

Case 9.1

A 4 year-old boy from Bangkok

Chief complaint: Right hemilateral limb atrophy for 6 months



Present illness:

Six months prior to presentation his mother observed that the patient's right upper and lower limbs looked smaller than his left side. He could participate in normal daily life activities and had no history of previous trauma.

Past history:

Normal delivery without complications
Proper vaccination
Normal growth and development

Physical examination:

T 37°C, active child, BW 14.6 kg
HEENT: Not pale, no jaundice
Lymph nodes: Not palpable
Heart: Normal S1S2, no murmur
Lungs: Clear

Abdomen: Soft, no hepatosplenomegaly

Extremities:

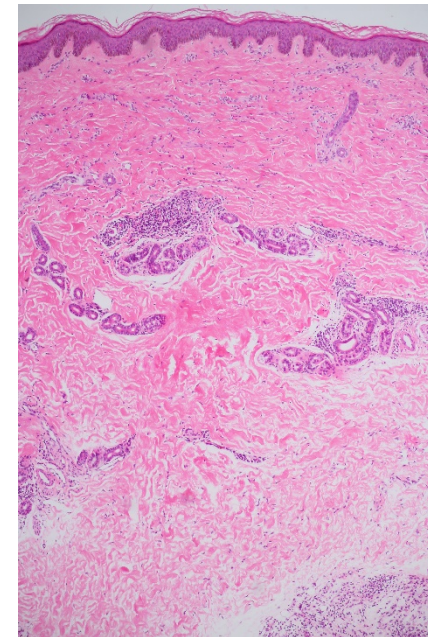
Arm circumference: Right 14 cms, Left 15 cms

Thigh circumference: Right 25 cms, Left 26 cms

Skin examination:

- Diffused sclerotic skin-colored to hypopigmented plaques on right upper and lower extremities with prominent veins.

Histopathology: (S16-17629A, right arm)



- Dense superficial and deep perivascular and interstitial inflammatory-cell infiltrate of lymphocytes and a few plasma cell in the dermis.
- Thickened homogenized collagen bundles (sclerosis) in the

upper and mid dermis.

Diagnosis: Linear morphea

Investigation:

- Hb 11.7 g/dL, Hct 36.3%
- AST44 U/L, ALT 15 U/L
- ANA positive 1:320 homogenous pattern
- Anti dsDNA negative
- Pre-treatment evaluation with 15 Hz ultrasound on both arms and thighs: Skin and subcutaneous tissue thickening at the lateral aspect of right thigh than left thigh.

Treatment:

- UVA phototherapy initiated at 10 J/cm² twice weekly
- Oral methotrexate (0.3-0.6 mg/kg per week) 2 tabs (2.5 mg/tab) per week
- Folic acid (5mg) 1 tab oral OD
- Consult pediatric orthopedist for evaluation of joint involvement

Presenter: Thirawut Sirikham, MD

Consultant: Penpun Wattanakrai, MD
Amornsri Chunharas, MD

Case 9.2

A 55 year-old Thai female from Bangkok

Chief complaint: Multiple erythematous to brownish sclerotic plaques on her trunk and extremities for 6 months



Present illness:

The patient developed multiple, mildly itching, erythematous to brownish indurated plaques on right forearm for 6 months. The lesion spread to the right arm, trunk, back and left leg. She denied previous trauma, any prolonged fever or drug intake prior to the onset of the lesions.

Past history:

Underlying AR, asthma, HT, dyslipidemia all well controlled

Family history:

No other family members show similar skin lesions

Physical examination:

GA: Middle-aged, healthy looking female, BW 74.9 kg

HEENT: not pale, no jaundice, no oral ulcers

Lymph nodes: not palpable

Heart and lungs: WNL

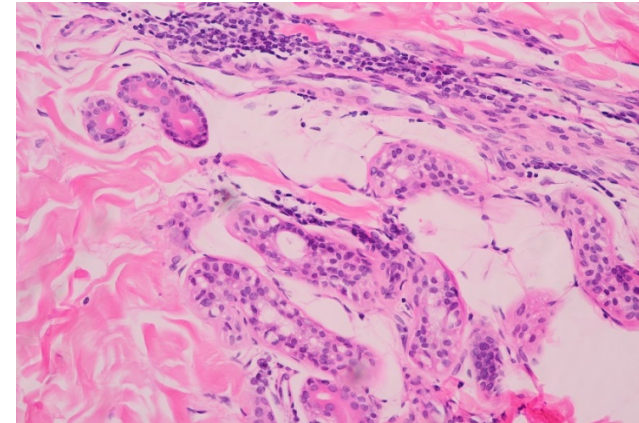
Abdomen: no hepatosplenomegaly

Skin examination:

Multiple, ill-defined, discrete, erythematous to brownish sclerotic plaques on the right forearm, arm, trunk, back and left leg.

Investigations:

- Hb 13.4 g/dL, Hct 41.4%
- AST 26 U/L, ALT 29 U/L
- ANA and 12 specific ANA negative all
- Anti HCV, HBsAg Negative

Histopathology: (S16-30991A, right arm)

- Mild superficial and deep perivascular and interstitial inflammatory-cell infiltrate of lymphocytes and a few plasma cell in the dermis.
- Subtle dermal sclerosis in the reticular dermis.

Diagnosis: Generalized morphea**Treatment:**

- Oral methotrexate (2.5mg/tab) 3 tabs per week
- Folic acid (5mg) 1 tab per day
- Emollient and topical calcipotriol applied twice daily

Presenter: Thirawut Sirikham, MD

Consultant: Penpun Wattanakrai, MD

Discussion:

Morphea or localized scleroderma is a connective tissue

disorder of unknown aetiology, characterized by sclerosis of the skin and subcutaneous tissue, often affecting the underlying muscle and bone.¹⁻³ The disease is differentiated from systemic sclerosis by the absence of sclerodactyly, Raynaud phenomenon, nail fold capillary changes and organ involvement.⁴ The pathogenesis of morphea is multifactorial, involving genetic factors and environmental exposures, which lead to small vessel damage, the release of profibrotic cytokines and disruption of the balance of collagen production and destruction.⁵ Transforming growth factor- β (TGF- β) has been found to be increased in lesions of localized scleroderma. TGF- β stimulates fibroblasts to produce an increase amount of glycosaminoglycans, fibronectin, and collagen while decreases extracellular matrix breakdown; and it diminishes fibroblasts susceptibility to apoptosis.⁷⁻¹⁰

The term 'morphea' was first introduced by Wilson.¹¹ In 1942, Klemperer and colleagues included scleroderma in the group of collagen diseases. Peterson and colleagues proposed first data collection on the epidemiology of morphea and classification of morphea.¹

There are five morphea variants: circumscribed, linear, generalized, pansclerotic and mixed as shown in table 1.³

We presented two cases with different subtypes of morphea. Case 9.1 was diagnosed as linear morphea (LM), also known² as linear scleroderma, which is common in children and can present in the first or second decade. The three most commonly described variants of LM are en coup de sabre, progressive hemifacial atrophy also known as Parry-Romberg syndrome, and linear limb involvement. All three variants are commonly accompanied by underlying tissue atrophy.⁴ The direction of the linear bands are usually transverse in the trunk and longitudinal in the extremities.⁸ In more than 90% of patients, the involvement is unilateral. LM may result in the following findings and complications: atrophy of soft tissue, muscle, periosteum and bone.

LM may cross joint lines and sometimes lead to contractures. Hammer toes or claw hands may develop if the toes or fingers are involved. Joint contractures can be a significant cause of morbidity and deformities.⁴ Children with head and neck morphea should have regular ophthalmologic and neurological examinations to monitor for asymptomatic involvement that may lead to irreversible damage if not aggressively treated.⁵ Case 9.2 was diagnosed generalized morphea which is a rare and more severe variant in which widespread and diffuse sclerosis of the skin occurs with no systemic involvement. It is mainly seen in adults. It can start insidiously, often on the trunk, with one or more plaques, and slowly progress to a much more extensive involvement. According to Laxer and Zulian, generalized morphea is defined as cases with 4 or more indurated plaques of more than 3 cm in diameter, involving 2 or more of 7 anatomic sites (head-neck, each extremity, anterior trunk, and posterior trunk).² The most commonly affected sites are the trunk, thighs, and lumbosacral region. The plaques are often distributed symmetrically and can coalesce into larger lesions. Contractures occur in limbs and can give rise to joint pains. In contrast to systemic sclerosis, Raynaud phenomenon, nail fold capillary dilation and telangiectasia are not characteristic features. Chronic graft-versus-host disease may result in generalized morphea.^{13,14}

Several laboratory tests may be abnormal in individuals with morphea, Erythrocyte sedimentation rate may be increased, especially in children with linear and deep morphea. Eosinophilia is seen in 15% overall, most often in the deep type.^{2,14,15} ANA positivity, especially speckled and nucleolar patterns, occurs in 26-59% of affected children and rheumatoid factor is positive in 16% of patients.^{2,14,15} Linear, deep and generalized morphea seem to be the subtypes associated with a higher prevalence of ANA; however, no correlation between these antibodies and the disease course has been observed.^{2,14,22} One of the major autoantigens for ANAs in

morphea is nuclear histone. Antihistone antibodies (AHAs) have been detected in 47% of patients with morphea, with a different prevalence in the various subtypes – higher in generalized morphea.¹⁶ Anti topoisomerase II antibodies have been detected in 76% of patients with morphea but these antibodies have been found in 14% of patients with systemic scleroderma and are detectable less than 10% of normal children and children with SLE or Juvenile DM.^{2,16,17}

Choice of therapy of morphea should be based on several factors: relative activity of the disease, depth of involvement, area of involvement and course.¹⁸ To date, methotrexate combined with systemic corticosteroid and UVA1 have the most convincing data supporting their use. Both of these medications should be reserved for patients with extensive involvement, facial involvement or involvement across joints.⁵

The systemic corticosteroids are given (either orally or pulse intravenous) for the first 2–3 months and methotrexate 0.3–0.6 mg/kg per week (either orally or intramuscularly) or 10-15 mg/m²/week initially and on a continuing basis. More than 90% of children with linear scleroderma show disease improvement.^{5,19,20} The mean time to response was 3 months, and relapses were seen after the methotrexate was discontinued.

UV phototherapy has been used in morphea for over more than 20 years, and there is a large body of evidence for its clinical efficacy. UV treatment should be considered primarily in morphea and should be combined with systemic treatment in deep variants of morphea. Based on previous studies on UV treatment in morphea, UVA1, PUVA, and narrow band UVB are considered

effective therapies for limited morphea, but UVA1 and PUVA are considered effective therapies for deep morphea. In the largest randomized UV trial for morphea, medium-dose UVA1 (30–50 J/cm²) yields significantly better results than narrow band UVB or

Main type	Subtype	Description
1.Circumscribed or plaque morphea	a. Superficial	Single or multiple, oval or round circumscribed area of induration limited to the epidermis and dermis, often with altered pigmentation and inflammatory changes.
	b. Deep	Single or multiple, oval or round, circumscribed, deep induration involving skin, subcutaneous tissue, fascia; may involve underlying muscle. Localized subcutaneous atrophy may be the leading symptom with minimal involvement of overlying skin.
2.Linear morphea	a. Trunk/limbs	Linear induration involving dermis, subcutis, muscle, underlying bone
	b. Head	'En coup de sabre' Parry–Romberg syndrome
3.Generalized morphea		Symmetrical, widespread, confluent induration and inflammation of the skin
4.Pansclerotic morphea		Circumferential involvement of limb(s) affecting the skin, subcutis, muscle and bone with severe sclerosis. May involve large areas of the body without internal organ involvement
5.Mixed morphea		Combination of two or more of the previous subtypes

low-dose UVA1 (10–20 J/cm²).²¹ But morphea frequently recurred after UV treatment, narrow band UVB and low-dose UVA1 given its lower carcinogenic potential. So both narrow band UVB and low-dose UVA1 have been proposed as safest treatments for morphea.²¹

Treatment with other systemic medications such as

penicillin, penicillamine, calcitriol, mycophenolate mofetil, cyclosporin A, chloroquine, retinoids, IVIG, rituximab, or imatinib have been published in small case series or case reports.^{4,5,22,23} Extracorporeal photopheresis has only been described in case reports of generalized morphea with or without bullous course of disease, with good individual responses.^{4,5,14,21,23}

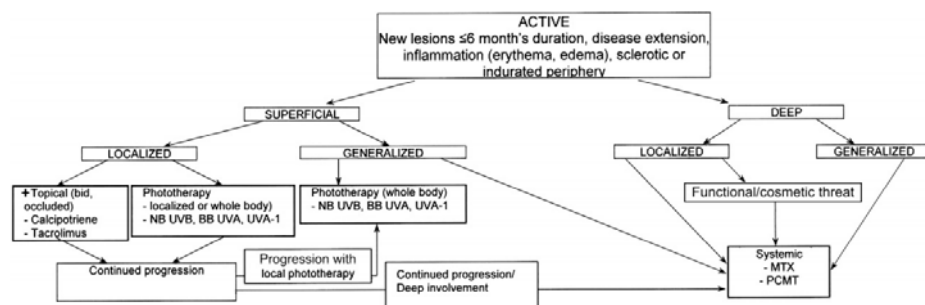


Figure 1: Therapeutic algorithm for morphea based on existing evidence.¹⁸

Other supportive treatments include deep connective tissue massage which can be helpful to improve dermal elasticity and joint movement.^{24,25} Regular physiotherapy is essential especially for linear morphea, to prevent the development of contractures. For established flexion deformities, splinting may be helpful. For those children with leg-length shortening, orthopedic surgical involvement is warranted. Particularly in patients with 'en coup de sabre' lesions, plastic surgery is an important adjunct to improve appearance, including excision of scar tissue, autologous fat transfer and the use of fillers.²⁵

For treatment of the boy with linear morphea, his parents decided to start UVA phototherapy 10 J/m² twice weekly and oral methotrexate 5 mg/week. After 4 weeks of treatment until now there is still no improvement. Pediatric orthopedist was consulted

for evaluation of joint involvement. In the case of generalized morphea, the option of phototherapy treatment was inconvenient therefore she was treated with oral methotrexate 7.5 mg/week and topical calcipotriol.

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