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Pregnancy-associated morphea: a case report and literature review

Anh Khoa Pham[1,2], Bhaskar Srivastava[3], April Deng[4]

Affiliations: [1] Department of Internal Medicine, Saint Vincent Hospital, Worcester, MA, [2] Section of Dermatology, Department of Surgery, Dartmouth-Hitchcock Medical Center, Lebanon, NH, [3]Yale School of Medicine, [4]Department of Pathology, University of Massachussetts Medical School, Worchester, MA

Corresponding Author: A. Khoa Pham MD, Section of Dermatology, Department of Surgery, Dartmouth-Hitchcock Medical Center, 1 Medical Center Rd., Lebanon, NH 03756, Email: anh.k.pham@hitchcock.org

Abstract

Morphea, also known as localized scleroderma, is a rare fibrosing disorder of the skin, the pathogenesis of which is incompletely understood. It is thought, however, to involve interplay of genetic disposition and triggering environmental factors, such as infections and autoimmunity. Pregnancy as a potential trigger has only been reported in four cases. Herein, we present a patient who developed morphea of the breasts during pregnancy, which rapidly resolved with a normal delivery. Our patient was distinct from some of the reported patients because her condition was tightly correlated with her pregnancy, as judging by rapid resolution after delivery. In addition, there was no apparent infection, history of autoimmunity, or development of autoimmunity during or after pregnancy. Although the pathogenesis of pregnancy-associated morphea is largely unknown, we explored potential mechanisms of this condition, which may involve mechanical injury, "microchimerism," and shifts in intrapartum hormones, such as TGF-β.

Introduction

Morphea, also known as localized scleroderma, is a rare fibrosing disorder of the skin and underlying tissue derived from the mesoderm. The pathogenesis of morphea is incompletely understood, but is thought to involve interplay of genetic disposition and triggering environmental factors. Disposing factors include autoimmune diathesis and possibly the presence of microchimerism. Reported environmental triggers include trauma, radiation, vaccination, and infection. Molecularly, the development of morphea is thought to begin with microvascular injury that leads to recruitment of immune cells generating a pro-fibrotic microenvironment.

Pregnancy has rarely been reported as a triggering factor for morphea. We report a patient that developed morphea of her breasts during pregnancy. This condition resolved rapidly after she gave birth. We hypothesize that pregnancy may cause mechanical and immunological changes that support the development of morphea.

Case Synopsis

Our patient was a 22 year-old G1P0 woman who presented to our office at 7 months gestation complaining of skin thickening on the breasts. This had been going on for 3-4 months. It started shortly after the patient found out she was pregnant and affected the inner aspect of both breasts. The changes had been slowly progressing but were not symptomatic. Ultrasound performed at 5 months gestation showed only skin thickening; trauma from bra wiring was hypothesized to be the cause.

Her past medical history was significant for alpha-thalassemia with anemia, gastroesophageal reflux disease, asthma, and eczema. Six months prior to becoming pregnant, the patient had been diagnosed with latent tuberculosis as judged by a positive tuberculin skin test and a negative chest X ray. She had begun isoniazid therapy, which she was on for three months before finding out she was pregnant, at which time she discontinued the treatment. Her only active medications included ranitidine and prenatal vitamins. She denied a history of Raynaud phenomenon or any family history of morphea or other autoimmune disorders. She denied any

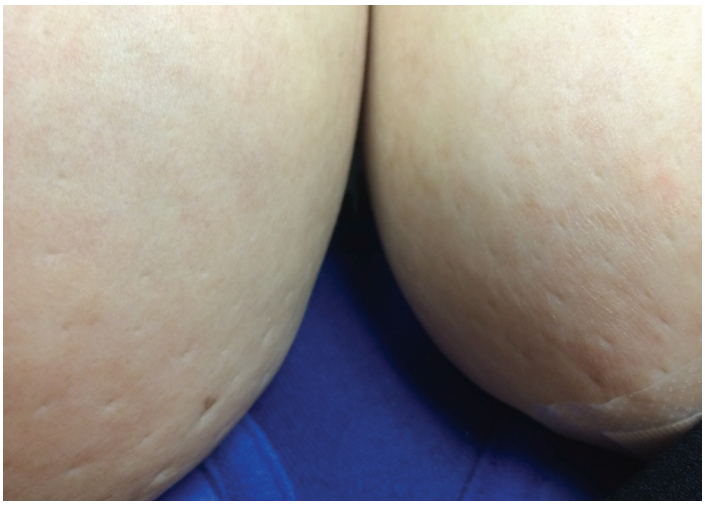

Figure 1. *Initial presentation with indurated, skin-colored plaques on the bilateral medial breasts. Patulous hair follicles and slight peau d'orange changes are evident.*

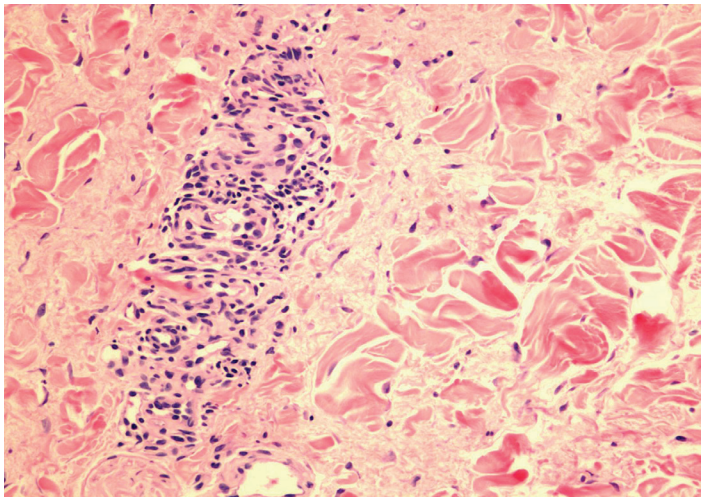

Figure 3. *A high-power magnification demonstrating perivascular lymphocytic infiltrates and thick collagen. H&E, 200x.*

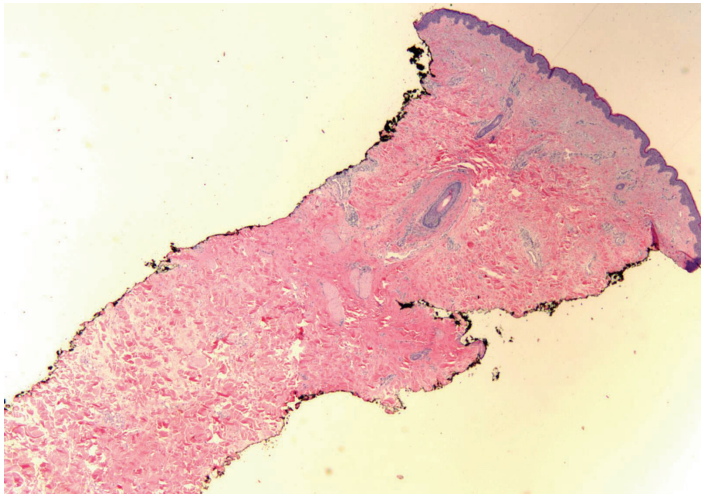

Figure 2. *A scanning view of the biopsy demonstrating an unremarkable epidermis and superficial dermis, but markedly thickened dermis and loss of subcutaneous fat. Increased dermal fibroblasts, vascular proliferation and ectasia were also observed. H&E, 20x.*

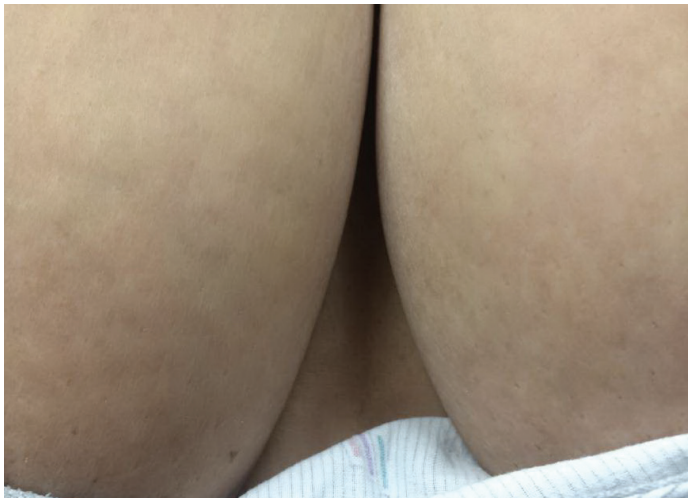

Figure 4. *Affected area six weeks after delivery. Only faint hyperpigmentation and slightly enlarged hair follicles are evident. Induration has resolved.*

systemic symptoms such as joint pains, muscle aches, or fatigue. Bloodwork, including basic metabolic panel, complete blood count, hepatic function tests, and coagulation panel were unremarkable.

On examination, she had indurated, poorly defined skin-colored subcutaneous plaques on the medial breasts, with the left more involved than right (**Figure 1**)

Patulous hair follicles and slight peau d'orange change were appreciated. The remainder of her skin, including her nailfolds, was normal. A punch biopsy was performed from the left breast (**Figure 2** and **3**), which revealed an unremarkable epidermis but markedly thickened dermis and loss of subcutaneous fat. High-powered view revealed thick collagen bundles, increased dermal fibroblasts, vascular proliferation and perivascular lymphocytic infiltrates. These findings confirmed the clinical suspicion of morphea.

Treatment options were discussed with the patient, including topical or intralesional corticosteroids. She wished to take a conservative approach and elected watchful waiting. She had an uncomplicated, full-term vaginal delivery and reported that within one day of giving birth, the lesions had become much softer. On examination 6 weeks after delivery, no induration remained. There was faint residual

hyperpigmentation. Hair follicles remained slightly enlarged, but less than the previous exam (**Figure 4**). No repeat biopsy or treatments were indicated.

Case Discussion

Our case highlights pregnancy as a possible trigger of morphea. Our patient developed morphea of the breasts a few months into pregnancy and the condition resolved shortly after giving birth. No other triggering factors such as infections or medications could be identified.

We identified four other reports of pregnancy-associated morphea [1-4]. Two reports involved patients with long-standing "en coupe de sabre" morphea who worsened during pregnancy [1, 2]. The first case [1] was associated with post-partum development of rheumatoid arthritis and the second [2] was accompanied by development of pemphigoid gestationis. Two cases of morphea arose de novo during pregnancy. In one case [3], a patient with a history of Grave disease and cytomegalovirus IgM positivity developed linear morphea of the right limb during her first trimester. The disease progressed despite miscarriage. In another case [4], which is the most similar to ours, a woman developed localized morphea of the left breast during her first month of pregnancy. This improved with topical corticosteroid therapy. Our patient was distinct from some of the reported patients because her condition was tightly correlated with her pregnancy, as judging by rapid resolution after delivery. Furthermore, there was no apparent infection, history of autoimmunity, or development of autoimmunity during or after pregnancy.

There are several reported mechanisms (reviewed in [5]) by which pregnancy could promote development of morphea. One factor might be mechanical injury associated with breast swelling and resultant trauma by bra wiring. This type of trauma might promote the vascular endothelial injury that is thought to initiate morphea. A second cause might be "microchimerism" in which fetal cells present in maternal tissues or circulation promote the development of morphea. A role for microchimerism in promoting morphea has been hypothesized due to the similarity of morphea to graft-versus-host disease, but definitive evidence is lacking. A third cause could be changes to the maternal immune system that promote tolerance to paternal alloantigens (reviewed in [6]). Regulatory T cells are important for maintaining tolerance to fetal tissue and can produce the pro-fibrotic cytokine TGF-β, which has been implicated in the pathogenesis of morphea (reviewed in [7]). It is possible that the immune changes caused by pregnancy promote the development of morphea.

Conclusion

Although apparently rare, it is important to be aware of morphea occurring during pregnancy and the possibility of improvement or resolution after delivery. Our patient was relieved to have a diagnosis and recovered without specific treatment. However, with a small number of reported cases, it is difficult to predict the course of morphea during pregnancy. Also, it is unclear whether morphea might recur or worsen during subsequent pregnancies. Thus, clinical vigilance is of utmost importance.

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