Clinical Characteristics and Prognosis of Morphea (Localized Scleroderma) in Adults: a Retrospective Study

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ABSTRACT

Objective: To study the clinical characteristics and prognosis of morphea in Thai adult patients.

Methods: The medical records of 81 morphea adult patients who visited Siriraj Hospital, Thailand, between 2006 and 2015, were retrospectively reviewed. The demographics, clinical features, treatments and outcomes were analyzed. Clinical improvement was categorized as excellent (>80%), partial (1%–80%), and no response.

Results: Circumscribed morphea was the most common subtype (34, 42%) of the 81 patients, followed by linear morphea (21, 26%), generalized morphea (14, 17%), en coup de sabre (11, 14%) and Parry–Romberg syndrome (1, 1%). Systemic treatment and ultraviolet A (UVA)1 phototherapy had satisfactory outcomes in 83% and 79% of cases, respectively, providing a partial to excellent response. For overall remission, one year after the treatment, 30% of patients achieved a partial to excellent response. After 2 years, this proportion rose to 50%. The median time to clinical response was 24 months.

Conclusion: Morphea is a difficult-to-treat dermatosis, with the majority of the patients having a partial clinical response and a high recurrent rate. Combination of treatment might be a worthy option.

Keywords: Morphea; prognosis; phototherapy; systemic; treatment (Siriraj Med J 2019; 71: 297-301)

INTRODUCTION

Morphea, or localized scleroderma, is a rare, chronic, autoimmune disease manifested by dermis and/or subcutaneous tissue sclerosis.[1] The incidence of morphea is approximately 2.7 cases/100,000 people.[2] Morphea is divided into five subtypes: (1) circumscribed morphea (including a superficial and deep variant); (2) linear morphea (including a limb/trunk variant and a head variant); (3) generalized morphea; (4) the pansclerotic subtype; and (5) the mixed subtype.[1] The different clinical manifestations of morphea have led to the development of different classifications and progressions of the disease.[1,3] Therefore, this study aimed to elucidate the clinical characteristics, treatment types, results after treatment, and prognosis of adult patients with morphea.

MATERIALS AND METHODS

Subjects

This study was approved by the Institutional Review Board, Faculty of Medicine Siriraj Hospital (Si 690/2015). The medical records of patients age ≥ 18 years diagnosed with morphea at the Department of Dermatology, Faculty of Medicine Siriraj Hospital, Mahidol University, between January 2006 and December 2015 were retrospectively reviewed. A total of 81 adult morphea patients, evidenced by clinical and/or pathological findings, were included.

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Demographic data, clinical manifestations, lesion sites, symptoms, treatments and clinical responses at final follow-up were collected. A telephone survey was conducted to follow up the relapse status after the last consultation.

The clinical responses were subjectively categorized as excellent (>80%), partial (1%-80%), and no response. Serial photographs before and after treatment were evaluated for clinical response by two dermatologists. Additionally, the effects of the UVA1 dosage on the clinical responses and recurrence rates were gathered. UVA1 phototherapy was categorized as low-dose (20-40 J/cm^2), medium-dose (>40-80 J/cm^2) and high-dose (>80-120 J/cm^2). UVA1 phototherapy was administered three to five times a week for 30 sessions.

Statistical analysis

Descriptive statistics, including frequency counts and tables, were used for demographic data, clinical manifestations, clinical responses, treatments, and disease recurrence. A Chi-square test or, if there were <5 responses in a cell, a Fisher exact test was used to examine the differences in the proportions and the association strength between the clinical response and disease recurrence, according to the treatment types and UVA1-phototherapy doses. A p value of less than .05 was set as the cutoff for statistical significance. All analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, N.Y., USA).

RESULTS

A total of 81 patients, aged 18-83 years and with a median age of 34 years, were included in the analysis. There were 64 (79%) females, and 17 (21%) males, making the female to male ratio 3.8:1. The median time between the initial disease manifestation and diagnosis was one month. The most common subtype of morphea was circumscribed morphea (34, 42%), followed by linear morphea (21, 26%), generalized morphea (14, 17%), en coup de sabre (11, 14%), and Parry-Romberg syndrome (1, 1%).

Morphea lesion was mostly found in the lower extremities, followed by the trunk, head and neck, and upper extremities. In circumscribed morphea, lesions were mostly found in the trunk. However, in the linear and generalized groups, lesions were mostly found in the lower extremities. Skin discoloration (79%), induration (43%) and atrophy (39%) were the top three, most common clinical symptoms of all of the types of morphea. None of the patients progressed to systemic sclerosis during the follow-up period.

The combination therapy was the most often used treatment for generalized morphea and linear morphea (Table 1). Topical corticosteroids (41%) were the most frequently prescribed topical treatment, followed by combined topical corticosteroids with a calcineurin inhibitor (24%), and then by a calcineurin inhibitor alone (11%). In the case of systemic treatment, colchicine (23%), corticosteroid (19%), and methotrexate (14%) were the top three prescribed medicines. Colchicine was the most commonly prescribed drug for systemic treatment in the circumscribed and en coup de sabre groups. As for linear and generalized morphea, oral prednisolone (23.8%) and methotrexate (35.7%) were the most used drugs, respectively.

Fifty-nine percent of patients achieved a partial clinical response, another 18% had no response, while 9% had an excellent response. Generalized morphea (Fig 1) displayed the most favorable response rate at 79%, followed by circumscribed morphea (70%), linear morphea (67%), and en coup de sabre (46%). The linear group had the shortest recurrence time, at 8 months, followed by en coup de sabre (10 months) and generalized (31 months). Circumscribed morphea had the longest recurrence time, at 47 months.

UVA1 phototherapy was administered in 24 (30%) cases. Eighteen (75%) patients received a medium dose (>40-80 J/cm^2) regimen of UVA1 (Table 1). For all types of morphea, the clinical responses did not differ significantly with different doses of UVA1 (p=0.490; Table 2). UVA1 phototherapy combined with systemic treatment (oral prednisolone, methotrexate, colchicine or chloroquine) provided a significantly better response than UVA1 alone (p= 0.044). The recurrence rate did not vary significantly (p=0.674) for morphea patients treated with just UVA1 or with UVA1 plus systemic treatment. Different doses of UVA1 also had no effect on the recurrence rate (p=0.850) (Table 2).

The Kaplan–Meier curve demonstrated the probability of a partial to excellent clinical response for the morphea patients overall. One year after the treatment, 30% of patients achieved a partial to excellent response. After 2 years, this proportion rose to 50%. The median time to clinical response was 24 months.

DISCUSSION

This retrospective study emphasizes the clinical features and prognoses of different types of morphea. We found circumscribed morphea to be the most common type, which was similar to results from the Korea and Netherlands.[4,5] However, a study from the United States found that generalized morphea was the most common subtype among adults.[6]

TABLE 1. Number and type of treatments by morphea subtypes.

	Type of morphea, n (%)				Total, n (%)
	Localized (n=34)	Linear (n=21)	Generalized (n=14)	En coup de sabre (n=11)	(n=80)
Demographics					
Mean age (range)	45 (18-83)	29 (18-52)	35 (21-65)	31 (18-49)	37 (18-83)
Male	6 (18)	5 (29)	1 (7)	5 (46)	17 (21)
Female	28 (82)	16 (76)	13 (93)	6 (55)	64 (79)
Mean age onset (range)	37 (4-81)	19 (2-52)	27 (9-58)	22 (8-37)	28 (18-83)
Mean duration of disease (months) (range)	98 (12-240)	124 (2-276)	93 (6-240)	118 (12-216)	107 (2-81)
Location					
Head and neck	9 (24)	2 (7)	2 (6)	11 (100)	25 (23)
Trunk	13 (35)	3 (11)	9 (27)	0	25 (23)
Buttock	1 (3)	2 (7)	0	0	3 (3)
Upper extremities	6 (16)	9 (34)	10 (31)	0	25 (23)
Lower extremities	8 (22)	11 (41)	11 (33)	0	30 (27)
Intertriginous area	0	0	1 (3)	0	1 (1)
Symptoms					
Tightness	1 (1)	6 (13)	0	0	7 (4)
Pain	1 (1)	2 (4)	0	0	3 (2)
Skin color change	29 (43)	16 (33)	12 (43)	6 (32)	63 (38)
Erythema/edema	5 (8)	6 (13)	5 (18)	1 (5)	17 (10)
Deformity	1 (1)	6 (13)	0	2 (11)	9 (6)
Induration	17 (25)	10 (20)	6 (21)	1 (5)	34 (21)
Atrophy	14 (21)	2 (4)	5 (18)	9 (47)	31 (19)
Type of treatment					
Topical treatment					
Corticosteroids	13 (38)	10 (48)	8 (57)	2 (18)	33 (41)
Calcineurin inhibitor	5 (15)	3 (14)	–	1 (9)	9 (11)
Corticosteroids plus calcineurin inhibitor	10 (29)	4 (19)	2 (14)	3 (27)	19 (24)
Others†	3 (9)	2 (6)	–	2 (18)	7 (9)
Systemic treatment					
Oral prednisolone	6 (18)	5 (24)	4 (29)	1 (9)	15 (19)
Methotrexate	3 (9)	3 (14)	5 (36)	–	11 (14)
Colchicine	9 (27)	3 (14)	4 (29)	2 (18)	18 (23)
Others†	11 (32)	9 (43)	8 (58)	4 (36)	32 (40)
Phototherapy (UVA1)‡					
Low dose	1 (3)	1 (5)	–	–	2 (2)
Medium dose	4 (12)	5 (24)	7 (50)	2 (18)	18 (28)
High dose	–	2 (10)	1 (7)	1 (9)	4 (5)
Other treatments					
Intralesional corticosteroids	1 (3)	–	–	1 (9)	2 (3)
Surgery for reconstruction	–	–	–	1 (9)	1 (1)
Clinical response					
Excellent (>80%)	2 (6)	1 (5)	4 (29)	–	7 (9)
Partial (≤80%)	22 (64)	13 (62)	7 (50)	5 (46)	47 (59)
No response	5 (15)	4 (19)	1 (7)	4 (36)	14 (18)
Loss to follow-up	5 (15)	3 (14)	2 (14)	2 (18)	12 (15)
Recurrence of disease					
Recurrence (months)	7 (29)	6 (43)	3 (27)	3 (60)	19 (24)
Time to recurrence (months) – median (min, max)	47 (4, 93)	8 (2, 26)	31 (19, 32)	10 (4, 15)	17 (2, 93)

† Other systemic treatments included chloroquine, hydroxychloroquine, isotretinoin, pentoxifylline, d-penicillamine and indomethacin

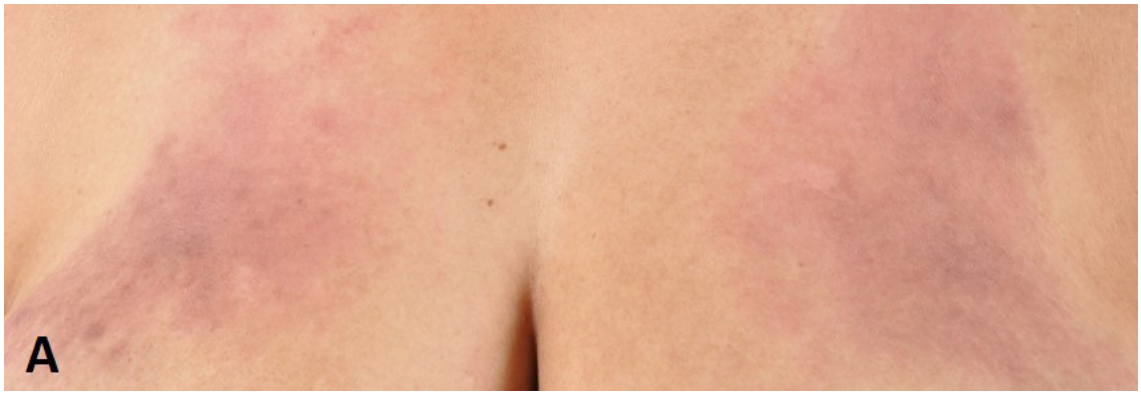
‡ UVA1 phototherapy was categorized as low dose (20–40 J/cm^2), medium dose (>40–80 J/cm^2) and high dose (>80–120 J/cm^2)

Abbreviation: UVA1= ultraviolet A1

TABLE 2. Clinical response and disease recurrence from UVA1 phototherapy.

	Clinical response, n (%)			*P*-value	Disease recurrence n (%)	*P*-value
	Excellent (>80%)	Partial (≤80%)	No response			
Treatment						
UVA1 plus systemic treatment	3 (33)	6 (67)	–	0.044*	5 (56)	0.674
UVA1	1 (7)	11 (73)	3 (20)		6 (50)	
Dose of UVA1†						
Low dose	–	2 (100)	–	0.490	1 (50)	0.850
Medium dose	3 (17)	12 (66)	3 (17)		8 (53)	
High dose	1 (25)	3 (75)	–		2 (50)	

† UVA1 phototherapy was categorized as low dose (20–40 J/cm^2), medium dose (>40–80 J/cm^2) and high dose (>80–120 J/cm^2)
* p-value ≤ 0.05 considered statistically significant
Abbreviation: UVA1 = ultraviolet A1



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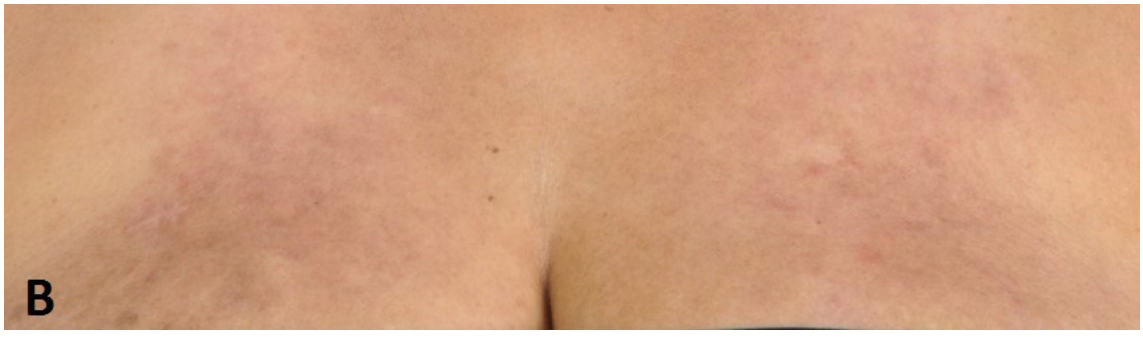

1B

Fig 1. Excellent response of generalized morphea on the breast. **A)** Baseline, indurated plaque on the breast. **B)** After treatment with oral prednisolone (30 mg/day) for 6 months, combined with methotrexate 7.5-10 mg/weeks for 12 months and medium dose UVA1 for 30 sessions. The morphea lesion left with postinflammatory hyperpigmentation.

In the present study, clinical responses, including partial to excellent responses, were detected in 59% of the treated morphea cases. The overall level of clinical improvement was similar to the aforementioned Korean study, which showed a 63% improvement.[4] Based on the Kaplan–Meier curve, approximately 50% of treated morphea cases obtained partial to excellent clinical responses within 2 years, regardless of the treatment employed. By comparison, Mertens et al., evaluated the clinical responses after treatment with methotrexate alone; and 62% of patients show a partial to excellent response after 2 years.[7]

UVA1 phototherapy is a commonly-used treatment for morphea.[8] Medium- and high-dose UVA1 phototherapy have proven to provide better outcomes for morphea than low-dose UVA1.[9] Our study showed that 80% of patients had a partial to excellent response to UVA1 (medium dose), similar to the efficacy results found in studies by Vasquez et al. (60%), Su et al. (82.9%) and Andres et al. (82%).[10-12]

Recurrence is common after morphea treatment. Mertens et al., reported a disease recurrence rate of 17% for adult-onset localized morphea, and 27% for pediatric-onset morphea.[5] Linear morphea was the most frequent type.[5] Methotrexate combined with systemic corticosteroids showed a recurrence rate of 30%, with a 6-month mean relapse time after methotrexate discontinuation.[13] Moreover, Vasquez et al., reported a recurrence of 46% for active morphea after successful UVA1 phototherapy.[10] UVA1 phototherapy combined with immunosuppressives may inhibit episodes of recurrence.[10] Similar to another study,[10] the present study found a recurrence rate of 50% after successful treatment with UVA1. Our study supports the view that UVA1 combined with a systemic treatment for morphea provides significantly more benefits than UVA1 alone.

This study is a retrospective chart review and there was a lack of standardized criteria to evaluate the treatment responses; so the evaluation of the effectiveness of the treatments could therefore be subjective. Lastly, there may be a recall bias from the telephone interviews. We recommend a further study should be performed using validated assessments of morphea activity to reduce any bias in collecting data, such as the ultrasound measurements of skin thickness.

CONCLUSION

Morphea is a difficult-to-treat dermatosis, with most patients having a partial clinical response and a high recurrence rate. Overall, the median time to achieve a partial to excellent clinical improvement was 2 years. UVA1 phototherapy combined with systemic treatment was found to be a worthy option for patients.

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Conflicts of interest: None

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