INVITED REVIEW

Rheumatology Quarterly

DOI: 10.4274/qrheumatol.galenos.2023.08370
Rheumatology Quarterly 2023;1(4):130-39

SKIN MANIFESTATIONS OF RHEUMATOLOGICAL DISEASES

Selami Aykut Temiz, Saliha Aslan, Recep Dursun

Necmettin Erbakan University Meram Faculty of Medicine, Department of Dermatology, Konya, Turkey

Abstract

Rheumatic diseases have very heterogeneous manifestations and diagnostic criteria. Rheumatic diseases have a wide range of involvement, including systemic (joints and internal organs), as well as skin, mucosa, hair, and nails. Some of these symptoms can cause severe comorbidities and significantly impair the quality of life. Skin findings are critical for early recognition or reinforcing the diagnosis of rheumatic diseases. At the same time, some skin lesions have particular importance as they may be the first and/or most serious comorbid symptom of the disease. Although most of these findings are not specific for rheumatic diseases (such as facial telangiectasia in scleroderma or nonscarring alopecia seen in systemic lupus) some findings may be disease-specific (e.g. discoid lesions in discoid lupus, malar rash in systemic lupus, and Gottron papules in dermatomyositis). Thanks to the contributions of dermatology, the skin findings of rheumatic diseases have become clearer in recent years, thus enabling the classification, phenotyping, and early treatment of rheumatic diseases. Considering all these, each dermatological finding should be taken into consideration and evaluated on a case basis in terms of suspected condition, diagnosis, treatment, and management of post-treatment comorbidities. In conclusion, both rheumatologists and dermatologists have a great responsibility in detailed anamnesis and dermatological examination for detecting the condition, classifying and phenotyping as when necessary, and developing early treatment options.

Keywords: Rheumatology, dermatology, lupus erythematosus, scleroderma, dermatomyositis, Sjögren's disease, morphea

INTRODUCTION

Rheumatic diseases have very heterogeneous manifestations and diagnostic criteria. Skin findings are critical for early recognition and reinforcing the diagnosis of rheumatic diseases (1). Thanks to the contributions of dermatology, skin findings of rheumatic diseases have become clearer in recent years, thus enabling the classification, phenotyping, and early treatment of rheumatic diseases. A detailed clinical observation of the skin is also essential in rheumatic diseases (2). Here we discuss the skin findings of lupus erythematosus (LE), dermatomyositis (DM), scleroderma (SCL), and Sjögren's disease.

1. Lupus Erythematosus

LE is a chronic, inflammatory, autoimmune rheumatological disease that can cause multiple organ involvement, various comorbidities, and mortality (3-5).

The etiology of LE is not yet fully known, but it is thought to be polygenic, with multifactorial factors involved (4). The key risk factor for LE is gender: a female-male incidence ratio of 7:1 in adults and 4:1 in children has been determined. Even in patients with isolated cutaneous lesions, the female-male ratio is 3:1 (5).

LE has a broad spectrum, including localized CLE on one side and systemic LE with severe involvement on the other (2-4). Of these, cutaneous lupus erythematosus (CLE) can be examined under

Address for Correspondence: Selami Aykut Temiz, Necmettin Erbakan University Meram Faculty of Medicine, Department of Dermatology, Konya, Turkey
Phone: +90 535 843 00 68 **E-mail:** aykutmd42@gmail.com **ORCID ID:** orcid.org/0000-0003-4878-0045
Received: 08.11.2023 **Accepted:** 15.12.2023

three subheadings, i.e., acute, subacute, and chronic cutaneous lupus erythematosus (CCLE), from skin involvement, diagnostic, prognostic, and therapeutic perspectives (1-3). Chronic CLE, on the other hand, covers discoid lupus erythematosus (DLE), lupus profundus (LEP), chilblain LE, and LE tumidus (LET) (3,5). Apart from these, there are less common variants such as lupus panniculitis, bullous LE, hypertrophic/verrucous discoid LE, mucosal discoid LE, and lichenoid CLE (5).

To classify by clinicopathological involvement, LE lesions can be divided into dermo-epidermal, dermal, and subcutis subtypes (1).

Acute Cutaneous Lupus Erythematosus

Acute cutaneous lupus erythematosus (ACLE) can be both localized and generalized, mostly associated with active subacute lupus erythematosus (SLE), and its exacerbations may co-exist with systemic involvement (3,5). Generally, ACLE occurs in the third decade (3). Antinuclear antibodies and anti-dsDNA antibodies are elevated in laboratory tests in most patients. Although ACLE lesions usually heal without scarring, post-inflammatory pigmentation disorder can sometimes be observed (1,5).

Possible skin findings in ACLE are as follows:

- Malar rash/butterfly rash is typical in ACLE and is a congestive erythema involving the cheeks and dorsum of the nose while sparing the nasolabial folds and eyelids. Reversible and sensitive to sunlight, these lesions can sometimes be observed on the forehead and front of the neck (1,5).
- Mild edema or red-purple discoloration, sometimes accompanied by papules
- Poikiloderma
- Telangiectasias
- Dyspigmentation
- Widespread hair thinning
- Mucosal ulcerations
- Photosensitive lupus dermatitis/maculopapular lupus rash:

They are itchy, light-sensitive, symmetrically located maculopapular lesions that spread to the neck, and this rare form of ACLE may resemble drug rashes (3,5) (Figure 1). They are called inverse Gottron because, although the involvement of these lesions, especially those on the hands, is similar to DM, it does not affect the distal interphalangeal joint, proximal interphalangeal joint, and metacarpophalangeal joints that DM affects (3,5).

- Cuticle hypertrophy
- Reduced peripheral vascularity
- Erythema and dilated vessels are other rare nail findings (3).

Subacute Cutaneous Lupus Erythematosus

Its common points with SLE are that it mainly affects the young/middle-aged female population and causes light sensitivity (1,3). The lesions affect the areas exposed to the sun upon exposure, but interestingly, the scalp, mid-face area, and lower waist are generally spared. Subacute cutaneous lupus erythematosus (SCLE) has two forms: papulosquamous and annular, but sometimes both forms can co-exist. The annular type is in the form of erythematous, annular polycyclic plaques that tend to merge and form a polycyclic arrangement. (Figure 2). The papulosquamous type presents as psoriasiform papulosquamous without induration. As with some SLE skin lesions, it tends to heal, leaving only dyspigmentation and/or telangiectasis without atrophy, tissue hardening, and scarring. Immunologically, anti-RO (SS-A) positivity was found to be higher in this type, unlike others. Therefore, it will likely overlap with Sjögren's syndrome or be seen in primary Sjögren's patients (1,3,5).

Chronic Cutaneous Lupus Erythematosus

CCLE includes DLE, LEP, CCLE, and LET. Among these, the most common cutaneous lesions of CCLE are DLE (3).

Discoid Lupus Erythematosus

DLE usually occurs during the 4th and 5th decades, a decade later than SCLE (3). DLE has a better prognosis than other chronic subtypes, and DLE lesions have localized and generalized forms, of which the generalized form is relatively more likely to progress

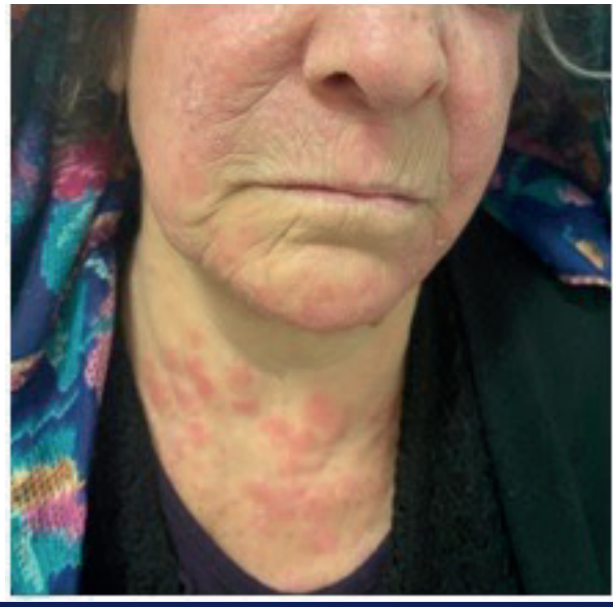

Figure 1. Itchy, photosensitive, symmetrically located drug rush-like maculopapular lesions in an elderly female patient with a generalized form of ACLE
ACLE: Acute cutaneous lupus erythematosus

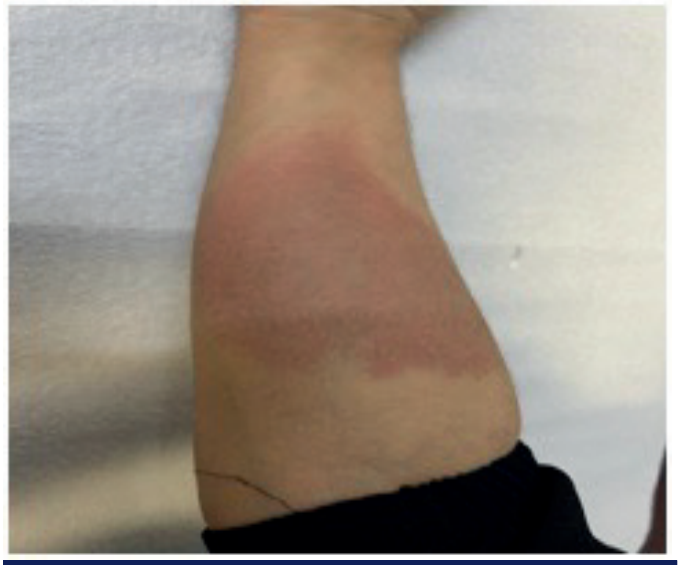

Figure 2. SCLE on the flexor of the right arm of a female patient
SCLE: Subacute cutaneous lupus erythematosus

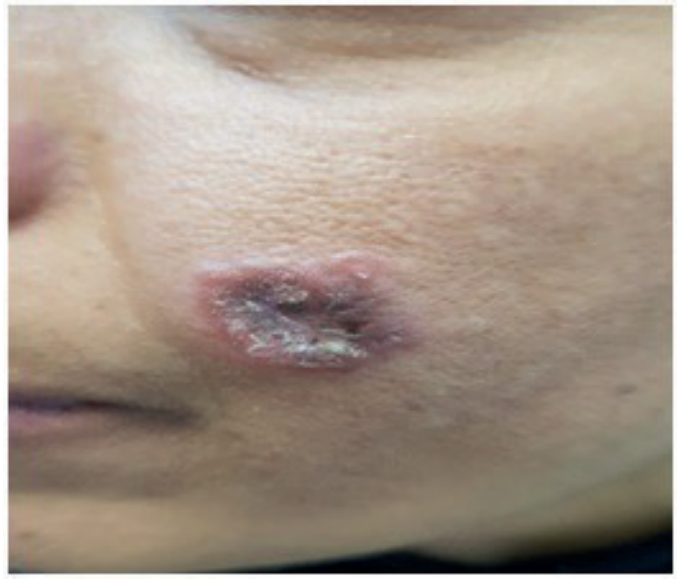

Figure 3. Atrophic hyperkeratotic plaque on the face of a female patient with discoid lupus erythematosus

to DLE (1,3). In addition to sun-exposed areas such as the head, neck, scalp, ears, extensor surfaces of the extremities, and hands, mucosal involvement can also be observed, including genitals, conjunctiva, oral, nasal, and genital mucosa protected from sunlight (3,5) (Figure 3). DLE plaques tend to specifically involve the hair follicle, and scarring alopecia may develop due to a chronic course. Lesions that can be triggered by sun, heat/cold exposure, infection, thermal burn, and trauma have erythema, follicular hyperkeratosis, atrophy, hyperpigmentation at the periphery, and discoid plaques with hypopigmentation in the center (1,3,5).

Buccal Mucosal Discoid Lupus Erythematosus

It may mimic lichen planus in the affected areas and lesion type but can be distinguished by erythematous, centrally located white papules and lesions in the form of plaques or erosion with white radial lines extending from there (3,5).

Verrucous/Hypertrophic Discoid Lupus Erythematosus

Usually on the extremities and face, lesions in the form of hypertrophic, hyperkeratotic, or papulonodules, similar to keratoacanthoma and hypertrophic lichen planus in some points, are observed (3,5). Because there is a risk of developing squamous cell carcinoma in long-term DLE lesions, especially mucosal lesions, it is essential to closely monitor the lesions (3,5).

Lupus Profundus or Lupus Panniculitis

It is generally seen in the 3rd-4th decades. Although it especially affects areas with a fat build-up, such as the extremities, face, and chest, the extremity distal is generally preserved. Painful hard subcutaneous nodules, deep scars that sometimes progress to lipoatrophy with a discoid plaque on the overlying skin, often appear as ulcerations in depressed tissue (1,3,5).

Chilblain Lupus Erythematosus

It is a rare subtype of CCLE with clinical features similar to those of frostbite. Lesions, which can be itchy or painful, appear mainly on the fingers, toes, nose, ears, and sometimes on the heels and knees exposed to cold. Erythematous swellings, purplish erythematous papules, plaques, and nodules, as well as central erosion and ulcerations developing from these lesions, can be observed (3,5).

Lupus Erythematosus Tumidus

It is a CCLE subtype with a relatively male gender bias compared with other CLE subtypes. It is generally expected to have a benign course, and relapses occur with sun exposure. It presents as erythematous, edematous, urticaria-like polycyclic plaques with a raised edge or smooth surface, with no squaring and follicular plug (3,5). Lesions generally appear on the face, neck, and trunk exposed to sunlight (5).

Bullous Lupus Erythematosus

It is a rare form found in 5% of SLE patients. Although the lesions, which are not itchy and are generally not expected to leave a scar, prefer sun-exposed areas such as the face, chest, and extremities, they can also be located on the vermillion border or oral mucosa

(5). To manage treatment, it is important to distinguish bullous LE from lupus subtypes with other cutaneous findings showing epidermal separation, especially the toxic epidermal necrosis (TEN) variant of LE (5).

Toxic Epidermal Necrosis Variant of Lupus Erythematosus

It is similar to severe cutaneous adverse reactions of Steven-Johnson syndrome and TEN, with extensive erythematous skin lesions showing epidermal separation. Although they are difficult to distinguish, histopathological findings, preservation of mucosal barriers/minimal focal involvement, and lesions affecting areas with significant light exposure may clinically support lupus diagnosis (5).

2. Sjögren's Syndrome

Sjögren's syndrome is a chronic, inflammatory, autoimmune rheumatological disease that may cause the involvement of exocrine glands, including the oral mucosa, salivary glands, and lacrimal glands in the orbit, especially the nose, ear, skin, vagina, respiratory, and gastrointestinal tract, and various comorbidities (6-10).

The etiology of Sjögren's syndrome is controversial, and its etiology pathogenesis, and risk factors are still not fully elucidated. However, polygenic factors and multifactorial factors that may cause chronic lymphocytic infiltration in the exocrine glands are thought to play a role (7-10). Although it can affect anyone, an exceptionally high female dominance rate of 9:1 was observed. In women, the disease is particularly prominent during the menopausal period, i.e., the 4th and 5th decades (7-10). It also peaks in the 2nd-3rd decades (10).

Because many immunological and clinicopathological features of Sjögren's syndrome are similar to those of other connective tissue diseases, diagnosis may be challenging (7,8). Sjögren's syndrome is classified as primary or secondary, depending on whether there is any accompanying autoimmune disease. While there is no other accompanying systemic autoimmune disease in primary Sjögren's syndrome, the most common autoimmune diseases accompanying secondary Sjögren's syndrome are rheumatoid arthritis, followed by other connective tissue diseases such as SLE, SCL, and DM (7,8,10).

Although symptoms related to the involvement of the salivary and lacrimal glands, i.e., "keratoconjunctivitis sicca", are the prominent clinical symptoms, skin findings may occur long before the specific findings of Sjögren's syndrome. The most common of these are xerosis, Raynaud's phenomenon, cutaneous vasculitis, localized nodular amyloidosis lesions on the skin, and annular erythema (7-11).

Skin findings that can be seen in Sjögren's syndrome are as follows (7-11):

- Xerosis cutis (seen in approximately half of the patients with primary Sjögren's syndrome, but its etiology is not fully known).
- Although cutaneous vasculitis presents with different types of vasculitis (such as cryoglobulinemic vasculitis, urticarial vasculitis, Waldestrom's cutaneous leukocytoclastic vasculitis or hypergammaglobulinemic purpura), the leukocytoclastic vasculitis type (small vessel vasculitis) is more common and prefers the lower extremities.
- Purpura and cutaneous ulcerations (vasculitis findings vary depending on the size of the involved vessel).
- Raynaud's phenomenon.
- Urticarial papules and plaques.
- Transient macular or papular purpura (mostly presenting as concentric circular purpuric rings).
- Annular erythema (ring-shaped/doughnut-like or polycyclic-shaped erythema that may be accompanied by papulosquamous lesions, as in subacute cutaneous lupus).
- Pruritus.
- Granuloma annulare.
- Oral candidiasis.
- Erythema multiforme and persistent lesions.
- Nodular amyloidosis localized to the skin (rarely in the genital area, other than that, single or multiple nodules of different sizes, which are primarily seen in the trunk, extremities, tongue, face, breast, glandular structures and internal organs).
- Angular cheilitis (Perleche).
- Erythema elevatum diutinum.
- Livedo reticularis.
- Subcorneal pustular dermatosis.
- Tongue depapillation (secondary to xerostomia).
- Vaginal xerosis.
- Erythema nodosum, granulomatous panniculitis, and other types of panniculitis.
- Sweet syndrome (acute febrile neutrophilic dermatosis)
- Oral mucosal erosion and ulcerations (secondary to xerostomia).
- Photosensitivity (especially on the face and upper extremities exposed to the sun).
- Pernio.
- Anetoderma.
- Xerotic cracked tongue and lips (secondary to xerostomia).

•Signs of other autoimmune skin diseases, such as psoriasis, lichen planus, vitiligo, and alopecia.

3. Dermatomyositis

DM is a multisystemic, idiopathic inflammatory myopathy primarily affecting the skeletal muscles and skin, with heterogeneous cutaneous and systemic findings (12-15). Its etiopathogenesis is not fully known, as in many inflammatory rheumatic diseases, but it is thought to be multifactorial, with microangiopathy and autoantibodies affecting the skin and muscles involved in the pathogenesis (15). Mostly affecting women, with a male-female ratio of approximately 2:1, this disease can also be seen in children and adults (16-19). This myopathy can occur at any age and has different juvenile and adult sub-forms with onset at ages 5-15 and 40-60 years (13,19).

It is classified as classical, amyopathic, and myopathic DM according to the coexistence of muscle and skin involvement, and there is also paraneoplastic DM, which accompanies paraneoplastic conditions, especially internal organ malignancies (13,17,19). Apart from these known subtypes, different subtypes, such as DM sinus dermatitis, hypomyopathic DM, and post-myopathic DM, have also been defined (13). While both skin findings and muscle involvement can be seen together in classical DM, distinct skin findings without or before significant muscle involvement are observed in amyopathic and, even more recently, skin-predominant DM. In the myopathic type, which has a smaller percentage, typical muscle involvement is observed without skin lesions (13,17,19).

The pathognomonic skin findings of DM are as follows (13,17,19):

•Gottron papules: These are flat purple-violet papules and plaques that cover the dorsal or dorsolateral surface of the interphalangeal and/or metacarpophalangeal joints, to which slight pressure can be applied and may be accompanied by telangiectasis. DM lesions are generally itchy and sensitive to sunlight and may cause dyspigmentation, atrophy, and scarring during healing.

•Gottron's sign: Symmetrically located violet maculae/plaques that may be accompanied by squads and edema covering the dorsal surface of the interphalangeal and/or metocarpophalangial joints, olecranons, medial malleoli, and patellas, i.e. the extensor surfaces of the extremities. They may also be accompanied by erythema and telangiectasia.

•Heliotropic rash: Violet erythema, which may be accompanied by edema in the eyelids and periorbital tissue, significantly affects the upper eyelids and may also affect the nose and cheeks.

The characteristic nail findings of DM include (12,13,17):

•Dystrophic cuticles and diffuse periungual changes.

•Prominent periungual telangiectasias without a dystrophic cuticle.

•Haemorrhagic nail fold and infarcts.

•Distorted nail fold capillaroscopy findings (showing a SCL pattern: low-density capillaries, irregular giant ring-shaped capillaries, and microhemorrhages).

Other skin findings that can be observed in DM (12,13,17,19):

•"V" neck sign/shawl sign: Purple-colored or diffusely erythematous symmetrical maculae/patches on the posterior shoulders, deltoids, neck, upper back, and additionally on the proximal lateral aspects of the upper extremities create this appearance by affecting the front neck in a "v" shape. They even form the poikilodermic "sheath sign" with its symmetrical placement on the lateral thighs and thighs. All these lesions can be exacerbated by UV/sunlight exposure.

•Poikiloderma/poikiloderma vasculare atrophicans/poiklodermatomyositis (coexistence of hypopigmentation, hyperpigmentation, superficial atrophy and widespread telangiectasia) usually occurs in the lateral upper arms and upper chest area.

•Walker's foot: Hyperkeratotic lesions that stimulate callosity on the plantar surface of the feet and fingers.

•Machinist's hand.

•Mechanic's hand sign: Chronic irritant dermatitis-like painful fissures on the palmar surface of the hands and hyperkeratotic lesions located on the lateral side of the palmar surface of the hands and fingers.

•Sunburn symptom: Bright red diffuse facial inflammatory erythema and subsequent post-inflammatory hyperpigmentation that affects the light-sensitive areas on the forehead, cheeks, nose, and chin, as defined in hispanic DM, but does not go beyond the nasolabial folds.

•Sunbed sign: Erythematous patch or plaque-shaped lesions where intertriginous areas and transverse skin folds are preserved; previously described in other diseases and now used in DM.

•Angel wing sign: Generalized erythema over the lumbar region and shoulders, typically separating the area around the scapulae.
Apart from these, some less common or more nonspecific skin findings are as follows:

•Vascular/vasculopathic changes (e.g., cutaneous vasculitis).

•Vesiculobullous and necrotic lesions.

•Skin erosion and ulcerations (e.g., in the digital pulp, periungual area).

•Erythroderma.

•Panniculitis and subsequent calcification lipodystrophy, sometimes simultaneously .

•Inverse Gottron and ulcerated Gottron papules.

•Photosensitivity and pruritus.

•Raynaud's phenomenon (episodic vasospasm in the fingers and toes resulting from exposure to cold).

•Painful calcinosis cutis (in the form of white papules and nodules in bone spurs and infection areas).

•Diffuse hair loss (may cause mild to moderate non-scarring alopecia).

•Koebner phenomenon positivity.

•Petechiae, palpable purpura.

•Oral mucosal changes (gingival telangiectasis, leucoplakia, erosion and ulcerations, oval palatal patches).

•Painful palmar papules.

•Whiplash erythema (linear erythematous maculae and patches on the back).

•Palmar hyperkeratosis.

•Psoriasiform plaques.

•Follicular hyperkeratosis [Pitriasis rubra pilaris (PRP)-like hyperkeratotic papules on the extensor surfaces, especially in Wong type DM].

•Contractures.

4. Systemic sclerosis/scleroderma

Systemic sclerosis (SSc) is an autoimmune, multifactorial, and multisystemic chronic inflammatory connective tissue disease in which microvascular damage and excessive fibrosis are pronounced (18,19). Differential diagnosis includes many immune-mediated, inflammatory, toxic, drug-induced, genetic, vascular, and paraneoplastic conditions with abnormal accumulation, which can be confused with SSc because they cause cutaneous sclerosis (CS) (14).

SSc is a condition whose etiology is not fully known, in which microvascular damage is observed, especially in the skin and internal organs, resulting in excessive collagen accumulation (14). A very small portion of SSCs have a pediatric onset, most of which typically occurs in the 3rd-5th decades (14).

SSc is evaluated in three subcategories based on the intensity and distribution of CS: localized CS (Morphea), limited cutaneous SSc (Crest Syndrome), and generalised cutaneous SSc. Because CS manifests itself with oedema that does not leave pits on the skin, swollen, puffy fingers, and a decrease in facial wrinkles are observed (14,19). Depigmentation and hypopigmentation, which may resemble vitiligo but with the perifollicular area is preserved and generalised, sometimes follicular hyperpigmentation, which is more dominant in sun-exposed areas, and a typical finding, the "salt-pepper sign", forms. In addition, cutaneous appendages, such as sweat glands, other than the hair follicle in shiny and hard skin diminish/disappear (14,19).

Skin thickening and hardening, starting symmetrically and extending proximally from the metacarpophalangeal joints of both hands, may tend to spread to the extremities, face, and trunk, but involvement of the entire skin is rare. Again, progressive nail folding and nail changes constitute the "SCL pattern" in capillaroscopic examination (14,18,19). Dyspigmentation, telangiectasis, cutaneous ulceration, calcification, purpura, and atrophic deep scars in the form of ice picks that are difficult to heal caused by progressive vasculopathy can be expected in the involved skin (14,19). The characteristic cutaneous findings in limited cutaneous SSc are limited to the hands, upper extremities, and face, whereas in diffuse SSc, spread, albeit slowly, to the upper extremities, the face, as well as the lower extremities, and trunk, can be observed (14,18,19). Cutaneous calcifications can progress to affect the fingers, forearms, elbows, and knees (14). The main findings of limited cutaneous SSc, also known as Crest syndrome, include calcinosis, Raynaud's phenomenon, esophageal motility disorder, sclerodactyly, and telangioctasias (14,18,19). Among these, Raynaud's phenomenon is usually bilateral and severe and can involve acral areas, such as the fingers, earlobe, tongue, toes, nose, and ear, and can be encountered in the early stages (14). An ischemic phase, which begins as blanching upon exposure to cold, is followed by the asphyctic phase, which is a painful phase in which the purplish color predominates and is followed by widespread erythema that occurs as a result of revascularisation (Figure 4) (14). Raynaud's phenomenon, which has primary/idiopathic and secondary forms that are important for early diagnosis and treatment, can progress to digital ulceration and gangrene, and autoamputations (resorption of the terminal phalanges) along with sclerodactyly (thinning and tapering of the fingertips secondary to developing deformities) can be observed in the same primary site (14,18,19).

In patients with systemic SCL, changes are also detected in the nail fold and nail bed, and these are defined as an SCL-type pattern (large avascular areas hemorrhages curled giant capillaries, capillary abnormalities in the nail fold, capillary branching, irregularity in microvascular alignment, fibrosis) in capillaroscopy/dermatoscopy. Other nail findings that can be observed in SCL are as follows (14,18,19):

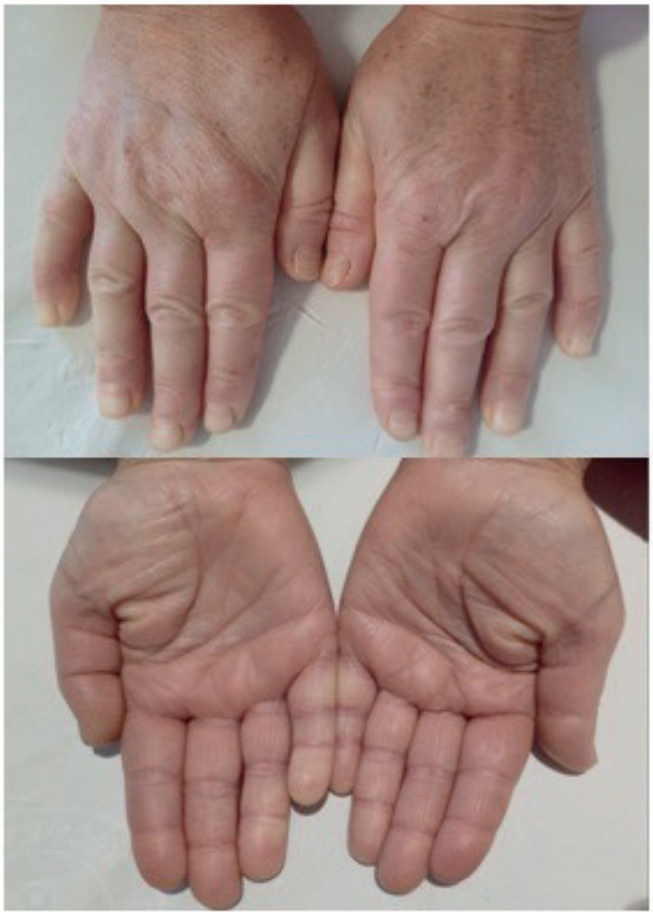

Figure 4. Raynaud's phenomenon in a female systemic sclerosis patient

- Trachyonychia (longitudinal protrusions),
- Sclero-onycholysis,
- Brachyonychia,
- Thickening of the nail,
- Hyperkeratosis in the hyponychium,
- Pterygiumversum unguis,
- Protruding, thickened, and distorted cuticles,
- Parrot beak appearance,
- Leukonychia,
- Red lunula,
- Dyschromia,
- Clubbing,
- Warping in the longitudinal axis,
- Splinter haemorrhages.

CS, with an initial phase in the form of pitting edema has three phases: indurative and atrophic (14). Because of recurrent ischemic attacks, the skin becomes shiny as it stretches and hardens, and its appendages disappear, taking on a wax-like appearance and progressing proximally, resulting in flexion contractures, ankylosis, and the complete disappearance of skin folds, giving the appearance of a claw hand (14).

Because of the involvement of the perioral soft tissue in CS, mouth opening decreases and microstomia develops, while vertical wrinkles begin to appear on the upper lip and a typical facial appearance occurs (Figure 5) (14,18,19). In the oral mucosa, increased tooth pocket openings and xerostomia lead to increased candidal and periodontal infections (14). Cutaneous telangioctasias are dermally located dilated capillaries that can be seen on the neck, palmar and dorsal surfaces of the hands, shoulders, face, thighs, abdomen, breasts, lips, and oral mucosa (14,18,19).

Calcinosis cutis appears as symmetrical white papules and subcutaneous nodules, which are their harder-consistency forms, mainly on the extremities and sometimes on the trunk (14,18,19).

Localized Cutaneous Scleroderma/Morphea

It is a connective tissue disease with fibrosis, where exogenous multifactorial causes and genetics are blamed, but its etiology is unknown. It primarily affects the skin and subcutaneous tissues, sometimes involving the bones, face, and head, and may also involve the central nervous system (14,20). There is a female dominance of 2-4.2:1 in the prevalence of the disease, and especially the white race is affected. The prevalence in children (highest incidence in 2-14 years) and adults (highest incidence in the 5th decade of life) was found to be similar, and the most common subtypes are linear-type and plaque-type morphea, respectively (14,20).

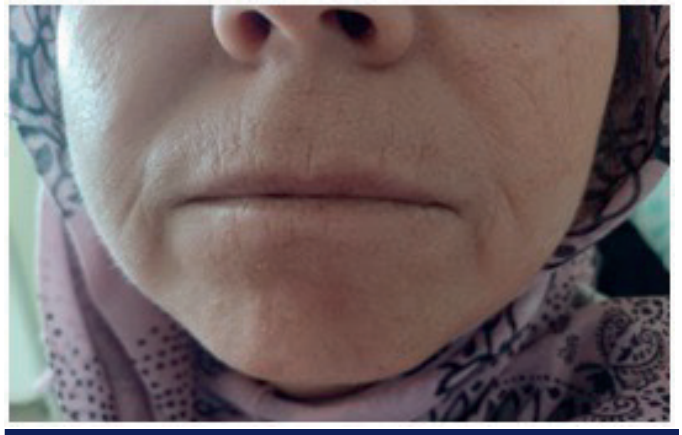

Figure 5. Perioral soft tissue involvement in a female patient with systemic sclerosis typical facial involvement (microstomy, vertical upper lip wrinkles)

Classification of morphea according to the most common classification (14,20):

•Plaque morphea /"en plaque" morphea (including gutta morphea, Pasini and Pierini atrophoderma, keloidal/nodular morphea, and lichen scleroatrophicus)

•Generalized morphea (more than two areas involved)

•Bullous morphea

•Linear SCL (including extremity involvement and en coup de saber)

•Progressive facial hemiatrophy, deep morphea (including morphea profunda, subcutaneous morphea, and eosinophilic fasciitis), and pansclerotic morphea.

Plaque Morphea/"En Plaque"Morphea

This type is generally located on the proximal part of the trunk and extremities and is the type most frequently encountered in adults (14,20). While it affects the dermis and above, the number of plaques often appearing in the pressure areas of clothing due to the Koebner phenomenon usually does not exceed three (14). In the early period, purple-colored, well-defined erythematous patches/plaques of various shapes become white in color with a sclerotic structure over time and are surrounded by a purple-colored inflammatory border called a lilac ring, which gradually expands and eventually disappears (14,20). When the fully active phase of the lesion ends, it appears as sclerotic plaques accompanied by post-inflammatory hyperpigmentation and as anhydrous and smooth as skin appendages such as hair follicles and sweat glands disappear (Figure 6) (14).

Guttate Morphea

It is a subform of plaque morphea with sharper borders but less induration, mostly seen on the upper body and above (14).

Keloidal/Nodular Morphea

In this rare type, which is also a subform of plaque morphea, nodular lesions resembling keloids are observed, unlike other forms (Figure 7) (14).

Pasini-Pierini Atrophoderma

It has sharp borders, is brown, and has a smooth surface. It is mainly located proximal to the trunk. Owing to the round-shaped atrophy, it is flattened compared with the skin, and when multiple lesions come together, it creates the appearance of "Swiss cheese" or "footprints in the snow" (14). Unlike others, structures such as hair follicles and tissue elasticity are preserved because it occurs before inflammation develops and does not reach the threshold of sclerosis (14).

Deep Morphea/Subcutaneous Morphea/Morphea Profunda

As its name suggests, it is the morphea form in which subcutaneous tissues are involved in addition to the dermis, and it is mostly depressed compared with the surrounding area and tightly connected to the underlying tissue, but the overlying skin may be normal, atrophic, or sclerotic (14).

Linear Morphea

There are three different variants depending on the location: head variant, extremity/trunk variant, and progressive

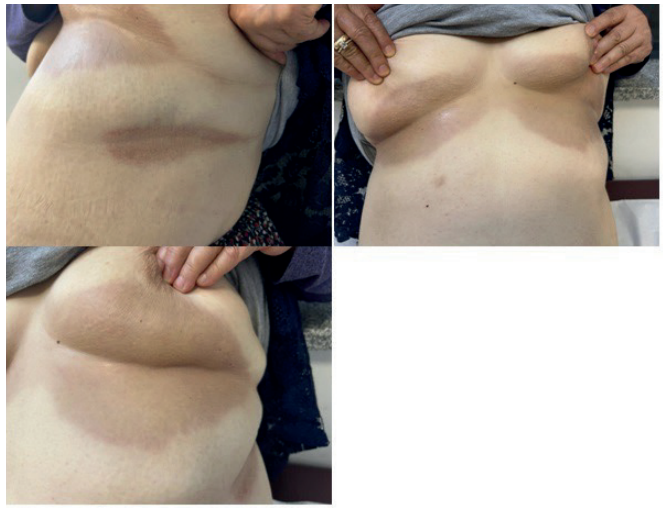

Figure 6. Sclerotic plaques accompanied by postinflammatory hyperpigmentation in a female patient with plaque morphea

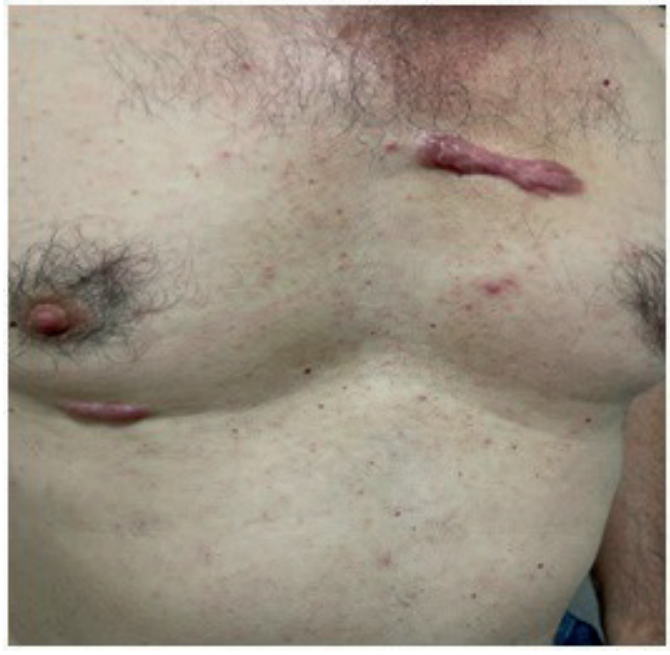

Figure 7. Keloid-like raised nodular lesions on the chest in a male patient with keloidal moraea

hemifacial atrophy, specifically named "en coup de sabre" and "Parry-Romberg syndrome" (14,20).

Lesions following Blascko's lines contain a linear cutaneous induration line extending into the subcutaneous tissue (14,20). The last variant is mostly seen in children and adolescents and is the most common morphea subtype in the pediatric population (14,20).

In linear morphea, which affects both genders, the lesions appear as an inflammatory erythematous linear line or a morphea plaque and adhere to the subcutaneous tissues with the effect of sclerosis, disrupting growth and development, and movements of the extremities (14,20).

''En Coup De Saber" Type of Linear Morphea

It is a subtype of linear morphea affecting the scalp, forehead, and paramedian of the forehead and can sometimes progress to the lips and gums, including the malar-nasal areas. It generally occurs at the age of 13 years, has a high rate of occurrence at menarche, and is more common in girls (14,20). In addition to the atrophic but smooth, hard, and unilateral linear plaque on the face, it may be accompanied by alopecia that leaves scars on the scalp (14,20).

Parry-Romberg Syndrome/Progressive Hemiatrophy

This syndrome mainly presents with unilateral involvement of the subcutaneous tissue of the dermatomes belonging to the trigeminal nerve and its branches and the elements of the musculoskeletal system, and ultimately unilateral atrophy. It exhibits clinical findings similar to En Coup De Saber and appears at the age of 13 (in the 1st-2nd decades), but unlike En Coup De Saber, it affects girls more commonly (14,20). The syndrome has a slow and progressive course but is self-limiting, and its etiology is still unknown (20).

In this syndrome, in which the periorbital skin is frequently affected, dyspigmentation and sclerosis may be observed in the affected skin, and the skin may maintain its normal structure but may be accompanied by ophthalmic and neurological complications (14,20).

Generalised Morphea

It manifests as four or more plaques located in more than one body part and/or plaques larger than 3 cm in size (14,20).

This type of morphea rarely involves the subcutaneous tissues and is mainly limited to the dermis; however, it has a progressive course covering the entire body surface and is relatively more common in women (14,20).

Although involvement in the hands has similar clinical manifestations as SCL, it can be differentiated by the absence of additional findings, such as other nail and vascular findings accompanying SCL (14,20).

Bullous Morphea

It is a rare subtype of Morphea, with tense, subepidermal localization on Morphea plaques and with contents varying from serous to hemorrhagic (14,20).

Mixed Variant Morphea

It is a Morphea subtype in which two or more Morphea subtypes are combined to different degrees (14).

Conclusion

Rheumatic diseases have several involvement, including systemic (joints and internal organs) and skin, mucosa, hair, and nails. Some of these symptoms can cause severe comorbidities and significantly impair quality of life. At the same time, some skin lesions are of particular importance as they may be the first and/or most serious comorbid symptom of the disease. Although most of these findings are not specific for rheumatic diseases (such as facial telangiectasia in SCL or nonscarring alopecia seen in systemic lupus), some findings may be disease-specific (e.g., discoid lesions in discoid lupus, malar rash in systemic lupus, and Gottron papules in DM). Considering all these, each dermatological finding should be considered and evaluated on a case basis in terms of suspected condition, diagnosis, treatment, and management of post-treatment comorbidities (21). In conclusion, both rheumatologists and dermatologists have a great responsibility in detailed anamnesis and dermatological examination for detecting the condition, classifying and phenotyping when necessary, and developing early treatment options.

Ethics

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: S.A.T., S.A., Concept: S.A.T., S.A., R.D., Design: S.A.T., S.A., R.D., Data Collection or Processing: S.A.T., S.A., R.D., Analysis or Interpretation: S.A.T., S.A., R.D., Literature Search: S.A.T., S.A., Writing: S.A.T., S.A.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Lenormand C, Lipsker D. Lupus erythematosus: Significance of dermatologic findings. Ann Dermatol Venereol 2021;148:6-15.

2. Lu Q, Long H, Chow S, et al. Guideline for the diagnosis, treatment and long-term management of cutaneous lupus erythematosus. J Autoimmun 2021;123:102707.

3. Okon LG, Werth VP. Cutaneous lupus erythematosus: diagnosis and treatment. Best Pract Res Clin Rheumatol 2013;27:391-404.

4. Grönhagen CM, Nyberg F. Cutaneous lupus erythematosus: An update. Indian Dermatol Online J 2014;5:7-13.

5. Dursun R, Temiz SA, Fındık S, Durmaz K, Oltulu P. Immunohistochemical Evaluation of TNF-α, IL-1, IL-12, IL-17, IL-23 Expression and Investigation of the Effect of Demodex in Patients with Discoid Lupus Erythematosus. Turkish Journal of Immunology 2023;11:23-8.

6. Concha JSS, Patsatsi A, Marshak-Rothstein A, et al. Advances in Cutaneous Lupus Erythematosus and Dermatomyositis: A Report from the 4th International Conference on Cutaneous Lupus Erythematosus-An Ongoing Need for International Consensus and Collaborations. J Invest Dermatol 2019;139:270-6.

7. DeWane ME, Waldman R, Lu J. Dermatomyositis: Clinical features and pathogenesis. J Am Acad Dermatol 2020;82:267-81.

8. Jhorar P, Torre K, Lu J. Cutaneous features and diagnosis of primary Sjögren syndrome: An update and review. J Am Acad Dermatol 2018;79:736-4.

9. Mathews SA, Kurien BT, Scofield RH. Oral manifestations of Sjögren's syndrome. J Dent Res 2008;87:308-18.

10. Paravar T. Less common rheumatologic disorders: Current concepts of skin and systemic manifestations. Clin Dermatol 2018;36:525-32.

11. Chua-Aguilera CJ, Möller B, Yawalkar N. Skin Manifestations of Rheumatoid Arthritis, Juvenile Idiopathic Arthritis, and Spondyloarthritides. Clin Rev Allergy Immunol 2017;53:371-93.

12. El-Banna G, Fiorentino D. Update on Cutaneous Signs to Assist in the Diagnosis of Dermatomyositis. Curr Rheumatol Rep 2022;24:156-65.

13. Iaccarino L, Ghirardello A, Bettio S, et al. The clinical features, diagnosis and classification of dermatomyositis. J Autoimmun 2014;48-49:122-7.

14. Ferreli C, Gasparini G, Parodi A, Cozzani E, Rongioletti F, Atzori L. Cutaneous Manifestations of Scleroderma and Scleroderma-Like Disorders: a Comprehensive Review. Clin Rev Allergy Immunol 2017;53:306-36.

15. Muro Y, Sugiura K, Akiyama M. Cutaneous Manifestations in Dermatomyositis: Key Clinical and Serological Features-a Comprehensive Review. Clin Rev Allergy Immunol 2016;51:293-302.

16. Volc-Platzer B. Dermatomyositis - update [Dermatomyositis-update]. Hautarzt 2015;66:604-10.

17. Kuhn A, Landmann A, Bonsmann G. The skin in autoimmune diseases-Unmet needs. Autoimmun Rev 2016;15:948-54.

18. Alves F, Gonçalo M. Suspected inflammatory rheumatic diseases in patients presenting with skin rashes. Best Pract Res Clin Rheumatol 2019;33:101440.

19. Careta MF, Romiti R. Localized scleroderma: clinical spectrum and therapeutic update. An Bras Dermatol 2015;90:62-73.

20. Dursun R, Mevlitoğlu İ. Morphea developing after hepatitis B vaccination. Selcuk Medical Journal 2005;21:83-7.

21. Yavuz S, Temiz SA, Ataseven A. Romatolojik dermatoloji ile ilişkili hastalıklar (sarkoidoz, amiloidoz, pannikülitler): Patogenez, klinik ve tedavide güncel yaklaşımlar. Aydoğan K, editör. Romatolojik Dermatoloji. 1. Baskı. Ankara: Türkiye Klinikleri; 2023. p.125-31.