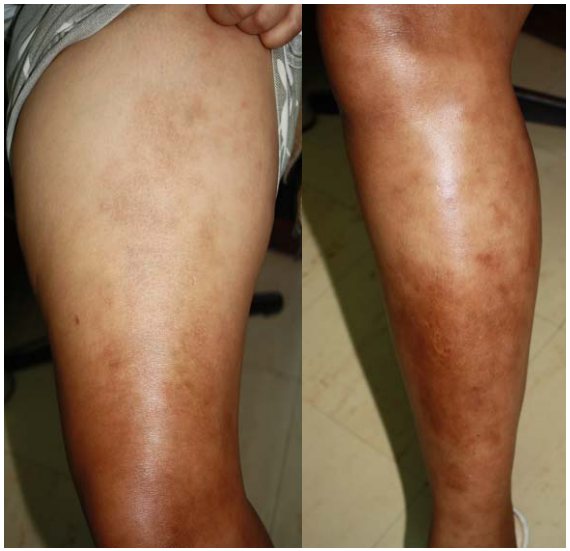
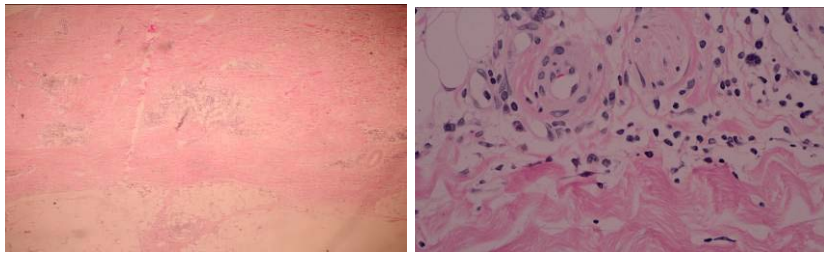
Case 4 .1
A 43-year-old woman from Bangkok
Chief complaint: Itchy band-like atrophic indurated brownish patches at left thigh and leg for 2 months
Past history: nil
Personal history: nil
Family history: nil
Physical Examination: A band-like indurated, atrophic brownish patches with some ivory and shiny spots at left thigh and leg
Histopathology: (S10-18311)
Perivascular and interstitial infiltrate of lymphocytes, admixed with some plasma cells and eosinophils in the dermis and subcutaneous tissue
Homogenized collagen bundles (sclerosis) throughout the dermis and in thickened fibrous septum of subcutaneous tissue

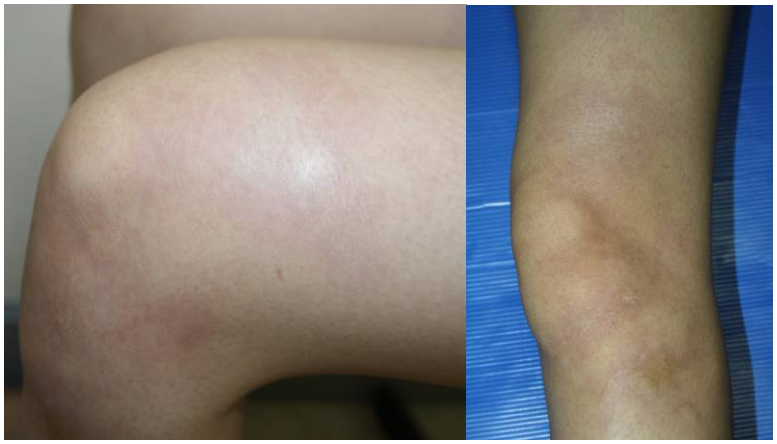


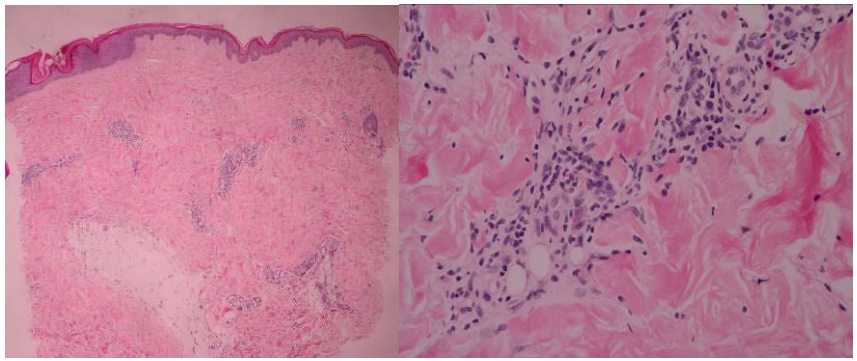


Investigation:
- ANA positive 1:320 Homogenous pattern, Antihistone antibodies negative, SCl-70 negative
- 15 Hz ultrasound on left thigh and leg (pre-treatment evaluation): Skin and subcutaneous tissue thickening at the lateral aspect of left thigh and anterolateral aspect of left leg
- 15 Hz ultrasound on left thigh and leg (4 months after therapy): Slightly decrease in thickness of skin and subcutaneous tissue

Diagnosis: Linear Morphea
Treatment: Methotrexate 15 mg/week for 7 months then decrease to 7.5 mg/week

Case 4.2
A 20-year-old woman from Bangkok
Chief complaint: Asymtomatic band-like atrophic brownish patches laid over left knee for 3 months
Past history: nil
Personal history: nil
Family history: nil
Physical Examination: A band-like indurated ivory and shiny brownish patches across left knee joint
Histopathology: (S11-08798)
superficial and deep perivascular and interstitial infiltrate of lymphocytes admixed with some plasma cells, as well as homogenized collagen bundles sclerosis throughout the dermis.





Investigation:
- 15 Hz ultrasound on left leg: Normal skin appearance at the hyperpigmented areas at the left proximal leg and lateral side of the left knee
Diagnosis: Linear Morphea

Treatment: Methotrexate 10 mg/week
Presenter: Wanjarus Roongpisuthipong
Consultant: Natta Rajatanavin
Discussion:
Morphea or localized scleroderma was differentiated from systemic sclerosis by the absence of sclerodactyly, Raynaud phenomenon, nailfold capillary changes and organ involvement.[1] The pathogenesis of morphea is multifactorial, involving genetic factors and environmental exposures, culminating in small vessel damage, the release of profibrotic cytokines and a disruption of the balance of collagen production and destruction.[2] Transforming growth factor-β (TGF- β) has been found to be increased in lesion of localized scleroderma. TGF- β stimulates fibroblasts to produce increased amounts of glycosaminglycans, fibronectin, collagen while

decrease extracellular matrix breakdown; and it diminishes fibroblast susceptibility to apoptosis.[3-7]

There are five morphea variants: circumscribed, linear, generalized, pansclerotic and mixed.[1]

Linear morphea (LM), also known as linear scleroderma, localized fibrosing disorder or regional fibrosis, is a thickening and hardening of the skin and subcutaneous tissues from excessive collagen deposition. LM is more 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.[1] Plaque formation is elongated into an appearance of linear bands. Linear bands direction is usually transverse in the trunk and longitudinal in the extremities.[8] LM is characterized by a discrete band-like skin induration often with pigment changes that primarily affects the extremities. Linear induration involving the dermis and subcutaneous tissue (may include muscle and bone). In more than 90 percent 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 leads 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.[1, 9] Central nervous system fibrosis most commonly affects those children with head and neck involvement. Children with head and neck morphea should have regular opthalmologic examinations to monitor for asymptomatic involvement that may lead to irreversible damage if not aggresively treated.[2]

A novel antibody, "*anti-DNA topoisomerase II alpha"*, has recently been described. Anti-DNA topoisomerase II alpha antibody is detected in 76 percent of all morphea patients. Anti-DNA topoisomerase II alpha antibody is much more prevalent in morphea patients than in patients with other autoimmune disorders (systemic sclerosis 14 percent, systemic lupus erythematous 8 percent and dermatomyositis 10 percent). The presence of anti-DNA topoisomerase II alpha antibody was associated with a greater total number of sclerotic lesions and number of plaque lesions in patients with morphea.[13]

Evidence-based treatment options of morphea are limited secondary to the rarity of the disease, and the lack of universally used validated outcome measures. Localized Scleroderma Cutaneous Assessment Tool (LoSCAT) is the only validated skin scoring tool for morphea. The most commonly used outcome measures are skin scores, computerized surface area measurement, durometer, cutometer, thermography, and ultrasound measurements. Ultrasound is a noninvasive technique used to measure the depth of lesion. 10-25 MHz ultrasound probes have been proven to have good interuser and intrauser reliability, and are sensitive to changes in the clinical examination.[2]

Choice of therapy for morphea should be based on several factors: relative activity of the disease, depth of involvement, area of involvement and course.[14] 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 those patients with extensive involvement, facial involvement or involvement across joints. [2]

Methotrexate, the immunomodulator, is used as monotherapy 15 mg per week. In uncontrolled trial for 24 weeks showed a significant improvement in the Modified Skin Score. [14] Combination therapy with systemic corticosteroids is supported by level IIB data. Randomized placebo controlled studies are needed to assess the efficacy of combination therapy.[2] The use of ultraviolet (UV) light therapy, with or without chemical agents such as psoralen, has been reported to be beneficial for localized or

superficial lesions in a number of studies. Narrowband UVB should be considered for superficial lesions, including early inflammatory and superficial dermal lesions. Broadband UVA/UVA-1 is more appropriate for deeper cutaneous lesions as a result of greater depth penetration, both in inflammatory and sclerotic disease.[2, 14] Besides medical therapies, physical therapy is often recommended in patients with morphea, particularly in linear limb, generalized, pansclerotic variants that can cause joint contractures.[2]

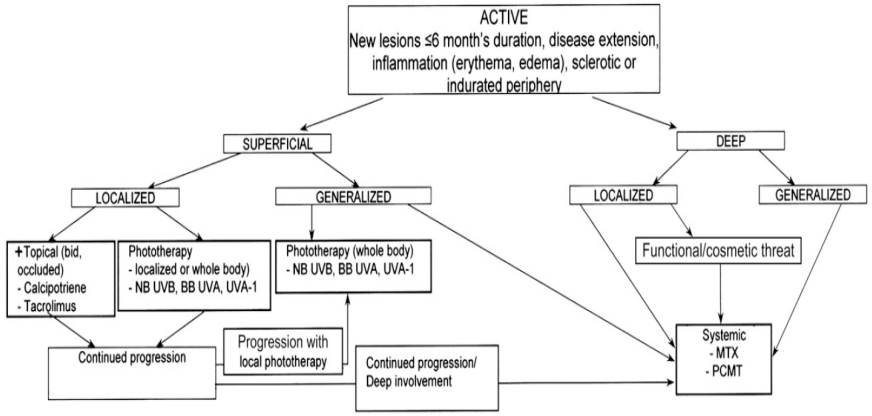


Figure 1: Therapeutic algorithm for morphea based on existing evidence.[14]

Reference

1. Fett N , Werth VP. Update on morphea: Part I. Epidemiology, clinical presentation, and pathogenesis. J Am Acad Dermatol 2011;64:217-28.
2. Fett N , Werth VP. Update on morphea: Part II. Outcome measures and treatment. J Am Acad Dermatol 2011;64:231-42.
3. Peltonen J, Kahari L, Jaakkola S, Kahari VM, Varga J, Uitto J et al. Evaluation of transforming growth factor β and type I procollagen gene expression in fibrotic skin diseases by in situ hybridization. J Invest Dermatol 1990;94:365-71.
4. Trojanowska M. Molecular aspects of scleroderma. Front Biosci 2002;7:d608-18.
5. Kemal Ozbilgin M , Inan S. The roles of transforming growth factor type β3(TGF-β3) and mast cells in the pathogenesis of scleroderma. Clin Rheumatol 2003;22:189-95.
6. Kawakami T, Soma Y, Baba T, Mizoguchi M, Matsuzaki K , Kumagai N. Immunohistochemical analysis of transforming growth factor β3 expression in solitary morphoea profunda with histological membranocystic changes. Br J Dermatol 2002;146:171-3.
7. Gilmour TK, Wilkinson B, Breit SN , Kossard S. Analysis of dendritic cell populations using a revised histological staging of morphoea. Br J Dermatol 2000;143:1183-92.
8. Serup J. Clinical appearance of skin lesions and disturbances of pigmentation in localized scleroderma. Acta Derm Venereol 1984;64:485-92.
9. Krafchik BR. Localized cutaneous scleroderma. Sem Dermatol 1992;11:65-72.
10. Falanga V, Medsger Jr TA, Reichlin M , Rodnan GP. Linear scleroderma: Clinical spectrum, prognosis, and laboratory abnormalities. Ann Intern Med 1986;104:849-57.
11. Sato S, Kodera M, Hasegawa M, Fujimoto M , Takehara K. Antinucleosome antibody is a major autoantibody in localized scleroderma. Br J Dermatol 2004;151:1182-8.
12. Sato S, Ihn H, Soma Y, Igarashi A, Tamaki T, Kikuchi K et al. Antihistone antibodies in patients with localized scleroderma. Arthritis Rheum 1993;36:1137-41.
13. Hayakawa I, Hasegawa M, Takehara K , Sato S. Anti-DNA Topoisomerase IIα Autoantibodies in Localized Scleroderma. Arthritis Rheum 2004;50:227-32.
14. Zwischenberger BA , Jacobe HT. A systematic review of morphea treatments and therapeutic algorithm. J Am Acad Dermatol. Forthcoming 2011 June 4.