

UC Davis

Dermatology Online Journal

Title

A patient with anti-NXP2-positive dermatomyositis and syphilis

Permalink

<https://escholarship.org/uc/item/0783v3nx>

Journal

Dermatology Online Journal, 26(2)

Authors

Nguyen, Mimi
Hai, Josephine
Bovenberg, Maria Sarah Sophie
[et al.](#)

Publication Date

2020

DOI

10.5070/D3262047413

Copyright Information

Copyright 2020 by the author(s). This work is made available under the terms of a Creative Commons Attribution-NonCommercial-NoDerivatives License, available at <https://creativecommons.org/licenses/by-nc-nd/4.0/>

Peer reviewed

A patient with anti-NXP2-positive dermatomyositis and syphilis

Mimi Nguyen¹ BS, Josephine Hai¹ BS, Maria Sarah Sophie Bovenberg² MD, Reason Wilken² MD, Maija Kiuru² MD PhD, Alain Brassard² MD FRCPC, Danielle Tartar² MD PhD

Affiliations: ¹School of Medicine, University of California Davis, Sacramento, California, USA, ²Department of Dermatology, University of California Davis, Sacramento, California, USA

Corresponding Author: Danielle Tartar MD, PhD, 3301 C Street, Suite 1400, Sacramento, CA 95816, Tel: 916-734-7463, Email: dtartar@ucdavis.edu

Abstract

Dermatomyositis is an auto-immune inflammatory myopathy that primarily affects the skin and muscle and can be triggered by exposure to various environmental factors. We present a patient with active syphilis infection who developed dermatomyositis and discuss the significance of anti-NXP2 autoantibody positivity.

Keywords: dermatomyositis, syphilis, infection

Introduction

Dermatomyositis (DM) is a multisystem autoimmune disorder that can be triggered by exposure to various environmental factors such as UV light, medications, drug use, infections, and malignancy and can be part of an overlap syndrome. The exact reasons for susceptibility to develop DM are unknown but there could be a genetic predisposition. Classically, DM presents with symmetrical proximal muscle weakness, and characteristic cutaneous manifestations, such as heliotrope rash and Gottron papules. Various clinical phenotypes have been described and are associated with specific autoantibodies [1]. To date, syphilis has only been associated with myositis and not with the clinical findings that are strikingly specific for DM. We present a case of anti-NXP-2-positive DM in the setting of an active syphilis infection.

Case Synopsis

A 28-year-old man was admitted to the hospital for weight loss, rash, anasarca, and generalized body pain and weakness. Two months prior to admission, he developed a rash that began on his bilateral knees that progressed to the arms, neck, chest, abdomen, and back. He reported discomfort from “tense” skin but denied any itching. During this time, he also experienced migrating joint pain in his knees and wrists and muscle weakness that was more significant proximally than distally. Additionally, he reported considerable fatigue, subjective fevers, diffuse swelling, and increasing difficulty swallowing.

His history was notable for a diagnosis of syphilis, for which he was treated with IM penicillin G benzathine

Abbreviations

CCP	cyclic citrullinated peptide
DM	dermatomyositis
dsDNA	double-stranded deoxyribonucleic acid
ESR	erythrocyte sedimentation rate
H/E	hematoxylin and eosin
HIV	human immunodeficiency virus
HTLV	human T-lymphotropic virus
IgG	immunoglobulin G
IgM	immunoglobulin M
NXP-2	nuclear matrix protein 2
PAS	Periodic acid–Schiff
PR3	proteinase 3
RNP	ribonucleoprotein
RPR	rapid plasma reagin
Sm	Smith

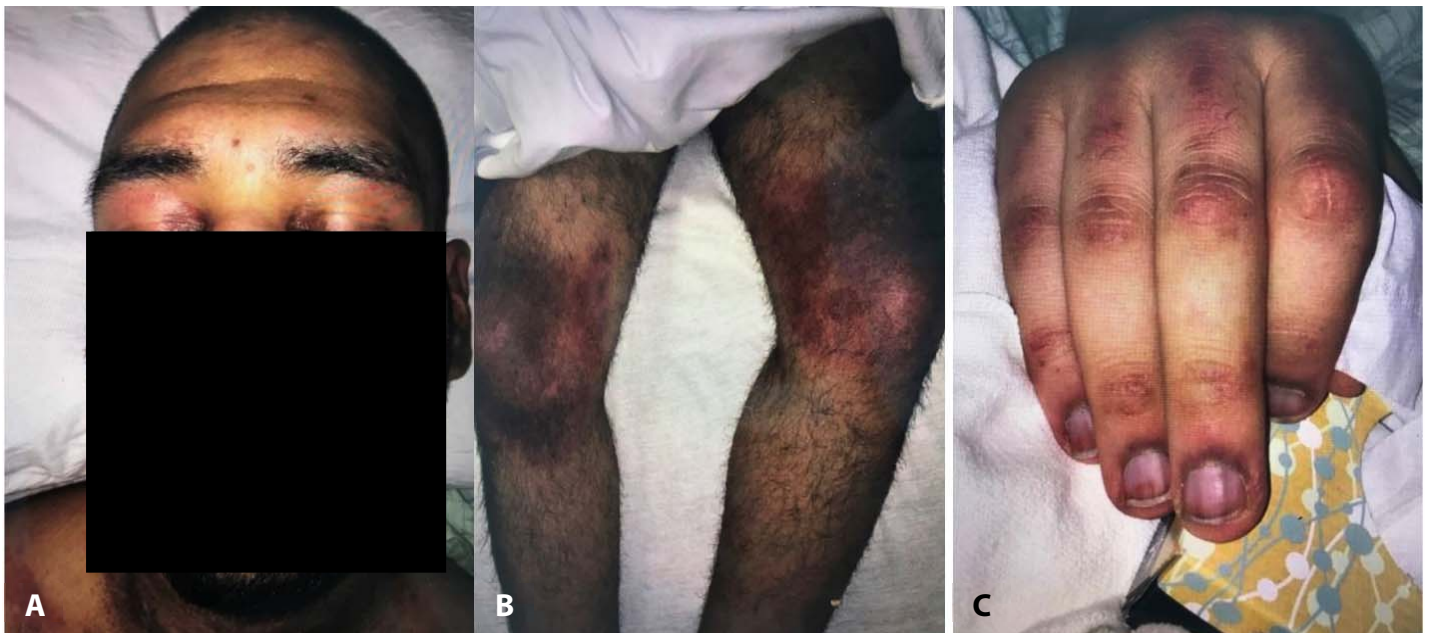


Figure 1. Physical examination findings of **A)** violaceous erythema over the eyelids (heliotrope rash), **B)** erythematous patches over the bilateral knees (Gottron sign), and **C)** erythematous patches over the metacarpophalangeal and interphalangeal joints (Gottron papules).

while in prison 10 months prior., He was sexually active with one female partner and had previously used methamphetamine, cocaine, and marijuana. He had no previous or family history of autoimmune diseases.

On physical examination, he exhibited generalized muscle weakness that was more prominent in the proximal muscles. On skin exam, he was found to have violaceous erythema over the eyelids (**Figure 1A**), erythematous, hyperpigmented patches with superficial erosion on the chest, back, and upper shoulders, and erythematous patches over the bilateral knees (Gottron sign; **Figure 1B**), metacarpophalangeal joints, and interphalangeal joints (Gottron's papules; **Figure 1C**).

A punch biopsy taken from the patient's chest showed sparse perivascular dermatitis with increased mucin and focal basement membrane thickening on H/E stain (**Figure 2A**), supporting the clinical impression of DM. Colloidal iron staining (**Figure 2B**) and PAS staining (**Figure 2C**) further highlighted the increased mucin and limited basement membrane thickening, respectively. Magnetic resonance imaging of the musculature of the bilateral thighs revealed diffuse bilateral myositis, also consistent with DM.

Additional physical examination findings of moth-eaten alopecia (**Figure 3**), mucous patch at the oral commissure, diffuse lymphadenopathy, and syphilitic penile chancre, along with positive rapid plasma reagin (RPR), (1:16) and syphilis IgM/IgG raised the possibility of active syphilis despite past treatment. His HIV screen was negative. Punch biopsies performed on the scalp and abdomen showed granulomatous and lymphoplasmacytic infiltrate, but stains for spirochetes, bacteria, mycobacterial, and fungal pathogens were negative. The patient was treated for active late-stage syphilis with a single dose of intramuscular penicillin G 2.4 MU.

Rheumatological evaluation revealed elevated PR3 and ESR, along with positive anti-nuclear, anti-Ro/SSA, dsDNA, chromatin, and Sm/RNP antibodies. Serology was negative for myeloperoxidase 3, rheumatoid factor, CCP, centromere, Jo-1, Scl-70, and anti-La/SSB antibodies. An extended DM panel later revealed the presence of anti-NXP2 antibodies.

Out of concern for syphilitic myositis, prednisone was delayed until a muscle biopsy was done. Muscle biopsy of the left thigh showed significant perifascicular atrophy and predominantly perivascular mononuclear inflammatory infiltrates.

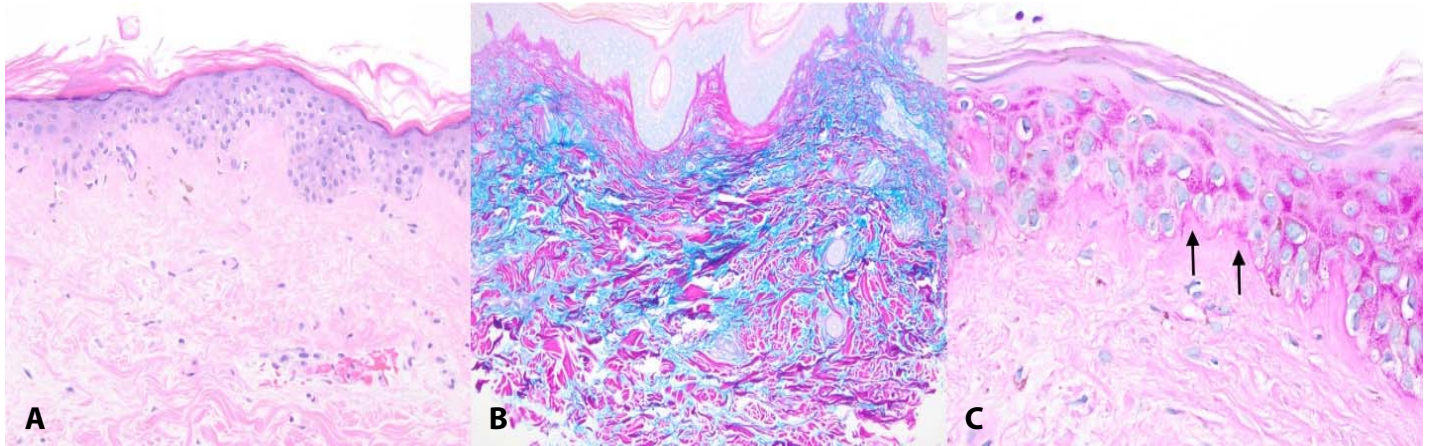


Figure 2. Skin, right chest (punch biopsy). **A)** Sparse perivascular dermatitis with increased mucin and focal basement membrane thickening, consistent with dermatomyositis, H&E, 100 \times . **B)** Colloidal iron stain highlighting increased mucin, which stains blue, 100 \times . **C)** Periodic acid-Schiff stain revealing limited basement membrane thickening (black arrows), 400 \times .

This was more consistent with DM, rather than syphilis-induced myositis, so the patient was initiated on prednisone, hydroxychloroquine, and trimethoprim/sulfamethoxazole for pneumocystis pneumonia prophylaxis.

The patient was discharged after about two weeks in the hospital. Ten days after discharge, he noted improved dysphagia, muscle strength, and hair growth, but continued to have pruritis on his hands, scalp, and knees.

Case Discussion

Dermatomyositis is an auto-immune inflammatory myopathy that primarily affects the skin and muscle. It is believed that environmental triggers in genetically susceptible individuals result in circulating autoantibodies that lead to complement deposition in the endothelium of blood vessels to the skin and muscle. This eventually causes inflammation and necrosis of the blood vessels and the supplied structures [2].

Although there have been cases of syphilitic myositis, syphilitic infection has never been previously reported as a trigger for dermatomyositis [3, 4]. Reported viral triggers of DM include coxsackieviruses, parvoviruses, enteroviruses, human T-lymphotropic virus (HTLV), and human immunodeficiency virus (HIV), [5]. Our patient was treated for syphilis while in prison and presented 10

months later with classic findings of DM, including symmetric proximal muscle weakness, heliotrope rash, Gottron papules and sign, dysphagia, and polyarthralgia [2]. However, given his history of syphilis and positive titers, syphilitic myositis was considered, and prednisone was held until it was ruled out by muscle biopsy. The presence of diffuse lymphadenopathy raised the concern of secondary-to-late stage syphilis versus DM-associated malignancy. Importantly, 20-25% of DM cases are associated with a coexisting malignancy discovered before, during, or after development of symptoms —



Figure 3. Moth-eaten alopecia of the scalp.

most frequently, solid organ malignancies, including adenocarcinomas, and lymphomas [2, 6]. In our patient, lymph node biopsy was consistent with a reactive rather than malignant process, supporting the diagnosis of active infection with syphilis.

Our patient's rheumatology workup was positive for the presence of anti-NXP2, an autoantibody specific for dermatomyositis. NXP2 is a nuclear matrix protein involved in the regulation of the p53-induced cellular apoptosis in response to oncogenic signals [1, 7]. Antibodies to NXP2 have been reported in up to 30% of cases of juvenile and adult dermatomyositis and is associated with distal weakness, more severe myalgias, peripheral edema, and a higher risk of dysphagia — the latter three of which were characteristics observed in our patient [8]. Although patients may have classic skin findings such as Gottron papules and heliotrope rash, anti-NXP2-positive DM patients tend to have less severe skin manifestations [1]. Other distinct characteristics associated with the NXP2 autoantibody include an increased risk of calcinosis cutis, which was not observed in our patient [1].

References

1. Tartar DM, Chung L, Fiorentino DF. Clinical significance of autoantibodies in dermatomyositis and systemic sclerosis. *Clin Dermatol*. 2018;36:508-24. [PMID: 30047434].
2. Bogdanov I, Kazandjieva J, Darlenski R, Tsankov N. Dermatomyositis: current concepts. *Clin Dermatol*. 2018;36:450-8. [PMID: 30047429].
3. Durston JH, Jefferiss FJ. Syphilitic myositis. *Br J Vener Dis*. 1975;51:141-2. [PMID: 1131681].
4. Yacyshyn E, Chiowchanwisawakit P, Emery DJ, et al. Syphilitic myositis: a case-based review. *Clin Rheumatol*. 2011;30:729-33. [PMID: 21210290].
5. Zampieri S, Ghirardello A, Iaccarino L, et al. Polymyositis-dermatomyositis and infections. *Autoimmunity*. 2006;39:191-6. [PMID: 16769652].
6. Hill CL, Zhang Y, Sigurgeirsson B, et al. Frequency of specific cancer types in dermatomyositis and polymyositis: a population-based study. *Lancet*. 2001;357:96-100. [PMID: 11197446].
7. Ghirardello A, Borella E, Beggio M, et al. Myositis autoantibodies and clinical phenotypes. *Auto Immun Highlights*. 2014;5:69-75. [PMID: 26000158].
8. Rogers A, Chung L, Li S, Casciola-Rosen L, Fiorentino DF. Cutaneous and systemic findings associated with nuclear matrix protein 2 antibodies in adult dermatomyositis patients. *Arthritis Care Res (Hoboken)*. 2017;69:1909-14. [PMID: 28129490].

Conclusion

Autoimmune disease occurs in the setting of a complex interplay between environmental, genetic, and immune factors. Many environmental factors, including ultraviolet light, medications, drug use, infections, and malignancy have been reported to trigger autoimmune diseases, including dermatomyositis, in genetically and immunologically susceptible individuals. Several infections have been linked to the development of dermatomyositis, likely through immune activation, including influenza, borrelia, toxoplasmosis, and other viral infections. To our knowledge, syphilis has never been previously reported as a trigger for dermatomyositis. In our patient, it is possible that his syphilis infection was the environmental stressor that triggered DM in this genetically and immunologically susceptible patient, again highlighting the complex interplay between internal and external factors that drive autoimmune disease.

Potential conflicts of interest

The authors declare no conflicts of interests.