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Anetoderma before development of antiphospholipid antibodies: delayed development and monitoring of antiphospholipid antibodies in an SLE patient presenting with anetoderma

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Abstract

Introduction: Anetoderma is an elastolytic skin disorder that has been associated with the presence of antiphospholipid antibodies (aPL). Patients with antiphospholipid antibody-positive anetoderma have been reported to develop symptoms of Graves disease, antiphospholipid syndrome, and other autoimmune conditions. The temporal relationship, however, between anetoderma onset and the emergence of aPL remains unclear, a clarification of which may have implications for the screening and monitoring of patients with anetoderma. Case: Herein we report a case of a patient with systemic lupus erythematosus presenting with anetoderma that preceded the development of aPL. The patient was found to have subsequently developed IgM cardiolipin antibodies at a serology follow-up approximately two years later. Conclusion and Relevance: This finding suggests that anetoderma can precede aPL seroconversion and that patients with anetoderma may require continued serology monitoring. Such long-term monitoring will be important for identifying laboratory indications that may portend the development of further autoimmune symptoms associated with anetoderma.

Keywords: anetoderma, antiphospholipid antibodies, lupus erythematosus

Introduction

Anetoderma is an elastolytic disorder in which focal destruction of elastin in the dermis results in flaccid outpouching or depression of wrinkled skin around 1-2cm in size [1]. The loss in elastic fibers is demonstrated on histopathology by elastic stains such as the Verhoeff's elastic stain [5]. Typical locations include the trunk, shoulders, and proximal upper and lower extremities. Anetoderma is categorized into primary and secondary anetoderma. Primary anetoderma arises from clinically non-diseased skin or from skin affected by nonspecific inflammatory processes, whereas secondary anetoderma arises from diseased skin, most commonly at sites of varicella or acne lesions [1].

Case Synopsis

A 20-year-old woman with a four-year history of systemic lupus erythematosus (SLE) with associated Jaccoud arthropathy presented with progressive atrophic hypoelastic skin over the knuckles, and thin hypoelastic skin over the elbows and distal interphalangeal (DIP) joints of the feet, lasting for the past year (**Figure 1**).

The patient's SLE had been diagnosed based on characteristic malar rash, discoid skin lesions, joint involvement, episodes of recurrent pleurisy, and positive serologies consistent with lupus (ANA 1:2560, +dsDNA, and +Ro). Her SLE had been treated with systemic corticosteroids, methotrexate, azathioprine, belimumab, and at time of presentation, with mycophenolate mofetil, hydroxychloroquine, celecoxib, and methylprednisolone for a recent flare. Her SLE had otherwise been quiescent.

The hypoelastic lesions that had developed over the past year were preceded by eruptive lesions that were pink, flat, and firm, per patient report. As described,

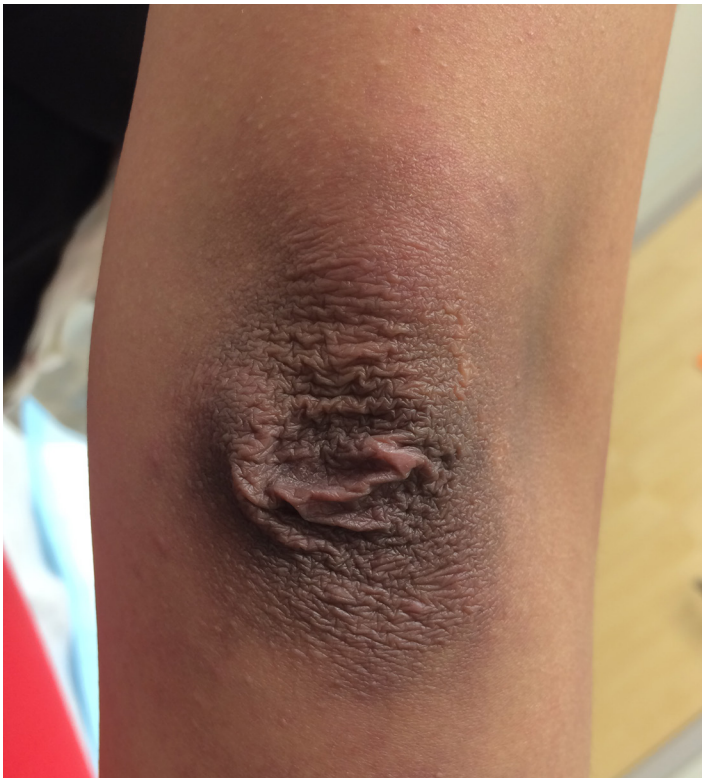

Figure 1. *Area of elbow after rapid loss of elasticity*

the pink eruptive lesions erupt and resolve, lasting a few weeks each episode, but leave the underlying skin flaccid and wrinkled, resulting in the hypoelastic lesions. The patient reports that the hypoelastic skin is not painful or pruritic.

Notable on physical exam was thin, atrophic, and hypoelastic skin over the knuckles, elbows, and DIP joints of the feet. As well, there was an 8-millimeter pink, blanchable patch on the right wrist that was positive for dermatographism.

Relevant laboratory included a positive ANA titer at 1:2560, positive anti-dsDNA at 1:10, and positive anti-Ro at 100.19. Anti-La, anti-Smith, anti-RNP antibodies were negative. CRP, ESR, C3, and C4 were all within normal limits.

A biopsy of the representative hypoelastic skin over the elbow was performed and showed dermal edema and elastic fiber loss (**Figure 2**). The elastic fiber loss was confirmed by Verhoeff's elastic stain (**Figure 3**). A diagnosis of anetoderma involving the elbows and digits was made.

Given the association of primary anetoderma with antiphospholipid antibodies (aPL) in SLE, we

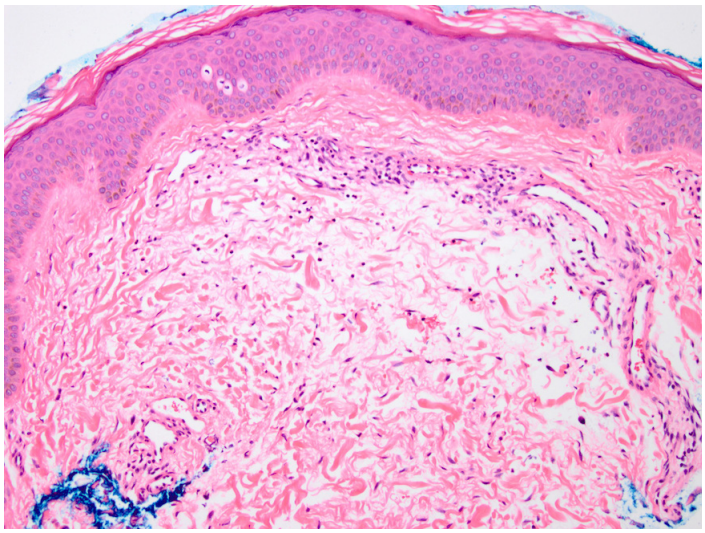

Figure 2. *Histology of involved skin over the elbow: Histologic section of the involved skin over the elbow shows mild perivascular infiltrate of lymphocytes and dermal edema (original magnification x 200, Hematoxylin and eosin stain).*

subsequently tested the patient for antiphospholipid antibodies (aPL) and found that the patient was negative for lupus anticoagulant and anticardiolipin antibodies IgM and IgG. However, at a serology follow-up approximately two years later, it was found that the patient went on to develop anticardiolipin IgM antibodies.

At the time of diagnosis, the anetoderma appeared to occur at sites of urticaria-like skin lesions, accounting for the patient's report of pink firm eruptive lesions that resulted in the hypoelastic skin. As such, the patient was started on topical mometasone for calming of the urticarial papules and was given

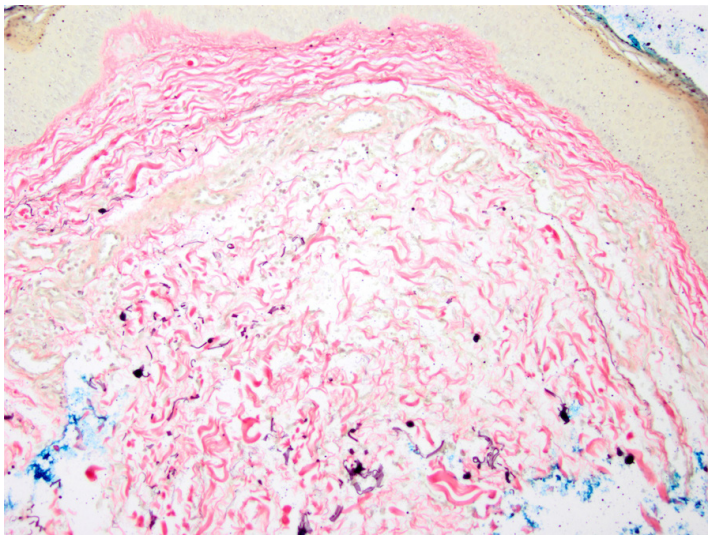

Figure 3.*Verhoeff's elastic stain of involved skin over the elbow: Elastic stain demonstrates loss of dermal elastic fibers (original magnification x200, Verhoeff's elastic stain).*

the option of anti-histamines to prevent urticarial outbreaks, thereby preventing further elastin loss and anetoderma development. The patient has so far responded well to treatment.

Case Discussion

The pathophysiology of anetoderma is unclear, although an immunologic mechanism has been suspected. Historically, anetoderma has been associated with several autoimmune diseases, most notably SLE [1]. However, it was suggested that anetoderma was more directly associated with the presence of antiphospholipid antibodies (aPL) as opposed to the presence of SLE [1-4, 6-7]. Specifically, Stephansson et al. found that anetoderma was associated with aPL-positive patients with or without SLE [1-3]. Furthermore, Hodak et al. showed that patients with anetoderma can go on to develop clinical symptoms associated with several autoimmune disorders including Graves disease, Hashimoto thyroiditis, alopecia areata, autoimmune hemolysis, systemic scleroderma, and antiphospholipid syndrome (APS). These patients were positive for aPL [4].

However, the temporal relationship between anetoderma onset and the presence of aPL remains unclear. It is unclear whether the presence of aPL causes elastic fiber destruction and anetoderma, and if so what the mechanism may be [7]. Herein, we report a case of anetoderma in a patient with SLE, who, around the time of anetoderma presentation, was negative for aPL but who later went on to develop aPL (IgM anticardiolipin). This finding suggests that anetoderma can precede aPL serologic conversion and that aPL may not necessarily cause anetoderma. However, the presence of anetoderma may portend possible development of aPL along with subsequent associated autoimmune symptoms. Our case report reinforces the need to be cognizant of the possible development of anetoderma lesions in patients with autoimmune conditions such as SLE. Importantly, however, our case demonstrates the possible temporal relationships between anetoderma and aPL – that anetoderma can precede the development of aPL. The case therefore suggests that continued monitoring of aPL serology in patients with anetoderma regardless of initial serology will be important - as such monitoring may provide us with early warning signs of future symptoms of autoimmunity.

References

1. Hodak E, David M. Primary anetoderma and antiphospholipid antibodies--review of the literature. Clinical reviews in allergy & immunology. Apr 2007;32(2):162-166. PMID: 17916987
2. Stephansson EA, Niemi KM, Jouhikainen T, Vaarala O, Palosuo T. Lupus anticoagulant and the skin. A longterm follow-up study of SLE patients with special reference to histopathological findings. Acta dermato-venereologica. 1991;71(5):416-422. PMID: 1684471
3. Stephansson EA, Niemi KM. Antiphospholipid antibodies and anetoderma: are they associated? Dermatology. 1995;191(3):204-209. PMID: 8534938
4. Hodak E, Feuerman H, Molad Y, Monselise Y, David M. Primary anetoderma: a cutaneous sign of antiphospholipid antibodies. Lupus. 2003;12(7):564-568. PMID: 12892400
5. Thornsberry LA, LoSicco KI, English JC. The skin and hypercoagulable states. Journal of the American Academy of Dermatology. 2013 Sep 30;69(3):450-62. PMID: 23582572
6. Staiger H, Saposnik M, Spiner RE, Schroh RG, Corbella MC, Hassan ML. Primary anetoderma: a cutaneous marker of antiphospholipid antibodies. Skinmed. 2011;9(3):168. PMID: 21675496
7. Eungdamrong J, Fischer M, Patel R, Meehan S, Sanchez M. Anetoderma secondary to antiphospholipid antibodies. Dermatology online journal. 2012 Dec 1;18(12). PMID: 23286816