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Case Presentation

Hypopigmented micropapules in apparently quiescent morphea lesions: A manifestation of disease activity.

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Abstract

We present two young patients with morphea or localized scleroderma undergoing systemic treatment, who developed papular lesions on pre-existing sclerotic plaques. Histology was compatible with a papular presentation of morphea and other entities in the differential diagnosis were ruled out. We believe this is a very uncommon presentation of activity in lesions of morphea and should be made known to clinicians so that activity and progression of the disease can be recognized and treated to avoid complications.

Introduction

Morphea or localized scleroderma is a rare fibrosing disorder of the skin and underlying tissues, characterized by skin thickening and hardening owing to an increased collagen density. It usually starts in childhood and the etiology and pathogenesis are not completely understood: autoimmunity, environmental factors, infection, and trauma may trigger cytokine production and release that are responsible for increased fibroblast and collagen synthesis. Transforming growth factor beta and alpha, among others, have been shown to regulate fibroblast proliferation and extracellular matrix deposition. Clinically, the condition is manifested by indurated, dyspigmented plaques with variable degrees of atrophy [1,2,3]. However, there are rare variants of morphea that pose diagnostic challenges owing to their different morphology. We present 2 cases of patients with generalized plaque and linear morphea undergoing treatment with systemic medications, who developed hypopigmented papules overlying clinically quiescent lesions.

Case 1

A healthy, 13 year-old girl presented to our clinic with a one-year history of hardening and discoloration of the right upper extremity, neck, and back. Physical examination showed linear sclerotic plaques, with erythematous and reticulated hyperpigmented areas with central “porcelain-like” lesions extending from the right shoulder to the right dorsum of the hand. Similar plaques were also present on the left forearm and left dorsum of the hand and circumscribed sclerotic and slightly depressed dyspigmented plaques were present on the neck and back. There was evidence of flexion contractures of both wrists and 3rd and 4th metacarpophalangeal and interphalangeal joints, bilaterally. Treatment with pulses of methylprednisolone (1 g IV per day 3 days per month, repeated for 3 months), methotrexate 15 mg PO weekly, and folic acid 1 mg PO daily was initiated. The methotrexate dose was increased to 25 mg, subcutaneously, weekly in the following 5 months and maintained. Her lesions became less indurated and less erythematous and shiny; she had improvement in her movement restriction. There was no evidence of new lesions while being treated for 15 months (Figure 1A). Eighteen months after initiation of treatment she was noted to have new asymptomatic, hypopigmented flat shiny papules, measuring 1-2 mm in size overlying previously existing lesions on the dorsum of both hands and the right arm and forearm (Figure 2). A biopsy was taken from these lesions and reported to show hyalinized collagen extending from the papillary dermis to the subcutis, with a moderate inflammatory infiltrate of lymphocytes, histiocytes, and eosinophils, compatible with active morphea.

Her treatment was augmented with mycophenolate mofetil 1 g PO twice daily (Figure 1B). After a few weeks of treatment all new lesions became smaller and flatter.

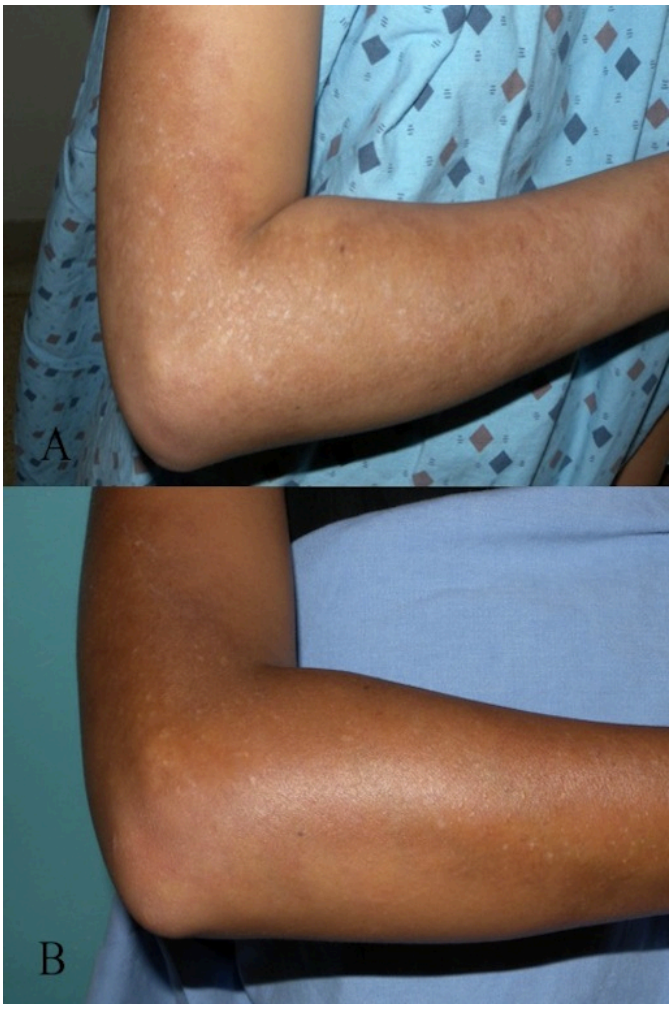

Figure 1. A. Pre-existing sclerotic hyperpigmented linear plaques with new hypopigmented flat shiny papules. B. Decrease in number and size of lesions after a few weeks of treatment with mycophenolate mofetil.

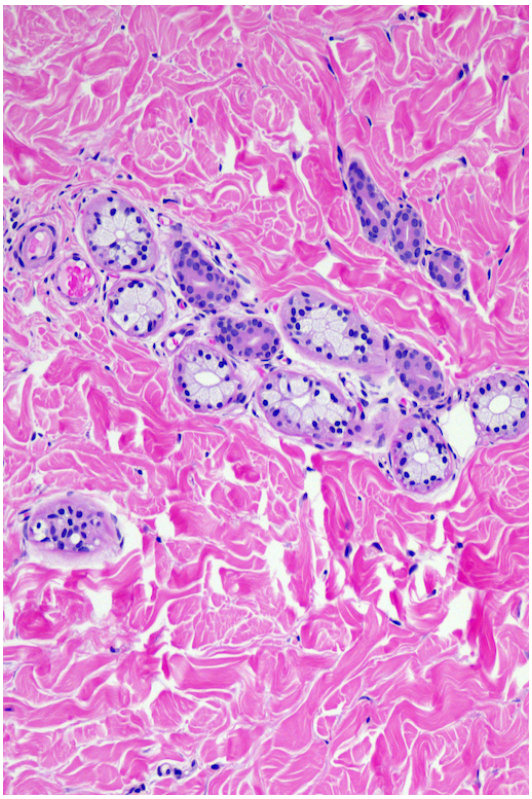

Figure 2. Biopsy showing hyalinized collagen extending from the papillary dermis to the subcutis entrapping eccrine sweat glands and a moderate inflammatory infiltrate.

Case 2

A healthy 7 year-old boy was diagnosed in our clinic with plaque and linear morphea on his left extremities and back. He had sclerotic, shiny, hyperpigmented plaques extending in a linear distribution from his left thigh to the ankle and foot; similar plaques were present on his left arm and the back. Treatment with pulses of methylprednisolone (1 g IV per day 3 days per month, repeated for 3 months), methotrexate 15 mg PO weekly, and folic acid 1 mg PO daily was initiated. His dose of methotrexate was increased to 20 mg PO weekly to adjust for the weight gain. After 5 years of continuous therapy he was noted to have new plaques developing in previously unaffected areas (right upper extremity and left side of the abdomen). A second course of methylprednisolone pulses was initiated and the methotrexate was increased to 25 mg, subcutaneously, weekly with significant improvement of his lesions (Figure 3A). Almost two years later, new lesions were noted, presenting as flat, hypopigmented, shiny tiny papules overlying quiescent lesions on his left shoulder, left arm, and left abdomen (Figure 4). The biopsy was reported to reveal densely packed and thick collagen in the superficial dermis entrapping eccrine sweat glands and a mild lymphohistiocytic infiltrate with scattered plasma cells, a picture compatible with active morphea (Figure 3B). Treatment with mycophenolate mofetil 720 mg PO twice daily was added to his regimen with complete clearance of the papules.

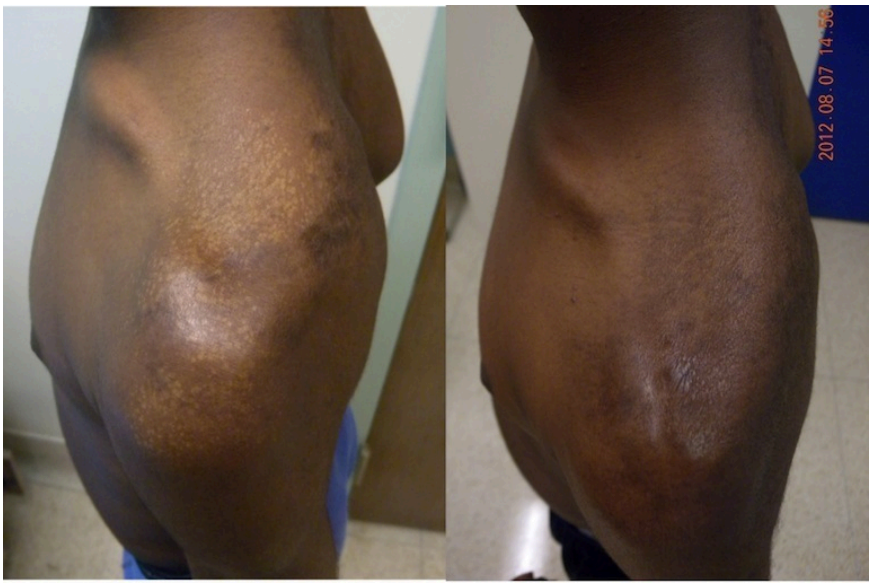

Figure 3. A. Flat, hypopigmented shiny papules overlying inactive morphea plaques. B. Complete clearance after adding mycophenolate mofetil to his treatment regimen.

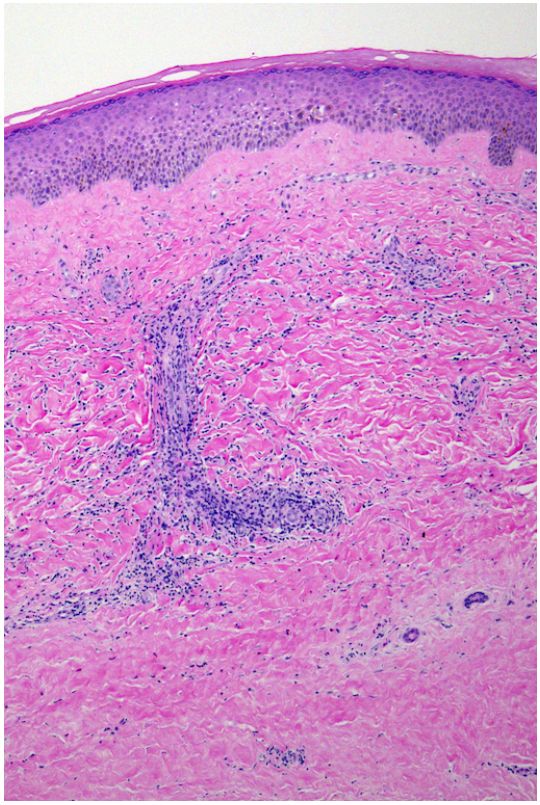

Figure 4. Biopsy showing densely packed, thick collagen fibers entrapping adnexal structures and a mild lymphohistiocytic infiltrate with scattered plasma cells.

Discussion

Morphea is a condition with an unpredictable natural history. Clinical activity usually persists for 3 to 5 years, but new lesions can develop even after longer periods of time. Lesions undergo different clinical stages: an initial inflammatory stage in which lesions are erythematous to violaceous, edematous, and warm to the touch. Over time the lesions become whiter and sclerotic with a characteristic violaceous ring. As the resultant damage is manifested, the plaques become white and sclerotic, showing postinflammatory hyper/hypopigmentation. The collagen deposition destroys adnexal structures such as hair follicles and glands [1,2,3,4,5,6].

Histologically, early lesions have a perivascular lymphocytic infiltrate with admixed plasma cells and rare eosinophils. In the late stages the inflammatory infiltrate disappears and the collagen bundles in the dermis become prominently eosinophilic, thickened, and crowded around adnexal structures and subcutaneous fat [1,2,3,4,5,6,7].

Progression or activity of morphea is difficult to measure, but clinical characteristics of the lesions such as changes in color (erythematous or violaceous hue), increase in size, increased induration, sclerosis, and dyspigmentation are used to determine activity.

Currently, treatment with methotrexate combined with systemic corticosteroids and/or UVA1 have the most convincing data supporting their use [6]. Methotrexate is an effective treatment for morphea [2,8,9], but even after having a good response, relapse rates can be as high as 28% after stopping methotrexate, especially in children who have linear lesions and present at an older age, like our first patient [9].

There is a subset of patients whose lesions have manifestations of clinical activity while on treatment (methotrexate-refractory morphea), and mycophenolate mofetil has shown to be effective in these cases [10]. However, the clinical picture of new micropapules on top of previous morphea plaques as a manifestation of activity of the disease, as demonstrated by our two cases, is extremely uncommon and could be easily mistaken for something else.

The differential diagnosis is wide and includes subtypes of morphea and conditions both associated and unassociated with the disease.

A subtype of morphea that can present with well-defined firm erythematous nodules in patients with scleroderma is the keloidal subtype. It is a fibrosing reaction, thought to be secondary to increased production of transforming growth factor beta (TGF-beta) and connective tissue growth factor (CTGF). These factors increase stimulation of fibroblast proliferation and production of extracellular matrix proteins, promote downregulation of matrix metalloproteinases, and enhance upregulation of proteinase inhibitors. Histological findings are variable, but usually characteristics of keloid scars are present, such as thick acellular collagen bundles arranged in a whorled pattern [11,12].

Nodular morphea is better characterized as small flesh colored papules or nodules arising in the setting of scleroderma, either in sclerotic plaques or in normal skin. It is more common in systemic sclerosis, but can also be found in localized sclerosis or morphea. Histology shows variable characteristic morphea features but not necessarily the thick, disorganized collagen that is found in keloids [12].

Although the terms nodular and keloidal morphea have been used interchangeably in the past, they should be differentiated [12]. It has been suggested that keloid scleroderma arises in patients who are genetically predisposed to developing keloid scar formation [11,12]; it is possible that the underlying pathologic process of nodular and keloid morphea is the same but the clinical appearance depends on this genetic predisposition.

Other conditions in the differential diagnosis of flesh-colored papules developing on previous sclerotic plaques are papular mucinosis and lichen sclerosus et atrophicus. There are reports of generalized scleroderma with papular mucinosis as a result of focal mucinosis deposition. Mucin accumulation is a frequent finding in localized and systemic scleroderma, but it is usually modest and focal and not a major clinical manifestation of the disease [13,14].

Concurrent lichen sclerosus et atrophicus and morphea lesions can present as atrophic porcelain-like papules overlying sclerotic plaques [15,16]. Infectious causes such as papules of molluscum contagiosum developing over morphea plaques could be possible as well and should be kept in mind.

Conclusions

We think our two patients developed the nodular subtype of morphea over their previous lesions. Their lesions do not have clinical or histological features of the keloid subtype of morphea, papular mucinosis, or lichen sclerosus et atrophicus. We

believe this uncommon presentation of morphea is likely related to partial suppression of the disease with therapy and should be made known to clinicians so that we are able to better recognize activity and progression of the disease and thus treat in a timely fashion. Whenever morphea lesions show changes that could be compatible with activity of the disease, they should be biopsied in order to diagnose adequately and escalate treatment as needed.

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