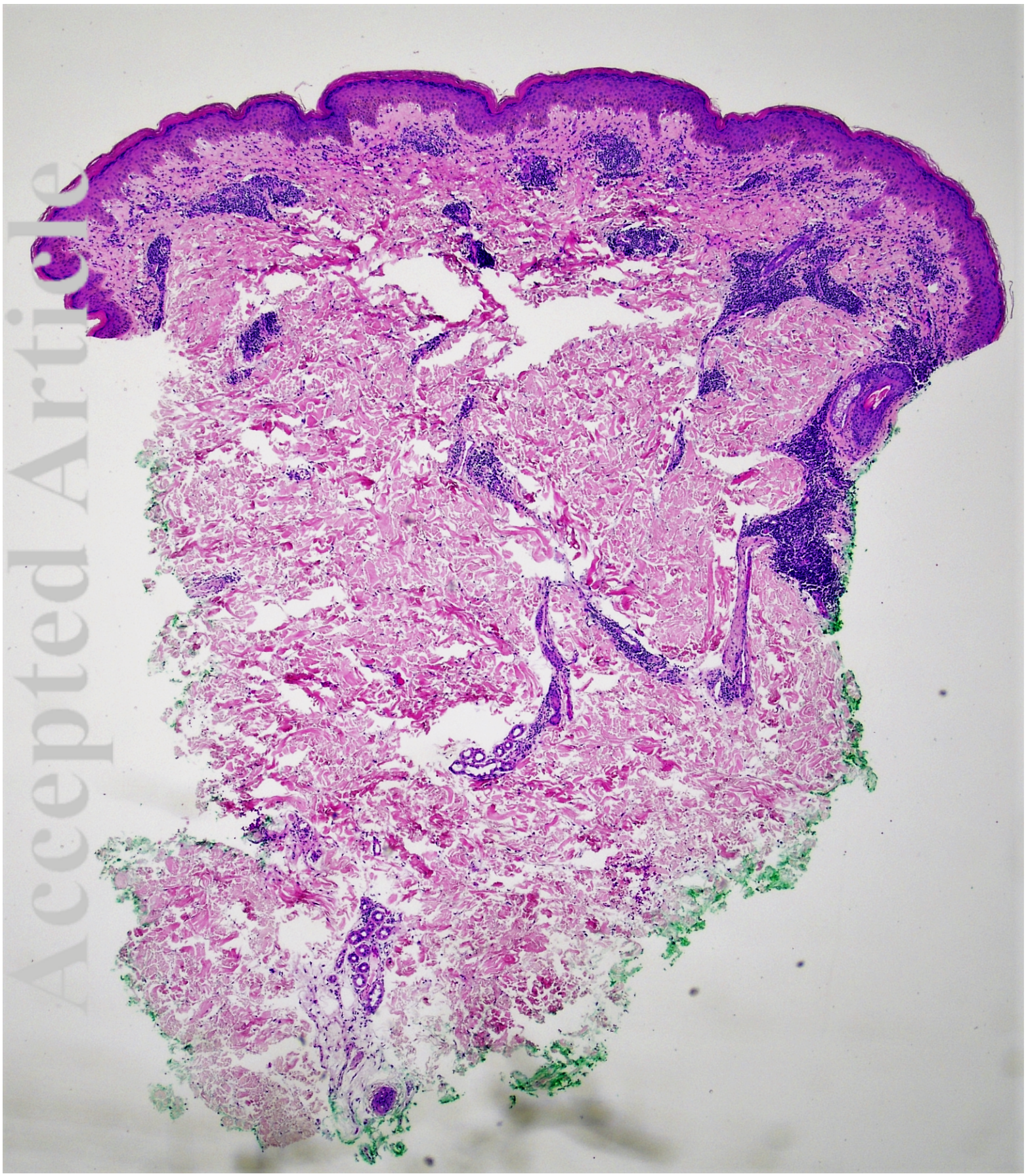

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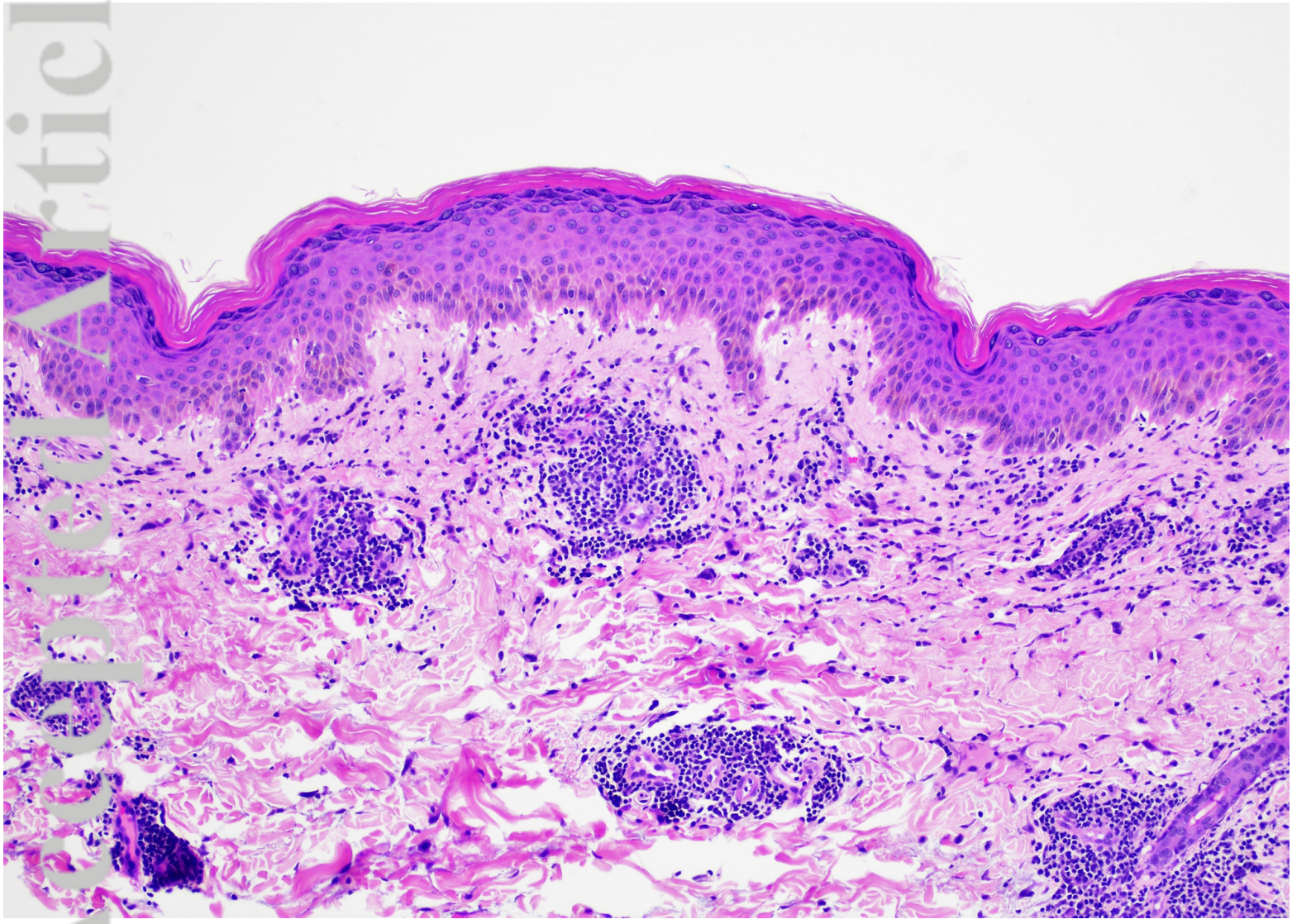

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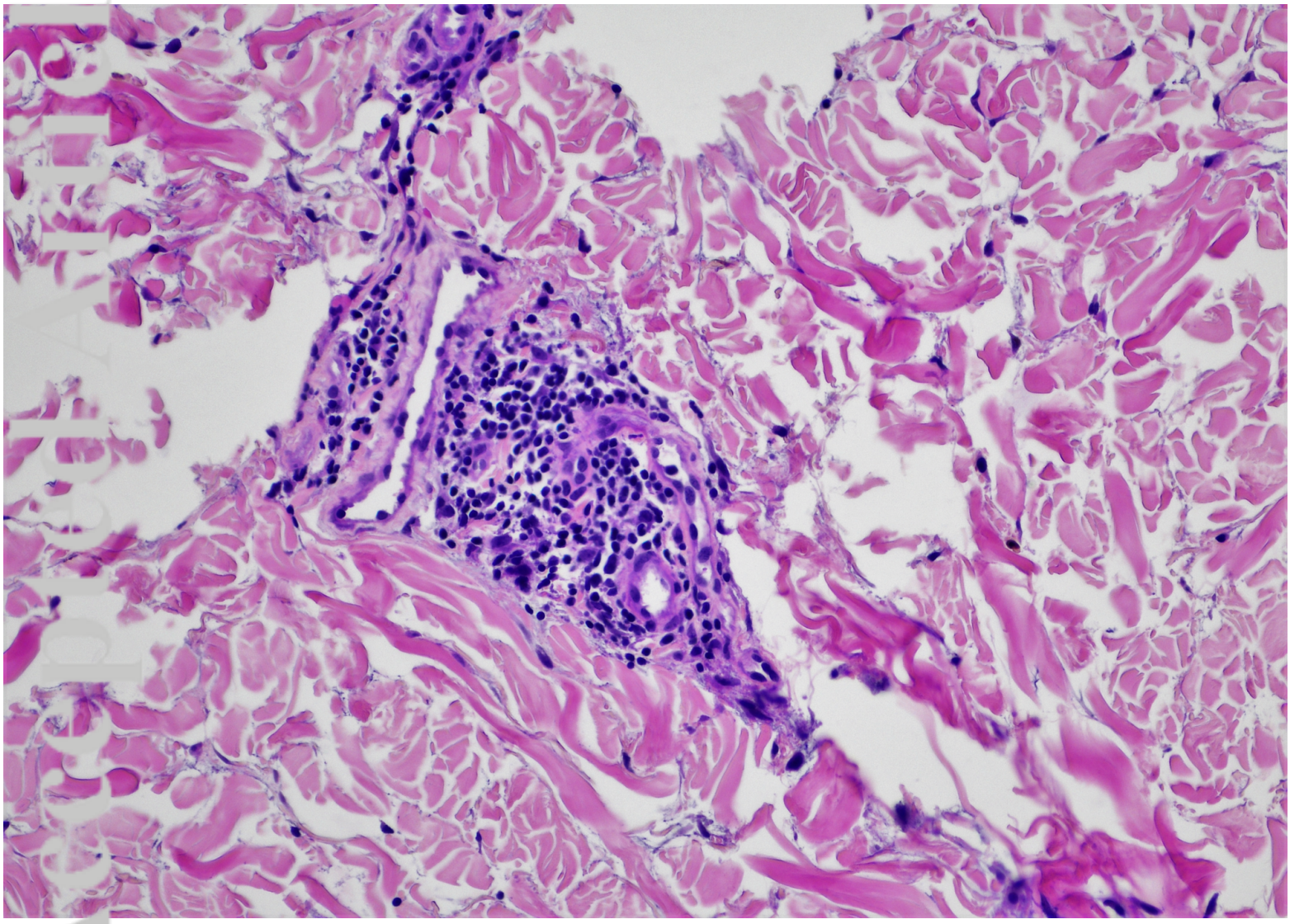

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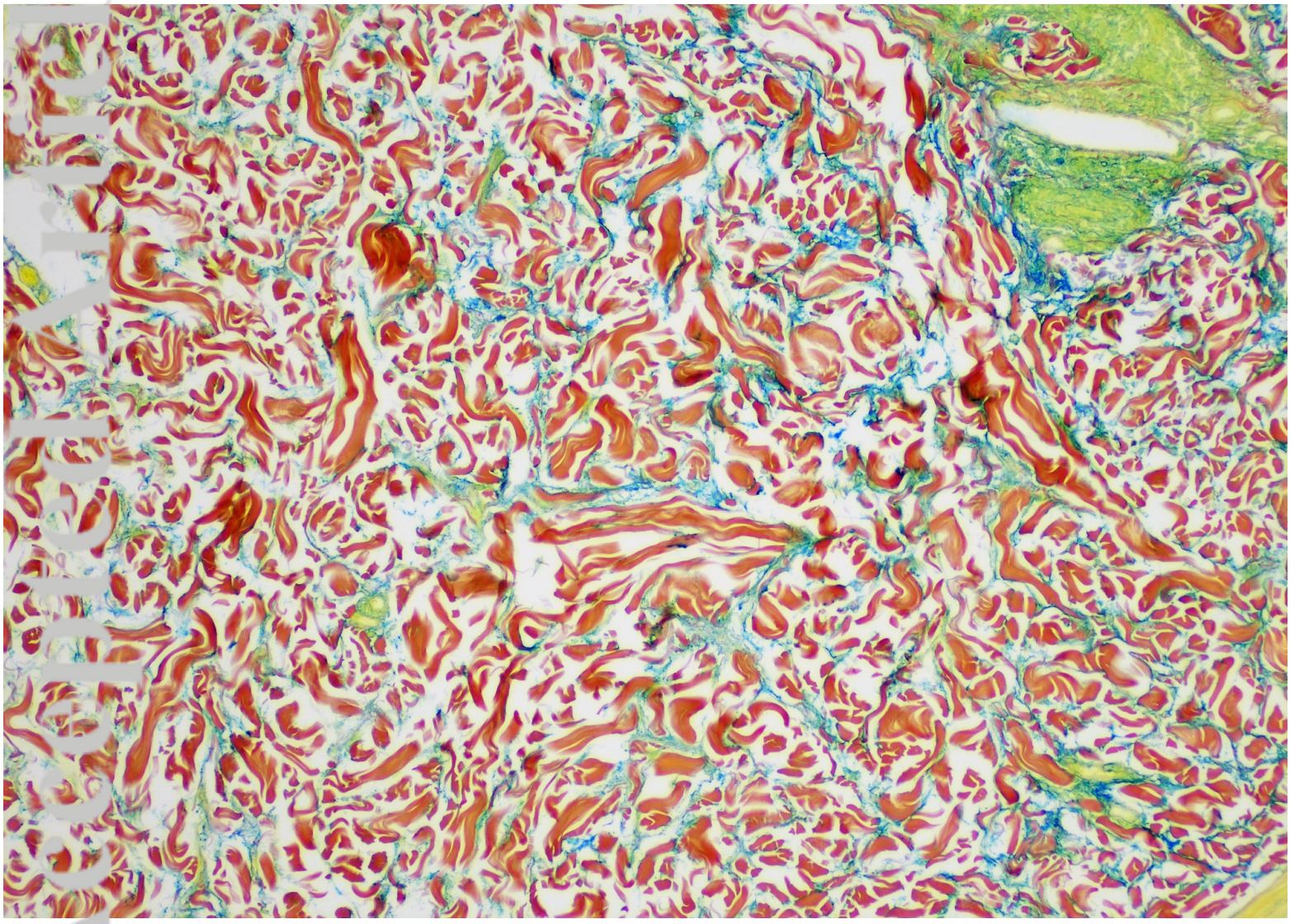

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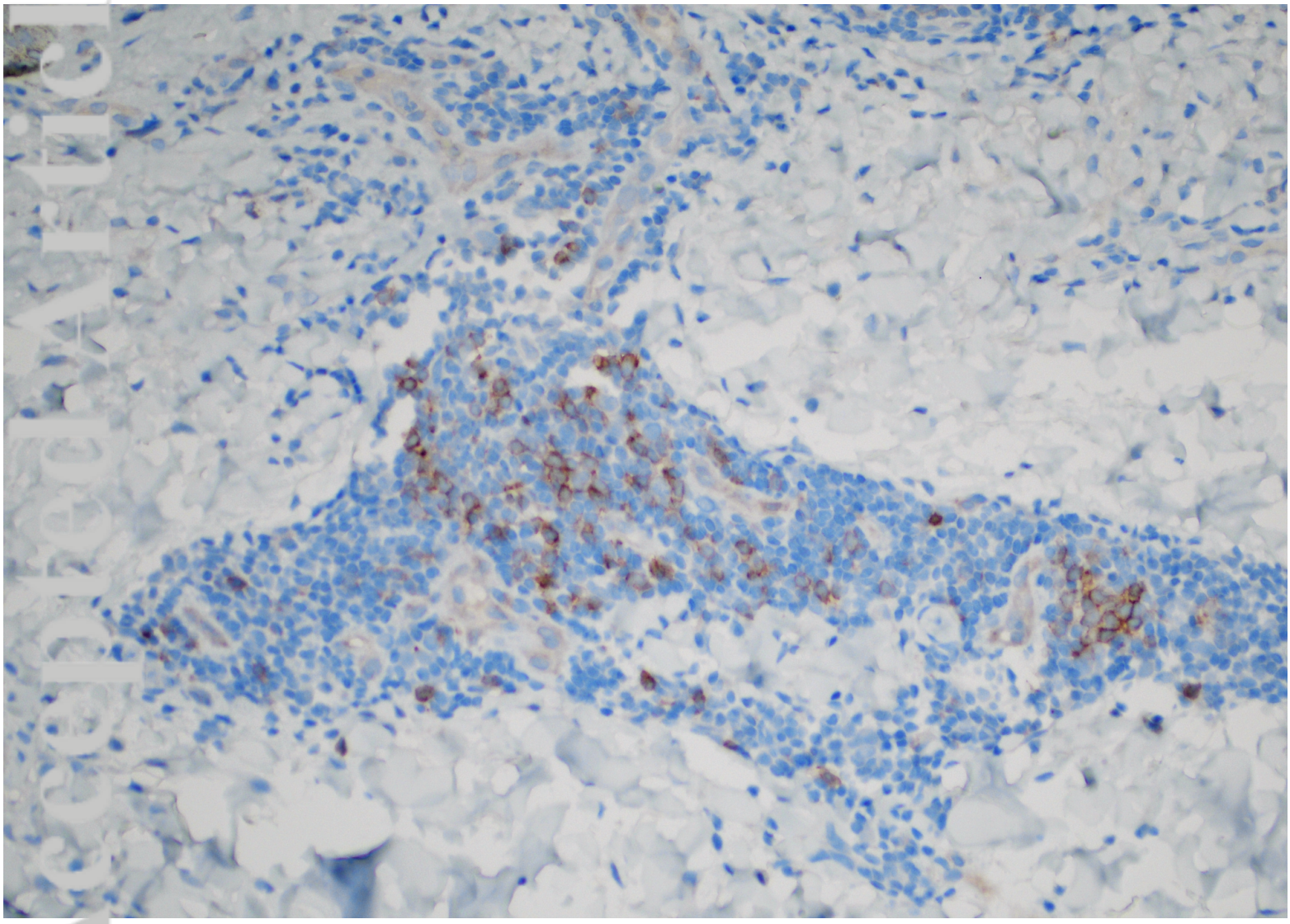

CUP_14281_Figure 6 (2).tif

Figure Legends:

Figure 1: Clinical photograph of the left arm, six weeks after vaccination.

Figure 2: This low magnification section shows superficial to mid-dermal perivascular and periadnexal lymphocytes. There is very scant deep peri-eccrine inflammation (hematoxylin and eosin, 20x).

Figure 3: Higher magnification of the superficial portion of the biopsy demonstrates vacuolar interface alteration and moderately brisk superficial perivascular and periadnexal lymphocytes (hematoxylin and eosin, 100x).

Figure 4: Higher magnification of the mid-dermis highlights the perivascular collections of lymphocytes. Spaces between the collagen and dermal mucin are evident (hematoxylin and eosin, 100x).

Figure 5: A special stain for colloidal iron highlights a mild increase in mid- to deep-dermal mucin (100x).

Figure 6: An immunostain for CD123 demonstrates clusters of positive plasmacytoid dendritic cells within the superficial infiltrate (200x).

Reference	Vaccine	Clinical Presentation	Histopathologic features	Treatment	Resolution
Current case	Pfizer	Erythematous and hyperpigmented, mildly edematous papules with no overlying scale, coalescing into flat-topped plaques	Vacuolar interface alteration, superficial to mid-dermal perivascular and periadnexal lymphocytic infiltrate with clusters of CD123 positive cells, and mildly increased dermal mucin	Topical corticosteroid	40 days
Annabi E, Dupin N, Sohier P, et al. 2021;35(12): e847-e850.	Pfizer	Erythematous indurated nodules/chilblains	NA / papillary dermal oedema, superficial and deep perivascular and perieccrine lymphocytic infiltrate	NA	7 days
	Pfizer	Diffuse erythematous rash (80% of BSA)	Vacuolar interface dermatitis, spongiosis, perivascular superficial lymphocytic infiltrate	Topical corticosteroid, phototherapy	Unknown
	Pfizer	Livedo racemosa of thighs	Epidermal dysmaturation, vacuolization of basal keratinocytes, apoptotic cells	NA	Persistence of post-inflammatory pigmented lesions at 2 months
	Moderna	Fixed drug eruption	Vacuolar interface dermatitis, perivascular superficial	Topical corticosteroid	5 days

			lymphocytic infiltrate with numerous eosinophils		
	Astra Zeneca	Diffuse maculopapular pustular exanthema (>80% of BSA)	Lichenoid interface dermatitis, intracorneal pustules, lymphocytic infiltrate with numerous eosinophils	Topical corticosteroid	30 days
Català A, Muñoz-Santos C, Galván-Casas C, et al. 2022;186(1): 142-152.	Moderna	Multiple red and indurated plaques at injection site	Perivascular and interstitial mixed-cell infiltrate with eosinophils and focal interface changes	Not reported	Unknown
	Moderna	Generalized, pruritic, morbilliform and PR-like	Perivascular lymphocytic infiltrate with vacuolar interface changes	Topical corticosteroid and antihistamines	Unknown
	Pfizer-BioNTech	Generalized eruption on trunk and extremities	Mixed-cell infiltrate with eosinophils, epidermal spongiosis, and vacuolar interface changes	Topical corticosteroid	Unknown
	Moderna	Generalized psoriasiform eruption	Perivascular mixed-cell infiltrate with eosinophils, papillary dermal edema, and vacuolar interface changes	Topical corticosteroid	Unknown

Table 1 : Summary of cases with reported lichenoid interface changes on histopathology.