Guttate Morphea in a 31-Year-Old Filipino Female: A Diagnostic Challenge in its Early Stage*

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ABSTRACT

Introduction: Morphea, also known as localized scleroderma, describes a distinctive inflammatory skin disorder that ultimately leads to sclerosis. It is differentiated from systemic scleroderma by the absence of vasculopathy and organ involvement. Initial erythema may precede the sclerotic stage by a few months causing initial diagnostic confusion. High index of suspicion and knowledge of disease evolution are essential. We report a case of morphea and its progression, the diagnostic approach and the importance of early treatment and long-term monitoring.

Case summary: A 31-year-old Filipino female who presented with multiple erythematous plaques on the trunk and extremities and arthralgia was initially diagnosed with cutaneous drug reaction. Prompt treatment led to partial relief of symptoms. However, two months later, eruption of multiple ivory-white small patches and plaques were noted on the same affected areas prompting an impression of morphea. Serum markers revealed elevated antinuclear antibody levels and negative anti-Scl70/anti-centromere serum autoantibodies. Skin biopsy showed homogenized thick dermal collagen bundles confirming the diagnosis of morphea. Topical therapy with calcipotriol + betamethasone dipropionate ointment showed remarkable improvement with decrease in erythema and softening of the lesions while adjunct narrowband-UVB phototherapy also provided relief due to its ability to reduce collagen synthesis and cytokine production.

Conclusion: Morphea may be easily misdiagnosed during the early stages especially if sclerosis ensues late in the disease. Characteristic clinical appearance of erythematous plaques with violaceous borders may not always be present. Histologic examination and serum autoantibodies help exclude other disorders with the same clinical and histopathological spectrum. Treatment is individualized depending on the severity and depth of skin involvement, early treatment and monitoring should be initiated before complications arise.

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CASE REPORT

INTRODUCTION

Morphea also known as localized scleroderma refers to a distinctive inflammatory disease that primarily affects the skin and underlying tissues that ultimately leads to sclerosis. It is differentiated from the systemic form of the disease by the absence of sclerodactyly, Raynaud phenomenon, abnormalities of the nail-bed capillaries, or internal organ involvement.[1] Both have a different clinical expression but they share a common pathologic and pathogenetic mechanism leading to vascular damage, immune activation, and excessive deposition of collagen. The cause is unknown however genetic background in association with exogenous triggers such as viral (EBV, varicella) and bacterial (Borrelia burgdorferi) infections, local trauma, surgical operations and vaccinations (BCG) has been suggested to play a role in morphea.[2]

CASE

A 31-year-old female sought consult at the University of the East Ramon Magsaysay Memorial Hospital (UERM) dermatology out-patient clinic (OPC) with multiple erythematous, irregularly shaped plaques associated with pruritus on her extremities and trunk of 2-weeks duration (Figure 1). There were no complaints of fever, swelling of eyes and lips, dysphagia, difficulty of breathing, chest pain or vaginal discharge. Medication taken prior to eruption of skin lesions was etoricoxib tablet which the patient takes as needed for her arthralgia. Initial impression was cutaneous drug eruption probably secondary to etoricoxib. A 3-mm skin punch biopsy of the skin on the left arm revealed spongiotic dermatitis with psoriasiform epidermal hyperplasia and focal areas of neutrophils subcorneally overlying parakeratotic stratum corneum (Figure 2) hence a spongiotic reaction to a drug was considered. Clearance of lesions were noted after giving a potent topical corticosteroid and a sedating antihistamine. Patient was advised to discontinue taking the etoricoxib. Rheumatology work-up revealed (+) antinuclear antibody (ANA), elevated erythrocyte sedimentation rate (ESR) and normal rheumatoid factor (RF) and C3; an inconclusive diagnosis of rheumatoid arthritis was conferred.

One month after discontinuation of previous medication and clearance of lesions, patient consulted again due to progression of previous lesions to multiple ivory-white small patches and plaques on bilateral hips, lower abdomen, back, and gluteal area (Figure 3). There was absence of sclerodactyly, Raynaud phenomenon, abnormalities of the nail-bed capillaries, and internal organ involvement. Patient still reported arthralgia with restricted mobility of the MCP and PIP joints.

Morphea was highly considered due to its limited cutaneous involvement and a negative anti-centromere (ACA) and anti-Scl70 autoantibodies. A 3-mm skin punch biopsy on the left hip confirmed a beginning homogenized thick collagen bundles that are present in the dermis and impinging into the adventitial layer (Figure 4).

Topical therapy with a combination of betamethasone dipropionate and calcipotriol twice daily was initiated to target the early inflammatory phase. Narrowband-UVB phototherapy was also initiated 3-5 times weekly at 200mJ/cm3 with weekly increments of 100mJ/cm3 on subsequent sessions until a maximum dose of 1,500 mJ/cm3 is reached.

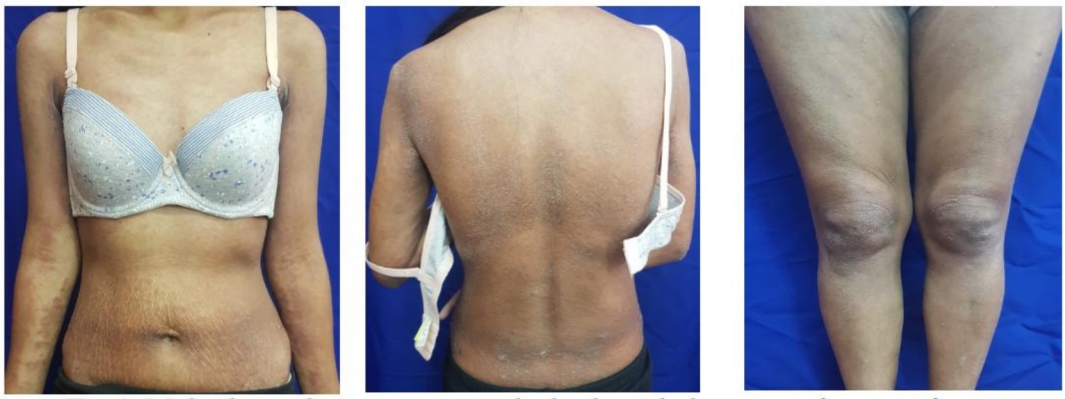

Fig 1. Multiple erythematous, irregularly shaped plaques on face, trunk and extremities on first consult

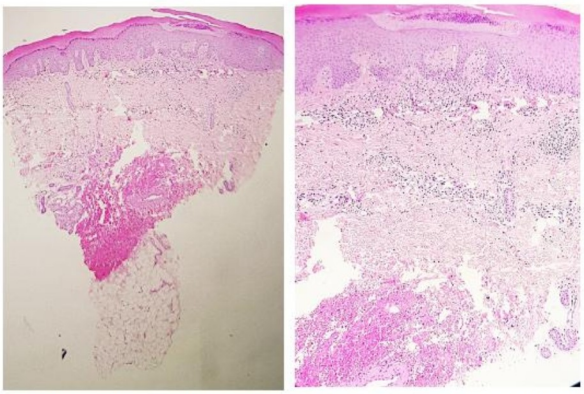

Figure 2. Spongiotic dermatitis with psoriasiform epidermal hyperplasia and focal area of neutrophils subcorneally overlying parakeratotic stratum corneum (H&E stain, 4x and 10x magnification)

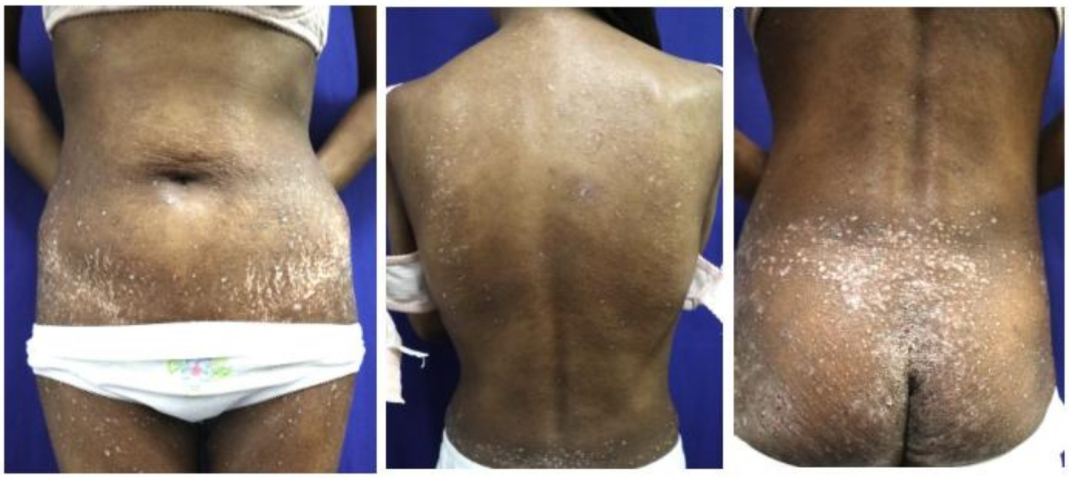

Figure 3. Progression of previous lesions to multiple ivory-white patches and plaques on second consult

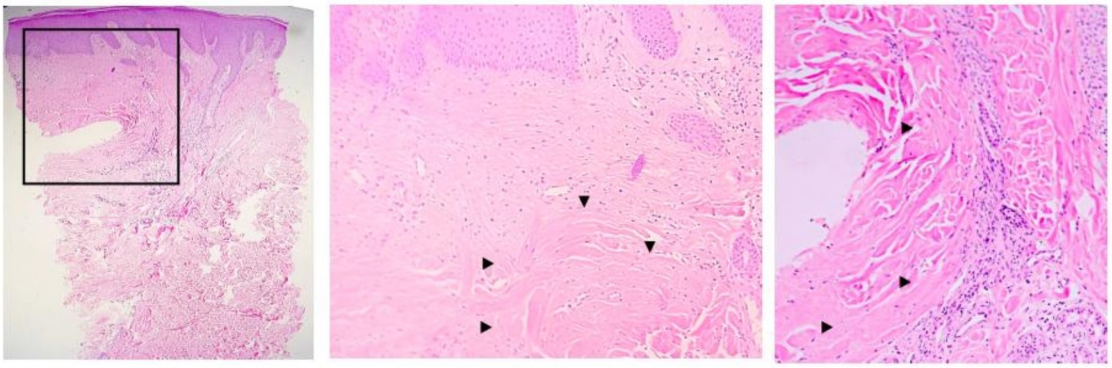

Figure 4. Section shows beginning homogenized thick collagen bundles present in the dermis impinging into the adventitial layer (black arrows) (H&E stain, 4x and 40x magnification)

Scleroderma is a chronic connective tissue disease of unknown etiology that causes widespread microvascular damage and excessive deposition of collagen in the skin and internal organs.[2] There are two types of scleroderma, a systemic form which is characterized by cutaneous sclerosis and visceral involvement and morphea which classically presents benign and self-limited evolution that is confined only to the skin and/or underlying tissues.[3] Morphea is a rare disease with an annual incidence rates between 3.4 and 27 cases per 1,000,000. Females are more frequently affected than males (ratio: 2.4–5.0 to 1).[6]

Subtypes are differentiated based on clinical presentation and depth of skin involvement. It is subdivided into linear scleroderma, plaque morphea, deep morphea, bullous morphea, and generalized morphea.[3] The most common subtype is the plaque type.

Three of the following must be established for the diagnosis of morphea: 1) presence of sclerodermatous skin changes, 2) histopathological examination that shows thickened and increased collagen fibers in the dermis and 3) these diseases can be excluded: systemic sclerosis, eosinophilic fasciitis, lichen sclerosus et atrophicus, keloid, (hypertrophic) scars and sclerosing panniculitis.[4]

This case report will highlight the importance of establishing the clinical and histopathologic diagnosis, the stages of its development and the treatment approach.

The patient presented with initial symptoms of recurrent arthralgia occurring for almost a year followed by an eruption of multiple erythematous pruritic plaques on the trunk and extremities. At this stage, the typical clinical and histopathological features of morphea is not yet fully seen therefore being able to identify the different stages of morphea is imperative for the clinician since misdiagnosis may happen.

According to Careta et al., there are stages in the development of sclerosis. In the inflammatory phase or in the early lesions, morphea clinically exhibits an erythematosus component (red, erythematous lesions) with a histologic picture that is not characteristic of scleroderma thus making a definitive diagnosis difficult. In the later stage, the presence of denser, homogenized collagen that is a little more eosinophilic, especially around vessels and adnexa is observed.

The patient's skin lesions have progressed to become multiple ivory-white oval plaques measuring 1-2cm on the previous affected areas two months after initial presentation. The size of the

lesions is described as guttate which is a subtype classification of plaque morphea in the Peterson et al. classification. Koebnerization was also observed as the lesions appeared in areas of pressure (hips, around the waist, and around the bra line)[10]. Anti-Scl70 and anticentromere serum autoantibodies, specific for systemic scleroderma and Raynaud phenomenon were negative hence a localized form was considered.

Histopathologic examination confirmed beginning homogenized thick collagen bundles that are present in the dermis, impinging into the adventitial layer. This explains that in later lesions, scleroderma can be established and a definitive histological diagnosis is possible. In summary, scleroderma lesions are characterized by an initial inflammatory stage that is followed by a fibrosis stage and results in the replacement of normal dermis and hypodermis structures by abnormal collagen.

Elevated ANA is also seen in the early phases of morphea lesions characterized by the influx of large amounts of mononuclear lymphocytes, plasma cells, and eosinophils because of widespread autoimmune reactivity seen in morphea patients.[7] Several laboratory tests that can aid in the diagnosis of scleroderma are the serum autoantibodies. They are still of limited use in morphea but they can help in excluding it from the systemic form. In the case of our patient, requested laboratories revealed a positive ANA indicating an early phase of morphea, a negative anti-centromere (ACA) and anti-Scl 70 hence a localized form is now established.

Recommended treatment for morphea should be based on disease activity and damage, depth of involvement, disease progression, systemic involvement and disease subtype. It is also important to differentiate active (new, erythematous, expanding lesions) from inactive or damaged (pigmentary changes, atrophy, static size) morphea.[8] Treatment options may be divided into topical and systemic therapy as well as ultraviolet (UV) phototherapy.

Corticosteroids is best used in the most superficial and limited forms of morphea and during the early, most inflammatory phase.[1] Plaque morphea is best treated with topical betamethasone dipropionate and calcipotriol hydrate combination therapy. The mechanism of efficacy for calcipotriol–betamethasone dipropionate is twofold as both components inhibit fibroblast proliferation and act as cytokine immunomodulators to decrease fibrosis and inflammation.[12] Therefore, it is considered suitable for the treatment of active morphea for our patient.

Another treatment option is phototherapy (level 1, randomized controlled trials: broadband ultraviolet (UV) A, narrowband UVB, and UVA-1). NB-UVB is considered for lesions affecting the superficial dermis (relatively thin on palpation or with sclerosis and inflammation in the papillary and superficial reticular dermis).[4] Based on the histopathologic exam of the patient, thick collagen bundles were seen in the dermis hence NB-UBV is still recommended. Although BB- UVA and UVA1 has greater depth of skin penetration, it is more useful on those types with deeper dermal lesions that are also affecting the subcutaneous, muscular and bone tissues.

Prognosis for morphea may have a remitting and relapsing course with periods of activity and reactivation over several years.[13] To monitor therapeutic success, disease activity and damage, an outcome measure known as localized scleroderma cutaneous assessment tool (LoSCAT) has been developed.[7] This tool can be used for my patient to monitor her disease progression and to evaluate clinical improvement after treatment.

Morphea presents a self-limited course with a tendency to spontaneous regression after 3 to 5 years but it may progress and recur especially when the onset of disease occurs in childhood.[3]

CONCLUSION

Morphea may be easily misdiagnosed during the early stages especially if sclerosis ensues late in the disease. Characteristic clinical appearance of erythematous plaques with violaceous borders may not always be present. Histopathologic examination is used to aid in making therapeutic decisions for the depth of involvement of the disease while autoimmune workup is employed to rule out other conditions with the same clinical spectrum. Treatment is individualized depending on the severity and depth of skin involvement and early treatment and monitoring should be initiated before complications arise.

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