Skin Manifestations of Rheumatological Diseases

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15.1 Introduction

There are many rheumatic diseases presenting with skin manifestations. This could be the first presenting feature of a systemic rheumatic disease. In addition, some of these skin manifestations could be an indication of an active disease or a sign of a serious medical emergency. In this chapter the skin manifestations of common rheumatic diseases will be described. Particular focus will be placed on rheumatic diseases with polyarthritis. The differential diagnosis of erythema nodosum will be discussed as this condition is observed in several disorders with arthritis. There are many drugs used in rheumatology, some of them like allopurinol can lead to life-threatening dermatological conditions. A quick review on some of these conditions will be outlined. At the end of this chapter, the reader should be able to recognize different dermatological signs associated with patients with arthritis, discuss the differential diagnosis of erythema nodosum, and recognize life-threatening dermatological conditions.

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15.2 Objectives

- To identify the dermatological signs in patients presenting with polyarthritis.
- To construct a diagnostic approach to patients presenting with erythema nodosum.
- To recognize life-threatening dermatological conditions.

15.3 Polyarthritis with Skin: (Diagram 15.1)

15.3.1 Rheumatoid Arthritis (RA)

RA is a chronic inflammatory disorder that affects the joints and causes symmetrical arthritis. It usually involves extra-articular structures like the skin, eye, lung, heart, kidney, blood vessels, and bone marrow. The skin manifestations of RA will be discussed here.

15.3.2 Pyoderma Gangrenosum

It presents as an inflammatory and ulcerative disorder of the skin. It's an uncommon neutrophilic dermatosis. It presents commonly as an inflammatory papule or pustule that progresses to a painful ulcer; it may also present with bullous, vegetative, peristomal, and extracutaneous lesions.

15.3.3 Rheumatoid Vasculitis

Inflammation of blood vessel is a central feature of RA, and it is considered as one of the primary events in the formation of rheumatoid nodule. Histologically it is characterized by mononuclear cell cuffing of postcapillary venule. It occurs in patients with long-standing joint-destructive RA. It affects vessels from medium vessel to small arterioles; it leads to ischemia and necrosis to blood vessel “occlusion.”

15.3.4 Rheumatoid Nodule

It is one of the most common cutaneous manifestations in RA. The nodule is seen on pressure area such as olecranon process and many other areas in the body. It is firm, with size varies between 2 mm and 5 cm; non-tender and moveable in subcutaneous tissue; it could be painful, interfere with function, and may cause neuropathy [1]. Around 75% of patients with Felty’s syndrome have a nodule [1], and a vast majority of

patient with nodule have positive RF [2]. Patients with nodule are more likely to have vasculitis [3] (Figs. 15.1 and 15.2).

15.3.5 Skin Ulceration

It may result from venous stasis, vasculitis, arterial insufficiency, and neutrophilic infiltration [4].

There are many cutaneous changes that occur in patients with RA such as granulomatous dermatitis and medication-induced skin changes, and also there are rare manifestations as linear bands or annular lesions, urticarial eruption, erythema elevatum diutinum, and dermal papule.

15.3.6 Systemic Lupus Erythematosus (SLE)

The dermatological manifestations are the most common presentation of SLE in general. They involve the skin, mucous membranes, and hair.

Fig. 15.1 The dermatological signs of patient presenting with polyarthritis. Source: Kelley’s textbook of rheumatology . available on:- www.medscape.com

Fig. 15.2 Periarticular skin-colored rheumatoid nodule

The new classification criteria of SLE contains acute cutaneous lupus erythematosus (ACLE) lesions, subacute cutaneous lupus erythematosus (SCLE), and chronic cutaneous lupus erythematosus as follows.

15.3.7 ACLE (Localized)

15.3.7.1 Malar Rash

Characterized by erythematous butterfly-shaped rash over the cheeks and nasal bridge sparing the nasolabial folds, it can be flat or raised, painful, and lasting for days to weeks [5].

15.3.7.2 Disseminated (Generalized) ACLE

This lesion is characterized by erythematous to violaceous, scaly maculo-papular widespread exanthum symmetrically involves trunk and

extremities. Other nonspecific lesions can be seen, for example; subungual erythema, ulcers, pitting scars stubby hair cheilitis, periorbital edema, and diffuse telogen effluvium [5].

15.3.7.3 SCLE

The clinical fissures of this type are characterized by circulating anti-Ro and anti-La antibodies and the HLA-B8 and HLA-DR3 haplotype. There are two variants that have been identified: annular variant and papulosquamous variant. The annular variant contains slightly raised erythemas with central clearing, while the papulosquamous variant consists of psoriasis-like or eczematous-like lesions. These two variants usually involve UV-exposed skin, including the lateral aspects of the face, the “V” of the neck, the upper ventral and dorsal part of the trunk, and the dorsolateral aspects of the forearms [5]. SCLE lesions commonly lead to hypopigmentation or depigmenta-

tion and never lead to scarring. The systemic symptoms are mild like arthralgias and musculoskeletal complaints [5].

15.3.7.4 CCLE

This is also called discoid CLE characterized by erythematous discoid plaque that becomes hyperkeratotic and finally leads to atrophy and scarring and can lead to dyspigmentation; it mainly involves the face, ears, and neck but may be widespread, and there are no relation of sun exposure. This lesion can affect the mucosal membranes including the lips, mucosal surfaces of the mouth, nasal membranes, conjunctivae, and genital mucosa. CCLE has several types like hypertrophic/verruccous lupus erythematosus, lupus erythematosus tumidus, lupus panniculitis/profundus, chilblain lupus erythematosus, and DLE–lichen planus overlap [5].

15.3.8 Others

15.3.8.1 Photosensitivity

Macular rash present only after sun exposure may appear on the face, arms, or hands and persist for more than 1 day [6].

15.3.8.2 Discoid Rash

Erythematous patches with keratotic scaling over sun-exposed areas, plaque-like in character with follicular plugging and scarring [6] (Fig. 15.3).

15.3.8.3 Alopecia

Mainly affects the temporal regions or creates a patchy pattern of hair loss [7] (Fig. 15.4).

15.3.8.4 Oral Ulcer

It is an important manifestation of SLE; it occurs more than three times per year and is usually painless [7].

Fig. 15.3 Discoid lesions of lupus erythematosus. Show dyspigmentation, atrophy, and scarring

15.3.8.5 Systemic Sclerosis “Scleroderma”

Scleroderma is a term used to describe a thickened skin. It may affect the skin and subjacent tissues, or it may be associated with systemic involvement [8].

15.3.8.6 Raynaud Phenomenon

Changes of the color of the digits due to abnormal vasoconstriction of digital arteries and cutaneous arterioles due to a local defect in normal vascular responses, (pallor, cyanosis and then redness). It is exaggerated by cold temperatures or emotional stress [9] (Fig. 15.5)

15.3.9 Telangiectasia

It may develop anywhere within the body but mostly seen in perioral area, hands, and anterior chest. It's small dilated blood vessels that locate beneath the dermis on skin (venule) (Fig. 15.6).

Fig. 15.4 Diffuse non-scarring alopecia

Fig. 15.5 Raynaud's phenomenon. Note the demarcation of color difference (pallor and cyanosis)

15.3.10 Sclerodactyly

It is a localized thickening and tightness of the skin of the fingers or toes. Sclerodactyly is commonly associated with atrophy of the underlying soft tissues. It is considered as a characteristic feature of scleroderma (Fig. 15.7).

15.3.11 Cutaneous Sclerosis

It is the formation of scar tissue in the skin or in tissues around joints (Fig. 15.8).

Note the tight and shiny appearance of skin.

15.3.12 Digital Ulcers

With scleroderma, repeated episodes of spasm of the fingers (Raynaud's) can cause pitted fingertip

scars, and in some people this results in fingertip ulcers [10].

15.3.13 Calcinosis Cutis

It is mostly asymptomatic and developed gradually, in which amorphous, insoluble calcium salt deposits in the skin and subcutaneous tissue [11]. It's usually firm, multiple, whitish dermal papules, plaques, nodules, or subcutaneous nodules. The lesion spontaneously ulcerated, and it may be tender and may restrict joint mobility. In severe cases it may cause cutaneous gangrene due to vascular calcification which diminishes the pulse.

Hyperpigmentation and finger swelling are also considered as skin manifestations which occur in systemic sclerosis.

Fig. 15.6 Telangiectasia

Fig. 15.8 Cutaneous sclerosis

Fig. 15.7 Sclerodactyly

15.4 Psoriasis

15.4.1 Scales (Fig. 15.9)

15.4.1.1 Nail Involvement

Nail disease is more common in patients with psoriatic arthritis [12]. There is usually involvement of the nail matrix or nail bed. Nail abnormalities may include: beau lines, leukonychia, onycholysis, oil spots, subungual hyperkeratosis, splinter hemorrhages, spotted lunulae, transverse ridging, cracking of the free edge of the nail, and uniform nail pitting.

15.4.1.2 Erythroderma

Patients commonly present with generalized erythema, then after the onset of erythema 2–6 weeks, scaling appears usually from flexural area. Pruritus commonly results in excoriations. If it persists for weeks, hair may shed, nails may become ridged, thickened and it may shed. Inflammation and edema in periorbital skin may occur resulting in ectropion (Fig. 15.10).

15.4.1.3 Guttate Lesion

It is a clinical presentation that is characterized by a distinctive, acute eruption of small, droplike, 1–10 mm in diameter, salmon-pink papules, usu-

ally with a fine scale. It occurs primarily on the trunk and the proximal extremities; also it may have general distribution on the body [13] (Fig. 15.11).

15.4.1.4 Psoriatic Arthritis

Psoriatic arthritis is one of the seronegative spondyloarthropathies which include ankylosing spondylitis and reactive arthritis. The prevalence of psoriatic arthritis among individuals with psoriasis is ranging from 7 to 48% [14–18]. There are several patterns of joint involvement in psoriatic arthritis patients [19]:

Fig. 15.10 Generalized erythroderma with scaly skin appearance

Fig. 15.9 Psoriatic plaques. Note the white to silvery scales over an erythematous base

Fig. 15.11 Guttate psoriasis. Small discrete papules and plaques with fine scales

- Distal arthritis which involves distal interphalangeal (DIP) joints.
- Asymmetric oligoarthritis.
- Symmetric polyarthritis.
- Arthritis mutilans, characterized by deforming and destructive arthritis.
- Spondyloarthropathy which includes sacroiliitis and spondylitis.

15.4.2 Dermatomyositis (DM)

15.4.2.1 Gottron's Papules

They are symmetrical erythematous eruptions which involve the extensor aspects of the metacarpophalangeal (MCP) and interphalangeal (IP) joints and may involve the skin between them; they may be associated with scale and ulcer if the eruption was prominent [20] (Fig. 15.12).

15.4.2.2 Heliotrope Eruption

Erythematous lesion occurs on the upper eyelids and may be associated with eyelid edema (Fig. 15.13).

15.4.3 Facial Erythema

This lesion can mimic the malar rash seen in SLE. To easily differentiate between both of them, look at the nasolabial fold; if it is involved, then the rash is mainly due to DM; however, if it is not involved, then the rash is mainly due to SLE (Fig. 15.14).

Fig. 15.12 Gottron's papules. Flat-topped papules over the proximal interphalangeal and metacarpophalangeal joints

Fig. 15.13 Heliotrope sign. Note the pink to violaceous discoloration over eyelids and forehead

Fig. 15.14 Facial erythema

15.4.4 Photodistributed Poikiloderma

Poikiloderma consists of both hyperpigmentation and hypopigmentation; it always occurs in upper chest, the V of the neck, and upper back (shawl sign); it may come as macular (nonpalpable) or papular erythema if it happens in early stages of cutaneous disease. It is usually associated with pruritus, and this is the difference between DM and photo-exacerbated eruption of lupus erythematosus. If the patient presents with poikiloderma on the lateral aspects of the thighs, this is now called Holster sign (Fig. 15.15).

15.4.5 Periungual Abnormalities

These are characterized by erythematous lesion with vascular changes in the capillary nail beds which also may be associated with areas of dilatation and dropout and with periungual erythema [21].

15.4.6 Psoriasiform Changes in Scalp

The scalp lesion in DM is diffuse, associated with prominent scaling and poikilodermatous changes.

Fig. 15.15 Photodistributed poikiloderma. Note the hyperpigmentation, hypopigmentation, telangiectasia, and atrophy

It may be difficult to distinguish from seborrheic dermatitis and psoriasis. It happens usually as a result of severe burning, pruritus, or sleep disturbance.

with glucocorticoids and immunosuppressive therapy; this lesion can be seen in other diseases like systemic sclerosis and SLE but more common with DM [22, 23].

15.4.7 Calcinosis Cutis

It is more common in juvenile DM than adult DM. It means deposition of calcium within the skin. It is associated with a delay in treatment

15.4.8 Reactive Arthritis

15.4.8.1 Circinate Balanitis

It is an asymptomatic genital lesion characterized by shallow ulcers in the penis [24].

15.4.8.2 Keratoderma

Hyperkeratotic skin rashes involve soles and palms [24] (Fig. 15.16).

15.4.9 Hepatitis C Virus (HCV)

15.4.9.1 Porphyria Cutanea Tarda

It is a skin lesion strongly associated with HCV and characterized by photosensitivity, bruising skin, fragility, facial hirsutism, and vesicles or bullae that can become hemorrhagic. It is a skin disease caused by a reduction of hepatic uroporphyrinogen decarboxylase activity [25].

15.4.9.2 Leukocytoclastic Vasculitis

This lesion is usually associated with palpable purpura and petechiae that usually involve the lower extremities and may happen in conjunction with essential mixed cryoglobulinemia; in skin biopsy, there is dermal blood vessel destruction associated with a neutrophilic infiltration in and around the vessel wall (Fig. 15.17) [26].

15.4.10 Lichen Planus

It involves mucus membranes, hair, and nails characterized by flat-topped, violaceous, pruritic papules with a generalized distribution. In skin biopsy, there is a dense lymphocytic infiltration in the upper dermis [27, 28] (Fig. 15.18).

Fig. 15.16 Keratoderma blennorrhagicum. Note the thick yellow scales on the soles

Fig. 15.17 Leukocytoclastic vasculitis. Note the scattered palpable purpura and hemorrhagic macules

15.4.11 Necrolytic Acral Erythema

This lesion is pruritic and characterized by sharply margined, erythematous to hyperpigmented plaques with variable scale and erosion which involves the lower extremities (Fig. 15.19) [29].

15.4.12 Polyarteritis Nodosa

15.4.12.1 Livedo Reticularis

It is characterized by tenderness and it does not blanch with active pressure [30–32].

15.4.12.2 Ulcerations

It usually involves the lower extremities [30–32].

15.4.13 Digital Ischemia

It may be associated with splinter hemorrhages and gangrene [30–32].

15.5 Sarcoidosis

It is a granulomatous disease and defined as presence of non-caseating granulomas in different tissues and organs such as lymph nodes, eyes, joints, brain, kidneys, lung, and skin. The signs that appear with sarcoidosis are as follows.

Fig. 15.18 Flat-topped, polygonal, and violaceous papules of lichen planus

15.5.1 Erythema Nodosum

It is the most common nonspecific lesion of sarcoidosis and characterized by inflammatory, tender, erythematous, subcutaneous plaques and nodules in the anterior tibial areas. The patient can present with low-grade fever, arthritis, and lower extremity edema (Fig. 15.20) [32].

15.5.2 Papular Sarcoidosis

It is the most common specific lesion characterized by numerous non-scaly, skin-colored, yellow-brown, red-brown, violaceous, or hypopigmented 1 to 10 mm papules, and the papules can demonstrate a slight central depression. The most common site is the face,

Fig. 15.19 Necrolytic acral erythema

with a predilection for the eyelids and nasolabial folds [33].

15.5.3 Nodular Sarcoidosis

Subcutaneous sarcoidosis or nodular sarcoidosis, all these terms describe the nodule arising from subcutaneous tissue [32]; it is one of the most common lesions in sarcoidosis, and it results from large collections of sarcoidal granulomas in the dermis or subcutaneous tissue characterized

Fig. 15.20 Erythema nodosum

as asymptomatic or mildly tender, flesh-colored, erythematous, violaceous, and hyperpigmented. The upper extremities are the most common site of nodular sarcoidosis [34]. It can be single or multiple, and its size could be about 1 and 2 cm in diameter. The differential diagnosis of subcutaneous sarcoidosis includes lipomas, cysts, cutaneous manifestations of lymphoproliferative malignancies, subcutaneous granuloma annulare, foreign body, or granulomas [35, 36].

15.5.4 Maculopapular Sarcoidosis

This lesion is characterized by raised papules that are often around 1 mm in diameter, slightly tender, pruritic, slightly hyperpigmented patches, red, brown, or violaceous in color [37]; the most common sites are facial and eyelid areas, and it may involve mucous membranes, neck, trunk, or extremities [32].

15.5.5 Plaque Sarcoidosis

This lesion is characterized by oval or annular shaped, indurated, different color such as flesh-colored, erythematous or brown rash that may have scale at the end stage. The most common sites involved are the arms, shoulders, back, and buttocks; it has common features with psoriasis, lichen planus, discoid lupus, granuloma annulare, cutaneous T cell lymphoma, secondary syphilis, and Kaposi's sarcoma [36].

15.5.6 Lupus Pernio

This lesion is characterized by erythematous, indurated papules, plaques, or nodules [38]; the most common sites involved are the face, nasal tip, alar rim, and cheeks, and it may involve ears and lips [39]. If this lesion is not treated, it will progress rapidly and increase in thickness, size, and induration. After the lesion is resolved, it will leave scar [37]. This lesion is associated more

with extracutaneous manifestations such as respiratory tract involvement and lytic and cystic bone lesions [40].

15.5.7 Hypopigmented Sarcoidosis

It affects mostly dark-skinned persons of African descent, and the lesion is characterized by round to oval, hypopigmented, well-demarcated patches and may have raised plaques [33, 41].

15.5.8 Atrophic and Ulcerative Sarcoidosis

This lesion is a combined lesion meaning it is involved with atrophic and ulcerated lesions, which are characterized by depressed plaques not elevated [42]; this lesion is associated with other mucocutaneous manifestations of sarcoidosis. The ulcerative lesion is more common in women and black patients [43].

15.6 Rheumatic Fever

Acute rheumatic fever is a non-suppurative sequela that occurs after 2–3 weeks of group A streptococcus and pharyngitis. It mostly affects children aged 5 to 15 years. This disease is characterized by arthritis, carditis, chorea, erythema marginatum, and subcutaneous nodules. The damage to the cardiac valve is chronic and it may progress [44].

To make a diagnosis of rheumatic fever, there is a special criterion called Jones Criteria, which involves major and minor manifestations which are as follows.

The major manifestations:

- Arthritis.
- Carditis.
- Chorea.
- Erythema marginatum.
- Subcutaneous nodules.

The minor manifestations:

- Arthralgia.
- Fever.
- Elevated acute phase reactants (erythrocyte sedimentation rate [ESR], C-reactive protein [CRP]).
- Prolonged PR interval.

In this chapter we will talk only about the rheumatological and dermatological manifestations, which are as follows.

15.6.1 Arthritis

It is the early symptom of rheumatic fever. The classical history of arthritis involves migratory polyarthritis within days to a week. The meaning of migratory is “it affects the joint then migrates to the other joint”; the most common joints involved are knees, elbows, and wrists [36]; the patient will complain of limitation in his movement because of the severity of the joint pain. The inflammation of each joint lasts no more than 1 week and the signs of inflammation are usually present [45].

15.6.2 Erythema Marginatum

This lesion appears early in the course of the rheumatic fever characterized by an evanescent, pink or faintly red, non-pruritic rash; the outer edge is sharp and the inner is diffuse; it has continuous margins and sometimes has a ring shape. It usually affects the trunk and may affect the limbs, but it is unlikely to affect the face [46]. The course of this lesion is intermittent meaning that it appears, disappears, and then reappears in a matter of hours [47].

15.6.3 Subcutaneous Nodules

This lesion is characterized by symmetrical, firm, painless lesions ranging from a few milli-

meters to 2 cm in size, and the average number of nodules is about three to four, and it has non-inflamed skin above it. The nodules present over the bony surface or prominence or near tendons. This lesion appears 1 week after the disease and is associated with severe carditis lasting no more than 1 month. We can distinguish rheumatic fever nodules from rheumatic arthritis nodules as the rheumatic fever nodules are smaller and more short-lived than the nodules of rheumatoid arthritis and almost involve the olecranon, while rheumatoid nodules are usually found 3 to 4 cm distally; finally all of them involve the elbows [48].

15.7 Behçet's Disease

Behçet's disease is a complex, multi-systemic disease that involves the mucocutaneous, ocular, cardiovascular, renal, gastrointestinal, pulmonary, urologic, and central nervous systems, the joints, blood vessels, and lungs. Men are more commonly affected by this disease than women, and it is more common in the third decade of life, but it can occur at any age. Signs and symptoms of this disease may precede the onset of the mucosal membrane ulcerations by 6 months to 5 years, and prior to the onset of the disease, the patient experiences generalized and various symptoms.

In patients with Behçet's disease, a variety of cutaneous changes appear on them [49].

15.7.1 Erythema Nodosum-like Lesion

It is red to violet and painful subcutaneous nodule. It occurs on the extremities especially the lower extremities; also it can present on the face, neck, and buttocks. It resolves spontaneously or it may ulcerate leaving a scar and hyperpigmentation area.

15.7.2 Acneiform Lesion

It may be more common in those with associated arthritis [50]. It consists of papules and pustules that are difficult to distinguish from ordinary acne [51].

15.7.3 Folliculitis-like Rash

It distributes on the back, face, neck, chest, and hairline of patients. It resembles acne vulgaris.

15.7.4 Papulopustular Eruptions

Pustular skin lesions are often not sterile and may contain *Staphylococcus aureus* and *Prevotella* spp. [52].

15.7.5 Erythema Multiforme-like Lesions

15.7.6 Superficial Thrombophlebitis

It is a migratory superficial thrombophlebitis of the skin. It may be associated with deep vein thrombosis that causes lower extremities edema.

15.7.7 Ulcers (Oral, Genital)

During physical exam:

- **Oral ulcer:** difficult to distinguish from common aphthae (Table 15.1).
- **The most common sites** are the tongue, lips, buccal mucosa, and gingiva; the tonsils, palate, and pharynx are less common sites. The interval between recurrences ranges from weeks to months.
- **Genital ulcers:** recurrent and painful, and it may cause scarring.

Table 15.1 Oral ulcer description on physical examination

Oral ulcer description on physical exam			
More extensive	More painful	More frequent	Appear singly or in crops
Lesions can be shallow or deep (2–30 mm in diameter)	Have a central, yellowish, necrotic base and a punched-out, clean margin	Evolve quickly from a pinpoint flat ulcer to a large sore	Located anywhere in the oral cavity
Subside without leaving scars		Persist for 1–2 weeks	

15.7.8 Pyoderma Gangrenosum

It is an ulcerative cutaneous condition starting from a small, red papule or pustule and then changing into an ulcerative lesion.

15.7.9 Positive Pathergy Reaction at Injection Site

Nonspecific inflammatory reaction to scratches and intradermal saline injection is a common and specific manifestation to these lesions.

15.7.10 Arthritis

During an exacerbation of disease, a non-erosive, asymmetrical arthritis occurs in about 50% of patients with this disease. It involves large and medium joints (wrist, knee, and ankle). Also for the patient with Behçet's disease, experiencing myalgias and migratory **arthralgias** without overt arthritis is common. On the other hand, **arthritis** occurs in about 50% of patients with Behçet's disease [53].

There are also genital, ocular, gastrointestinal, joint, and neurologic manifestations.

15.8 Inflammatory Bowel Disease

Inflammatory bowel disease (IBD) includes two major disorders, which are ulcerative colitis and Crohn's disease. This group of diseases cause many extraintestinal manifestations including eye, skin, joint, renal, and urologic conditions. In this chapter we will talk about skin and the **musculoskeletal** manifestations of IBD. The most common skin lesions presenting with IBD are erythema nodosum and pyoderma gangrenosum and other less common lesions such as Sweet syndrome, necrotizing cutaneous vasculitis, and psoriasis.

15.8.1 Erythema Nodosum (EN)

This lesion is equally present in ulcerative colitis and Crohn's disease, and it is characterized by raised, tender, red or violet subcutaneous nodules, which are around 1 to 5 cm in diameter. The most common sites involved are the extensor surfaces of the extremities, specifically over the anterior tibial area. The presence of erythema nodosum reflects the activity of the intestinal disease and usually disappears by management of intestinal manifestations. Also this lesion is diagnosed clinically, and if we take a biopsy, it will show focal panniculitis, which is rarely done [54].

15.8.2 Pyoderma Gangrenosum

This lesion is less common than EN, and it has a severe course because of its persistence, and it is an uncomfortable lesion preceded by trauma to the skin and initially appears as single or multiple erythematous papules or pustules [55]. The most common site involved is the legs, but it can appear at any site including

abdomen and at the site of surgical scars or at the stoma after colectomy. It may form deep ulceration that contains purulent material by subsequent necrosis of the dermis, and usually the culture of the purulent material is sterile. Pyoderma gangrenosum reflects the activity of IBD disease, and it needs a course of high-dose glucocorticoids over several weeks of treatment [56].

15.8.3 Oral Ulcer

It is a common manifestation in patients with IBD, especially patients with Crohn's disease.

15.8.4 Musculoskeletal Manifestations

The musculoskeletal manifestations of IBD are considered the most common extra-intestinal manifestation, and they include; non-destructive peripheral arthritis and axial arthritis, other less common **musculoskeletal manifestations** are osteoporosis, osteopenia, and osteonecrosis.

15.8.5 Arthritis

The joints that are involved are the spine, sacroiliac joints, and appendicular joints; there are two types of peripheral arthritis: type 1 is acute and remitting and type 2 is a chronic problem and causes frequent relapses; other joint pain can result from complications of IBD such as bacterial infection of the sacroiliac or peripheral joints or as adverse effects from chronic use of glucocorticoid such as osteonecrosis, and those complications must be distinguished from sterile inflammation [57].

15.9 Severe and Life-Threatening Conditions (Fig. 15.21)

15.10 Stevens-Johnson Syndrome (SJS) and Toxic Epidermal Necrolysis (TEN)

They are rare, acute immune complex mediated hypersensitive and life that are nearly always drug-related. Allopurinol is the most common cause [58]. They are a consequence of extensive keratinocyte cell death that results in the

separation of significant areas of skin at the dermal-epidermal junction, producing the appearance of scalded skin [59]. We can classify this disease simply into as follows:

- Stevens-Johnson syndrome (a minor form of toxic epidermal necrolysis): less than 10% body surface area (BSA) detachment.
- Overlapping Stevens-Johnson syndrome/ toxic epidermal necrolysis: detachment of 10–30% of the BSA.

Toxic epidermal necrolysis: detachment of more than 30% of the BSA.

Fig. 15.21 Severe and life-threatening conditions

The initial symptoms of Stevens-Johnson syndrome and toxic epidermal necrolysis that precede cutaneous manifestations by 1 to 3 days are fever, productive cough with thick purulent sputum, pain on swallowing, headache, arthralgia, and malaise.

A patient with SJS and TEN may complain of a rash, which appears first on the trunk, spreading to the neck, face, and proximal upper extremities. The following points are characteristic of cutaneous lesions:

15.10.1 Rash

It first appears as macules and then develops into papules, vesicles, bullae, urticarial plaques, or confluent erythema (erythroderma) (Fig. 15.22).

15.10.2 Bullous Lesions

It appears as flaccid blisters and may rupture leaving denuded skin (Fig. 15.23).

15.10.3 Urticarial Lesions (Not Pruritic)

It may be edematous, erythematous to pale area involving the dermis and epidermis (Fig. 15.24).

Fig. 15.22 Dusky to violaceous rash of toxic epidermal necrolysis

15.10.4 Erythema

Erythema and erosions of the buccal, ocular, and genital mucosae are present in more than 90% of patients.

15.10.5 Palpable Purpura

15.10.6 Edema (Face, Tongue)

15.10.6.1 Sloughing of Skin

- Skin looks like wet cigarette paper.
- Skin ulceration.
- Skin necrosis.
- Nikolsky sign: it should be sought by exerting tangential mechanical pressure with a finger on several erythematous zones and considered positive if dermal-epidermal cleavage is induced (Fig. 15.25).

15.11 Erythroderma Exfoliation

More than 90% of body surface areas are involved by generalized redness and scaling of the skin due to generalization of pre-existing dermatoses (such as psoriasis or atopic dermatitis), drug reactions, or cutaneous T-cell lymphoma (CTCL) [60]. The clinical features are as follows:

15.11.1 Erythema

15.11.1.1 Exfoliation and Scales (2–6 Days after Erythema)

There is variation in the size and the color of the scales. In acute phases, scales are usually large and crusted while in chronic states are smaller and drier. Occasionally, the cause of the erythroderma is suggested by the character of the scale:

- Fine scale in atopic dermatitis or dermatophytosis.
- Bran-like in seborrheic dermatitis.
- Crusted in pemphigus foliaceus.
- Exfoliative in drug reactions.

Fig. 15.23 Flaccid bullae with detachment of necrolytic epidermis

Fig. 15.24 Urticarial plaques (wheals)

Fig. 15.25 Nikolsky sign

15.11.2 Pruritus

Approximately 90% of patients complain from it, so it is the most frequent complaint. Thickness of the skin and areas of lichenification are seen in one-third of cases due to itching.

15.11.3 Pain

Most patients complain of severe skin pain.

15.11.4 Dyspigmentation

Hyperpigmentation area (45%) observed more frequently than hypo- or depigmentation (20%).

15.11.5 Palmoplantar Keratoderma

Hyperkeratosis of the palms and soles. Approximately 30% of erythrodermic patients present with it.

15.11.6 Nail Changes

They are related to the underlying cause of erythroderma, for example, pit in psoriasis or horizontal ridging in dermatitis. Most often “shiny” nails are observed, but discoloration, brittleness, dullness, subungual hyperkeratosis, Beau’s lines, paronychia, and splinter hemorrhages can be seen.

15.11.7 Diffuse Non-scarring Alopecia

It appears in 20% of patients with chronic erythroderma.

15.11.8 Systemic Manifestation

- Generalized peripheral lymphadenopathy.
- Pedal or pretibial edema.
- Facial edema.

- Tachycardia.
- Splenomegaly is rarely seen and occurs most often in association with lymphoma.

15.11.9 Complications

- Multiple seborrheic keratosis.
- Cutaneous infection with *Staphylococcus aureus*.
- Bilateral ectropion.
- Purulent conjunctivitis.
- Risk of cardiac failure.
- Anemia.

15.12 Gonococcal Arthritis

Considered as the most common form of septic arthritis in the United States and caused by gram-negative diplococcus *Neisseria gonorrhoeae*. It is composed of two forms:

- Bacteremic form (arthritis-dermatitis syndrome).
- Septic arthritis form (localized to the joint) [58]

Bacteremic form (arthritis-dermatitis syndrome)

- Migratory arthralgias and arthritis:
It presents as:
 - Polyarticular.
 - Asymmetric.
 - Upper extremities involvement more than lower extremities.
 - The most commonly affected joints are wrists, elbows, knees, and ankles.
 - It may evolve into a septic arthritis.
- Tenosynovitis:
An inflammation that involves the tendon and its sheath; it is almost always asymmetrical and commonly over the dorsum of the wrist and hands. Also, it can affect the ankle, knee, and metacarpophalangeal joints [60].
- Dermatitis:
Around 40–70% of patients with bacteremic form are affected.

It presents as:

- Tiny maculopapular, pustular, or vesicular lesions on an erythematous base.
- Painless and non-pruritic lesions.
- The lesion's center may become necrotic or hemorrhagic.
- The lesions may rarely resemble erythema nodosum or erythema multiforme [60].

Other presentations may include:

- Fever, rarely higher than 39 °C.
- Fitz-Hugh-Curtis syndrome (gonococcal perihepatitis).
- Sepsis with Waterhouse-Friderichsen syndrome.
- Gonococcal endocarditis (rare in the antibiotic era).
- Gonococcal meningitis (very rare in the antibiotic era).

Septic arthritis form:

It presents as an acute inflammation to the joints with signs of:

- Joint effusion.
- Warmth.
- Tenderness.
- Reduced range of motion.
- Marked erythema.

One form of complication is permanent joint damage. Other complications are pericarditis, perihepatitis, pyomyositis, glomerulonephritis, meningitis, endocarditis, and osteomyelitis [58].

DIP	Distal interphalangeal joint
DM	Dermatomyositis
CTCL	Cutaneous T-cell lymphoma
ESR	Erythrocyte sedimentation rate
CRP	C-reactive protein
IBD	Inflammatory bowel disease
EN	Erythema nodosum
SJS	Stevens-Johnson syndrome
TEN	Toxic epidermal necrolysis
BSA	Body surface area

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Abbreviations

RA	Rheumatoid arthritis
PND	Paraneoplastic neurological disorders
HCV	Hepatitis C virus
SLE	Systemic lupus erythematosus
ACLE	Acute cutaneous lupus erythematosus
SCLE	Subacute cutaneous lupus erythematosus
CCLE	Chronic cutaneous lupus erythematosus
DLE	Discoid lupus erythematosus

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