

CHAPTER 1

Bacterial Infections

CHAPTER MENU

- | | |
|---|--|
| <ul style="list-style-type: none">1.1 Staphylococcal and Streptococcal Infections<ul style="list-style-type: none">1.1.1 Impetigo Contagiosa1.1.2 Ostiofolliculitis (Bockardt)1.1.3 Pseudomonas (Gram-Negative) Folliculitis (Whirlpool/Hot Tub Dermatitis)1.1.4 Perianal Streptococcal Dermatitis1.1.5 Differential Diagnosis: Acne Papulopustulosa1.1.6 Differential Diagnosis: Pseudofolliculitis Barbae1.1.7 Ecthyma Gangrenosum1.1.8 Abscess1.1.9 Furuncle1.1.10 Carbuncle1.1.11 Erysipelas (Cellulitis)1.1.12 Phlegmon1.1.13 Necrotizing Fasciitis (Streptococcal Gangrene)^o1.1.14 Hidradenitis Suppurativa (Acne Inversa)1.2 Other Bacterial Infections: Corynebacteria<ul style="list-style-type: none">1.2.1 Erythrasma1.2.2 Pitted Keratolysis (Keratoma Sulcatum)1.2.3 Trichobacteriosis (Trichomycosis) Palmellina1.2.4 Erysipeloid1.2.5 Anthrax1.2.6 Nocardiosis1.2.7 Rhinoscleroma1.3 Rochalimaea/Bartonellae<ul style="list-style-type: none">1.3.1 Bacillary Angiomatosis and Cat Scratch Disease1.3.2 Verruga Peruana1.3.3 Differential Diagnosis: Pyogenic Granuloma (Lobular Capillary Hemangioma; Botryomycosis)1.4 Mycobacterial Infections<ul style="list-style-type: none">1.4.1 Tuberculosis Cutis1.4.2 Atypical Mycobacteriosis: Fish Tank (Swimming Pool) Granuloma1.4.3 Leprosy (Hansen Disease)1.4.4 Buruli Ulcer1.5 Actinomycosis | <ul style="list-style-type: none">1.6 Borrelia Infections (Lyme Disease)<ul style="list-style-type: none">1.6.1 Variant: Erythema (Chronicum) Migrans (ECM) (Stage I)1.6.2 Variant: Lymphadenitis Cutis Benigna (Pseudolymphoma, Lymphocytoma Cutis) (Stage I)1.6.3 Variant: Morphea/Scleroderma-Like Lesions (Stage II)1.6.4 Variant: Acrodermatitis Chronica Atrophicans (Stage III)1.6.5 Variant: Juxta-Articular Fibrous Nodules in Acrodermatitis Chronica Atrophicans (Stage III)1.6.6 Differential Diagnosis: Actinic Reticuloid^o1.7 Venereal Diseases<ul style="list-style-type: none">1.7.1 Gonorrhea1.7.2 Syphilis, Chancres1.7.3 Ulcus Molle (Chancroid)1.7.4 Granuloma Inguinale (Donovanosis; Granuloma Venereum)1.7.5 Lymphogranuloma Inguinale (Lymphogranuloma Venereum; Duran-Nicolas-Favre Disease)1.8 Rickettsial Infections1.9 Dermatoses Associated with Bacterial Infections<ul style="list-style-type: none">1.9.1 Staphylococcal Scalded Skin Syndrome (SSSS)1.9.2 Differential Diagnosis: Toxic Epidermal Necrolysis (TEN)1.10 Dermatoses Mimicking Bacterial Infections<ul style="list-style-type: none">1.10.1 Pyoderma Gangrenosum1.10.2 Infantile Acropustulosis1.10.3 Acute Generalized Exanthematous Pustulosis (AGEP)1.10.4 Psoriasis Pustulosa1.10.5 Localized Neutrophilic Eccrine Hidradenitis Associated with Mitoxantrone Treatment1.10.6 Erosive Pustular Dermatitis (Pustular Ulcerative Dermatitis) of the Scalp |
|---|--|

^ono pictures

1.1 Staphylococcal and Streptococcal Infections

1.1.1 Impetigo Contagiosa

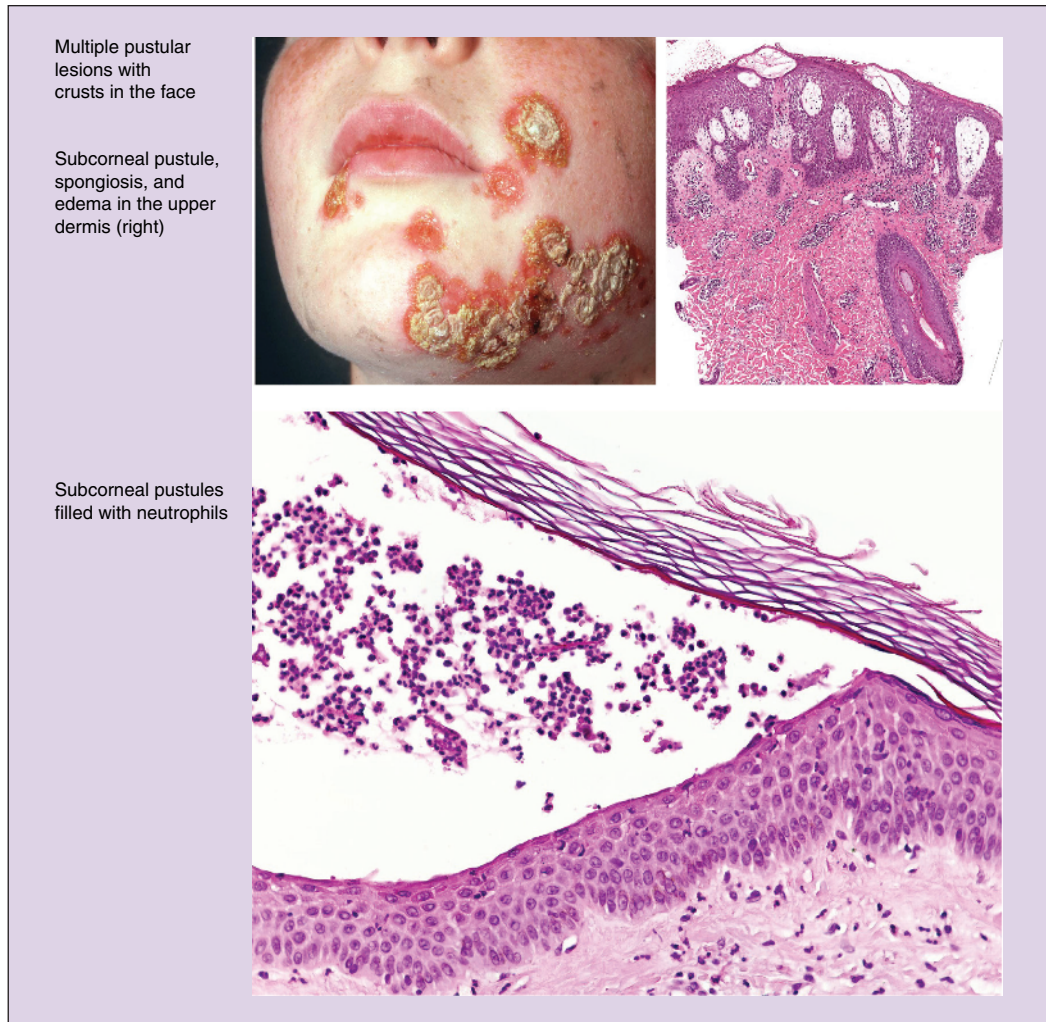


Figure 1.1.1.1 Impetigo Contagiosa.

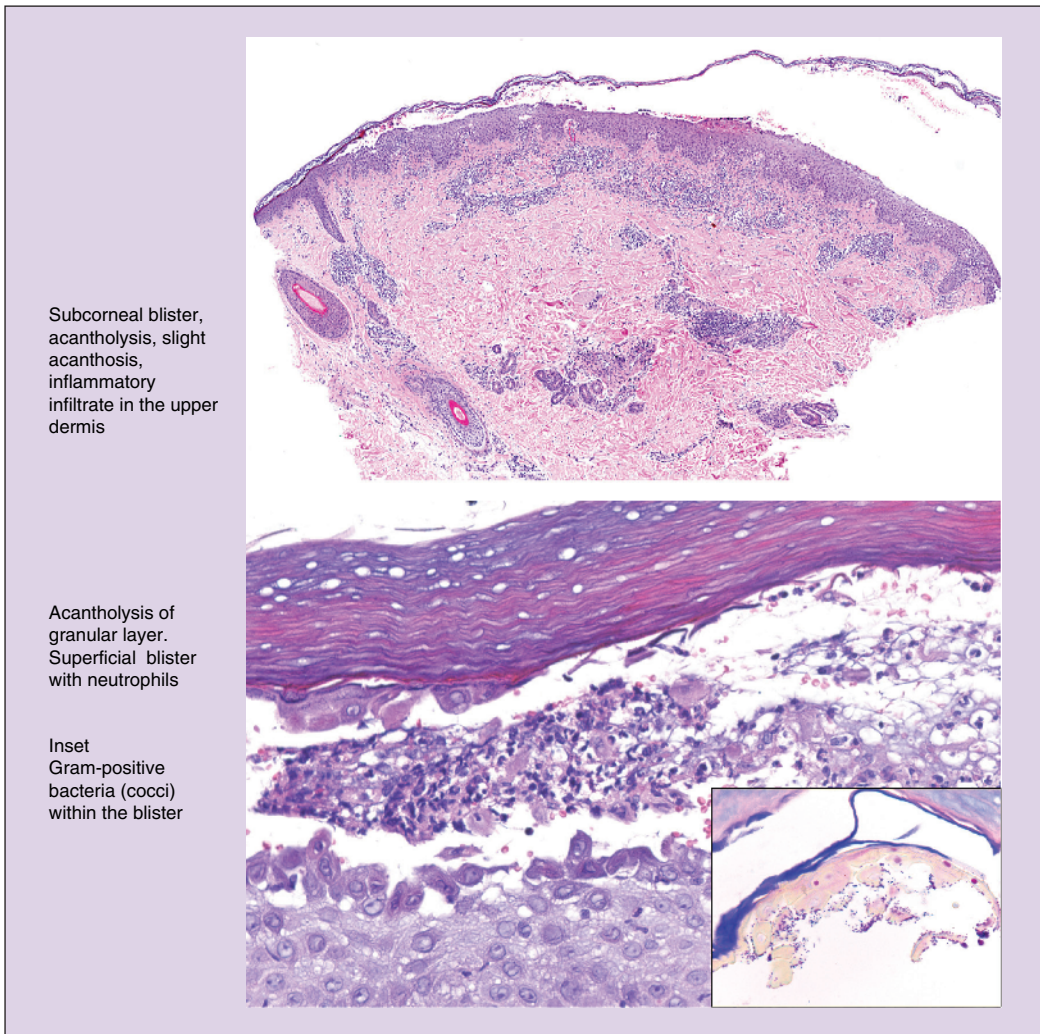


Figure 1.1.1.2 Impetigo Contagiosa.

CF: Streptococcal infections initially induce erythematous patches with fragile subcorneal tiny vesicles, which easily rupture and develop into yellowish crusts.

Bullous lesions with thicker blister roof are usually due to staphylococcal infection.

The face and extremities of children are the most common localizations.

Impetiginization of various inflammatory skin disorders is caused by secondary infection.

HF:

- Subcorneal vesicles filled with neutrophils
- Acantholytic changes in the granular layer
- The thin roof of the pustule is often detached and replaced by necrotic crusty debris
- Neutrophil-rich lymphohistiocytic infiltrate in the upper dermis

DD: Pemphigus foliaceus (similar histology, no bacteria, positive direct immunofluorescence).

Reference

Darmstadt, G. L., & Lane, A. T. (1994). Impetigo: An overview. *Pediatr Dermatol*, **11**(4), 293–303.

Durdu, M., Baba, M., & Seckin, D. (2008). The value of Tzanck smear test in diagnosis of erosive, vesicular, bullous, and pustular skin lesions. *J Am Acad Dermatol*, **59**(6), 958–964.

1.1.2 Ostiofolliculitis (Bockardt)

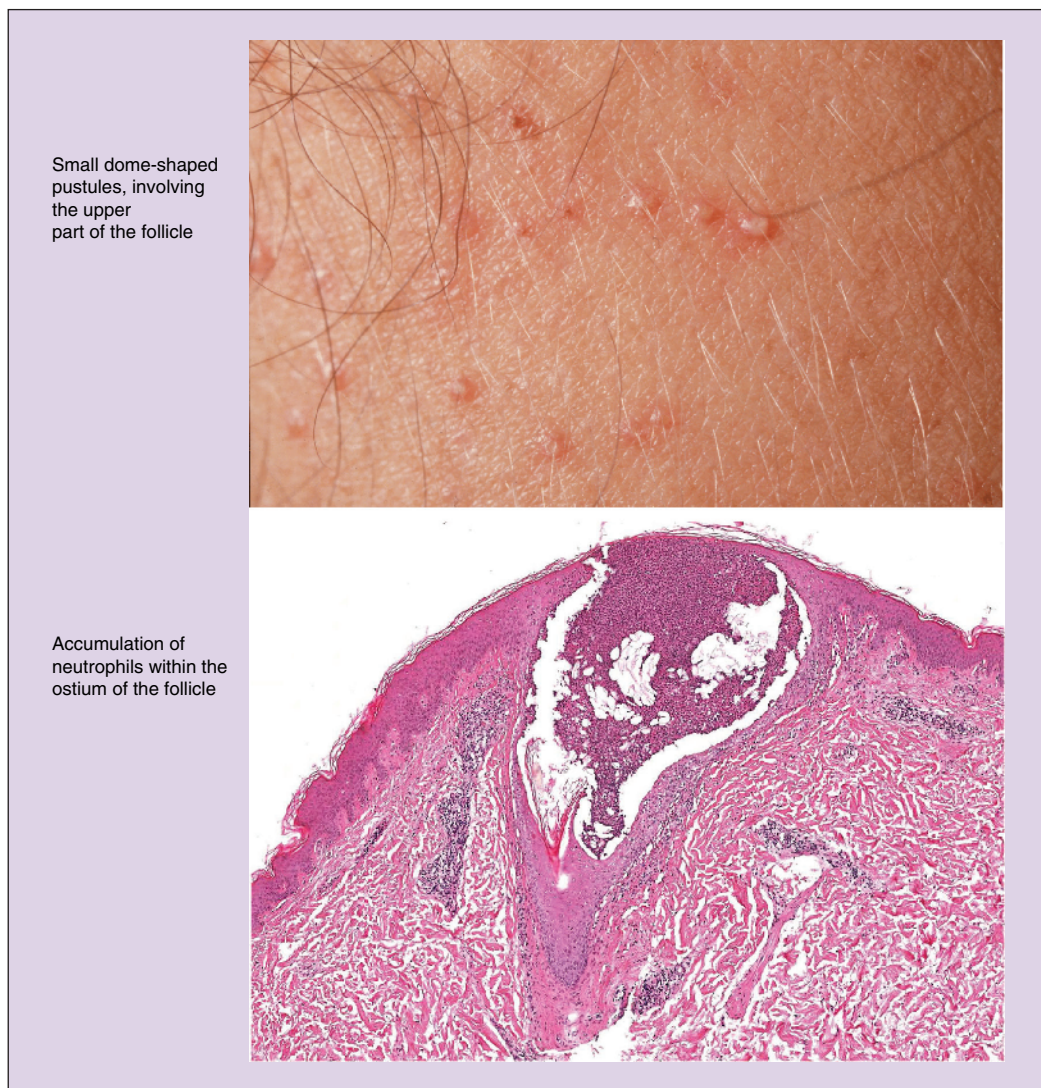


Figure 1.1.2 Ostiofolliculitis (Bockhardt).

Folliculitis is a general term, describing inflammatory reactions within and around follicular structures. There are many types of folliculitis, including

infectious, inflammatory, mechanical, or chemical ones. In infectious folliculitis bacterial, fungal or viral agents can be involved, mostly in conjunction with

predisposing factors like diabetes, atopic dermatitis, or immunodeficiencies.

Staphylococcus aureus, *Streptococcus pyogenes*, and *Pseudomonas aeruginosa* most commonly affect follicular structures, leading to acute superficial folliculitis, with or without deep abscess formation or chronic granulomatous inflammation. Bacterial and fungal folliculitis show similar microscopic features.

CF: Small yellow, dome-shaped pustules in a follicular distribution with the terminal or vellus hair in the center. Preferential localizations are scalp, face, and axillae.

HF: Bacterial and fungal folliculitis show similar microscopic features. Neutrophils are present in the upper part of the follicle, the infundibulum, or the subcorneal layer of the epidermis.

DD: Other forms of infectious, mechanical, or chemical folliculitis.

1.1.3 *Pseudomonas* (Gram-Negative) Folliculitis (Whirlpool/Hot Tub Dermatitis)

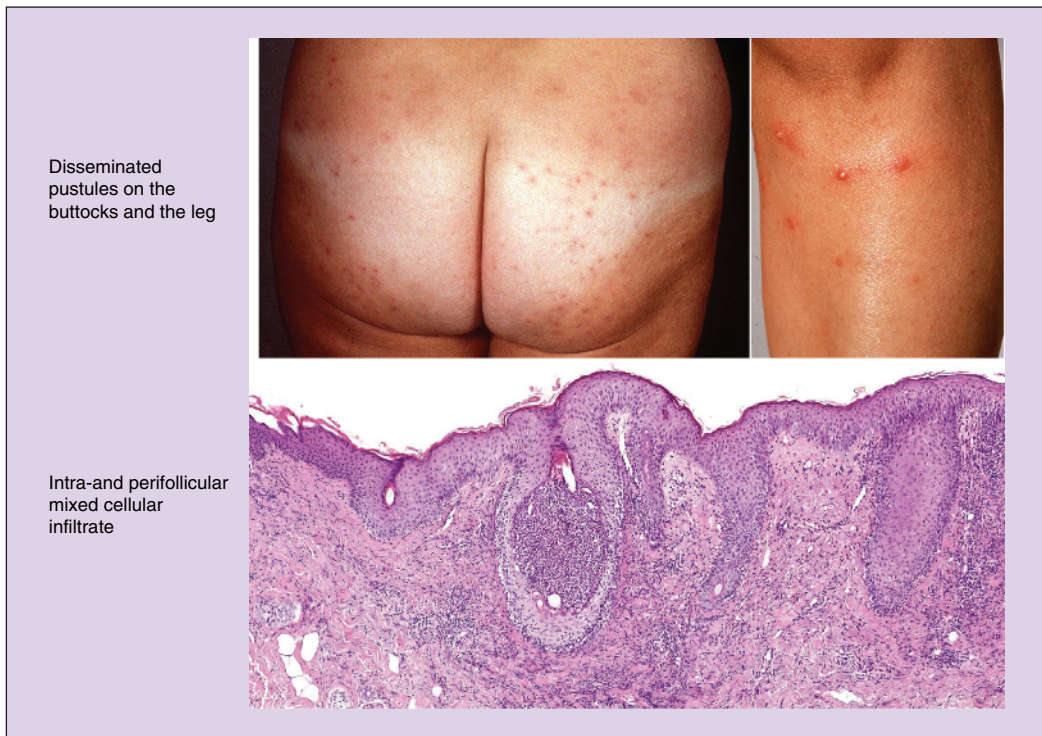


Figure 1.1.3 *Pseudomonas* (Gram-Negative) Folliculitis (Whirlpool Dermatitis).

Pseudomonas aeruginosa is a gram-negative bacterium which is part of the normal flora of the large skin folds and intertriginous areas. Under special local predisposing conditions or in patients with diabetes

or patients under immunosuppression, “whirlpool” or hot tub folliculitis may develop.

CF: Disseminated painful pustules, mostly at body sites covered by bathing suit.

HF:

- Follicles, with follicle walls partly ruptured
- Acneiform intra- and perifollicular inflammatory infiltrate, predominantly neutrophilic
- Plasma cells and eosinophils may be present

DD: Acne; other bacterial, fungal (pityrosporum) or viral (HIV-associated) folliculitis; demodex folliculitis.

Reference

- Mazza, J., Borkin, M., Buchholz, R., & Deleo, V. (2013). Pseudomonas folliculitis contracted from rubber gloves: A public health concern. *J Am Acad Dermatol*, **69**(2), e93–94.
- Yu, Y., Cheng, A. S., Wang, L., Dunne, W. M., & Bayliss, S. J. (2007). Hot tub folliculitis or hot hand-foot syndrome caused by Pseudomonas aeruginosa. *J Am Acad Dermatol*, **57**(4), 596–600.

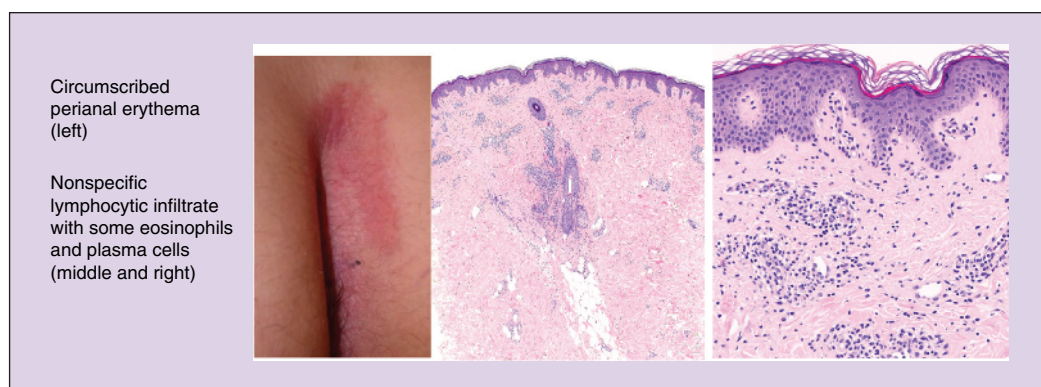
1.1.4 Perianal Streptococcal Dermatitis

Figure 1.1.4 Perianal Streptococcal Dermatitis.

This is caused by group B β -hemolytic streptococci. Similar symptoms may more frequently be caused by perianal allergic, toxic, seborrheic, or atopic dermatitis.

CF: Circumscribed pruritic eczematous erythema in the gluteal and perianal region, mostly by bacterial dissemination from the upper respiratory tract, most commonly in young children but also in adults.

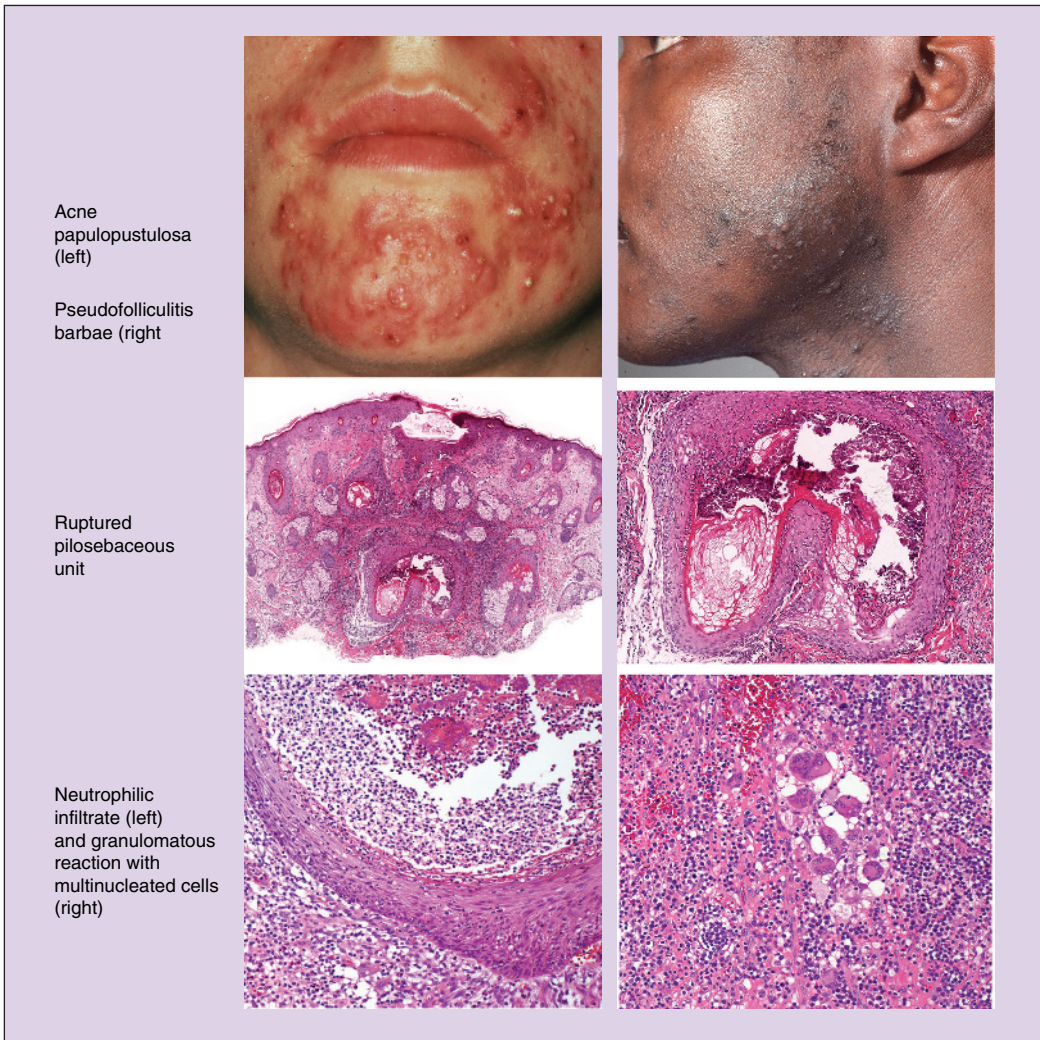
HF: Variable nonspecific histologic features. Diagnosis depends on positive swab for β -hemolytic streptococci. The rationale for taking a biopsy may lie in the exclusion of other conditions (differential diagnoses; see below).

DD: Erysipelas; fungal infection; contact dermatitis; psoriasis; Langerhans cell histiocytosis; zinc deficiency/acrodermatitis enteropathica; intertrigo; lichen planus.

Reference

- Kahlke, V., Jongen, J., Peleikis, H. G., & Herbst, R. A. (2013). Perianal streptococcal dermatitis in adults: Its association with pruritic anorectal diseases is mainly caused by group B Streptococci. *Colorectal Dis*, **15**(5), 602–607.
- Serban, E. D. (2018). Perianal infectious dermatitis: An underdiagnosed, unremitting and stubborn condition. *World J Clin Pediatr*, **7**(4), 89–104.

1.1.5 Differential Diagnosis: Acne Papulopustulosa



Figures 1.1.5 and 1.1.6 Differential Diagnosis: Acne Papulopustulosa and Pseudofolliculitis Barbae.

CF: Papulopustular lesions, preferentially in the face during puberty and in adolescence. Various grades of severity: acne comedonica (I); acne papulopustulosa (II); acne conglobata (III).

HF (acne papulopustulosa):

- Ruptured hair follicle
- Hyperparakeratosis in the ostium and infundibular parts of the hair follicles with keratin and cellular debris

- Microorganisms (*Propionibacterium acnes* and *Staphylococcus epidermidis*) surrounded by infiltration with neutrophils
- Foreign body (granulomatous) reaction

Reference

Leyden, J. J. (1995). New understandings of the pathogenesis of acne. *J Am Acad Dermatol*, **32**(5 Pt 3), S15–25.

1.1.6 Differential Diagnosis: Pseudofolliculitis Barbae

CF: Preferentially in black people with curly hair, recurrent papular and pustular, acneiform lesions occur in the beard area, secondary to razor shaving, and in the neck, where acne keloidalis nuchae is a frequent sequela.

HF:

- Fragments of hair, penetrating into the skin
- Perifollicular and follicular inflammatory infiltrate

- Foreign body reaction with multinucleated giant cells
- Fibrosis

Reference

Perry, P. K., Cook-Bolden, F. E., Rahman, Z., Jones, E., & Taylor, S. C. (2002). Defining pseudofolliculitis barbae in 2001: A review of the literature and current trends. *J Am Acad Dermatol*, **46**(2 Suppl Understanding), S113–119.

1.1.7 Ecthyma Gangrenosum

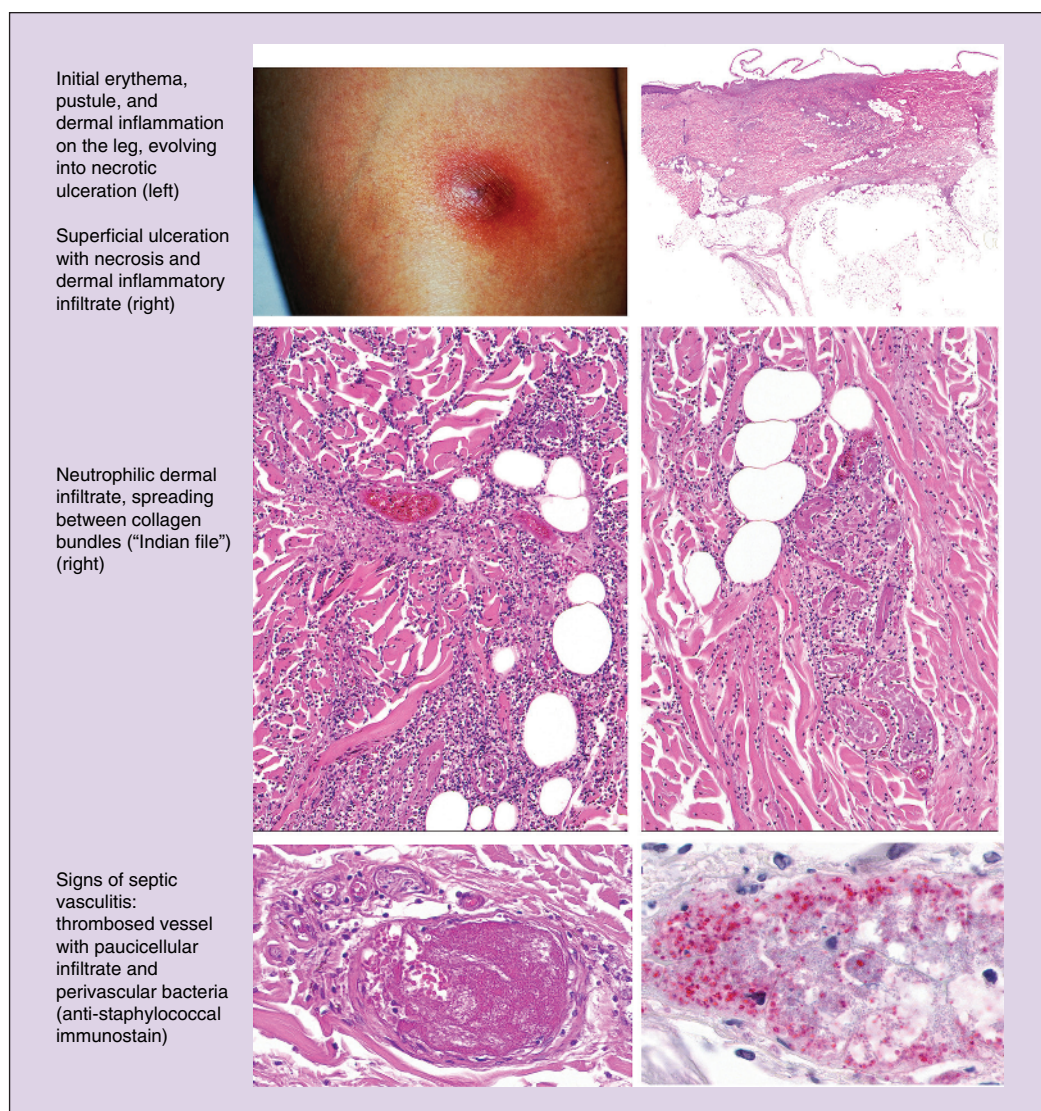


Figure 1.1.7 Ecthyma Gangrenosum.

The term *ecthyma* is used in various semantic combinations, which show different etiologies: Ecthyma simplex is a superficial ulcerating form of impetigo with “punched-out” sharp borders. Ecthyma contagiosum (orf) is caused by parapox infection (orf virus; see below).

Ecthyma gangrenosum is an ulcerative variant of septic vasculitis caused by group A streptococci or *S. aureus*. It commonly is found in tropical areas, in children, or in patients with impaired immunity.

CF: Starting with diffuse erythema, followed by massive edema, pustulation and rapid ulceration, often as sequela to minor trauma; rapid evolution into sharply circumscribed deep ulceration with distinct borders. The limbs of children (buttocks) are preferentially affected. Dissemination may occur (requiring rapid response with antibiotic treatment!). Healing with scar formation.

HF:

- Initially massive edema with subtle mixed inflammatory infiltrate

- Signs of septic vasculitis may be present (thrombosed postcapillary venules with very sparse adjacent inflammatory infiltrate)
- Gram-positive cocci, often adjacent to thrombosed vessels
- Sharply circumscribed “punched-out” deep ulceration
- Debris and necrotic material within the ulcer
- Mostly neutrophilic dermal infiltrate

DD: Ulcerating suppurative inflammation and septic vasculitis of other causes; reactive perforating dermatosis (acute prurigo).

Reference

- Greene, S. L., Su, W. P., & Muller, S. A. (1984). Ecthyma gangrenosum: Report of clinical, histopathologic, and bacteriologic aspects of eight cases. *J Am Acad Dermatol*, **11**(5 Pt 1), 781–787.

1.1.8 Abscess

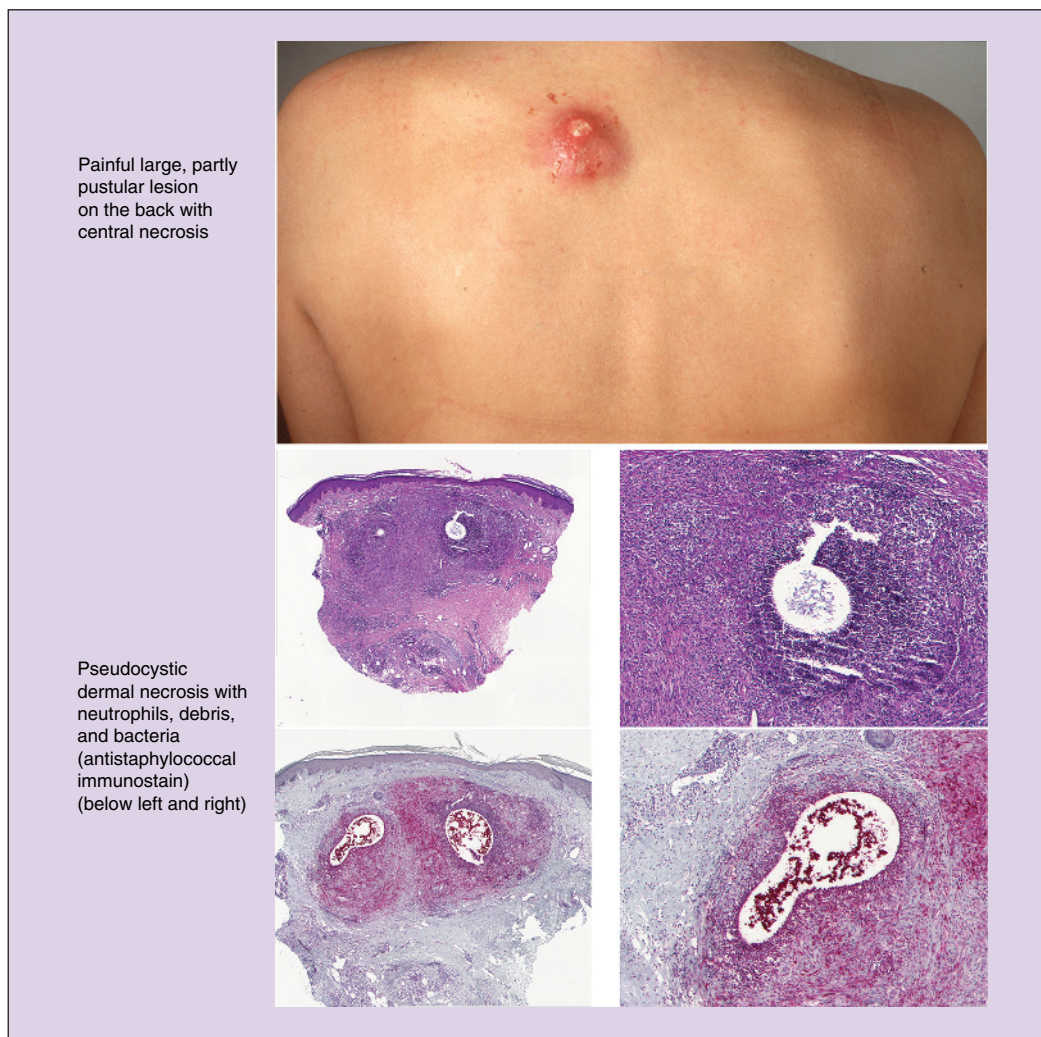


Figure 1.1.8 Abscess.

CF: Mostly painful and highly inflamed intradermal accumulation of pus, opening and draining to the surface.

HF: Intradermal necrosis and massive sup-puration with intradermal pseudocystic accumulation of neutrophils and debris.

DD: Furuncle; carbuncle; ecthyma.

1.1.9 Furuncle

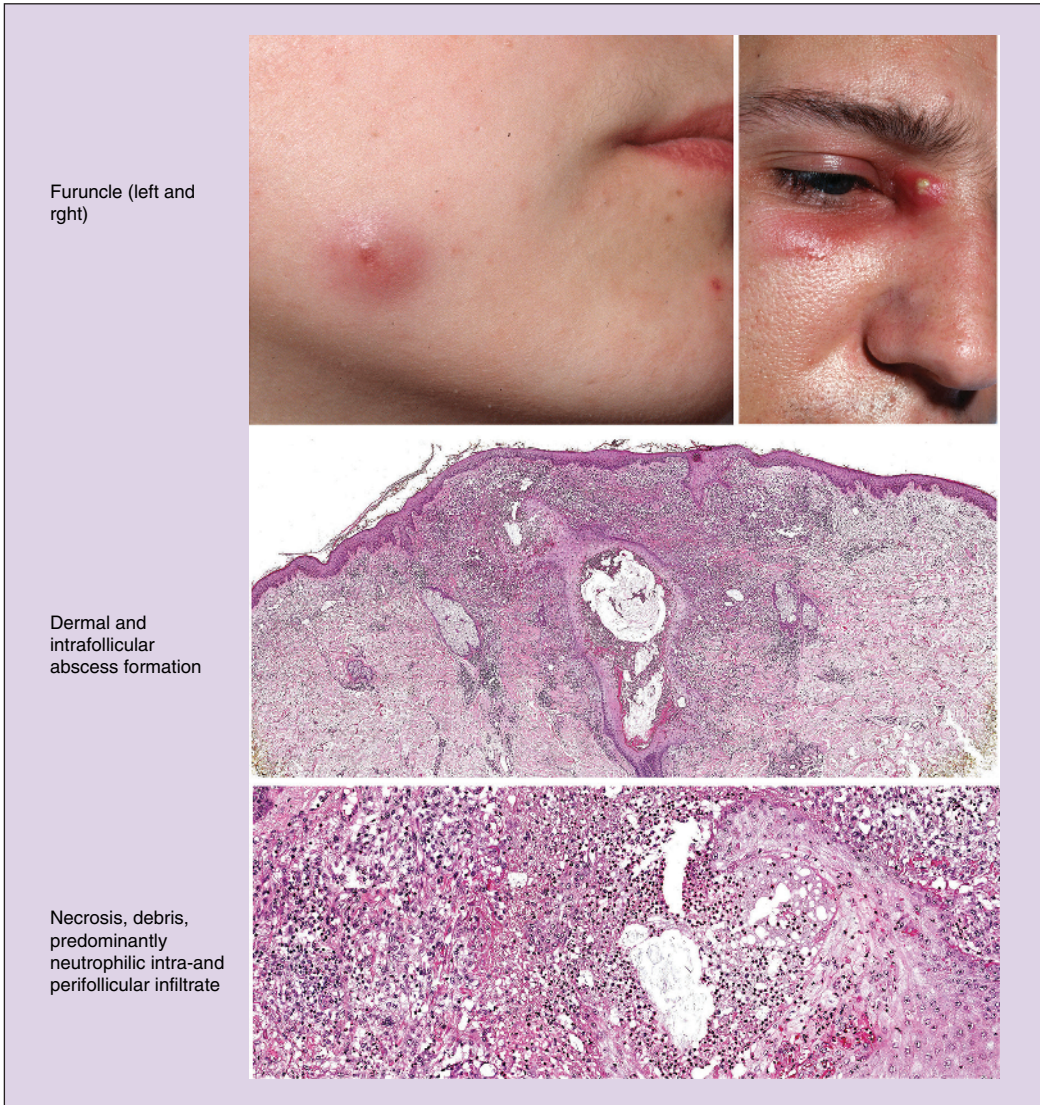


Figure 1.1.9 Furuncle.

CF: Under conditions of poor hygiene or in patients with diabetes or with reduced immune status, acute deep forms of folliculitis can develop, which – depending on the size and depth – is referred to as furuncle.

HF: Deep folliculitis is usually accompanied by follicular destruction and resolves with scarring.

- Mixed inflammatory intra- and perifollicular infiltrates

- Neutrophils predominate
- Follicular rupture with abscess formation
- Granulation tissue with giant cells
- Bacterial organisms
- Necrosis
- Scarring in late lesions

DD: Abscess; carbuncle.

1.1.10 Carbuncle

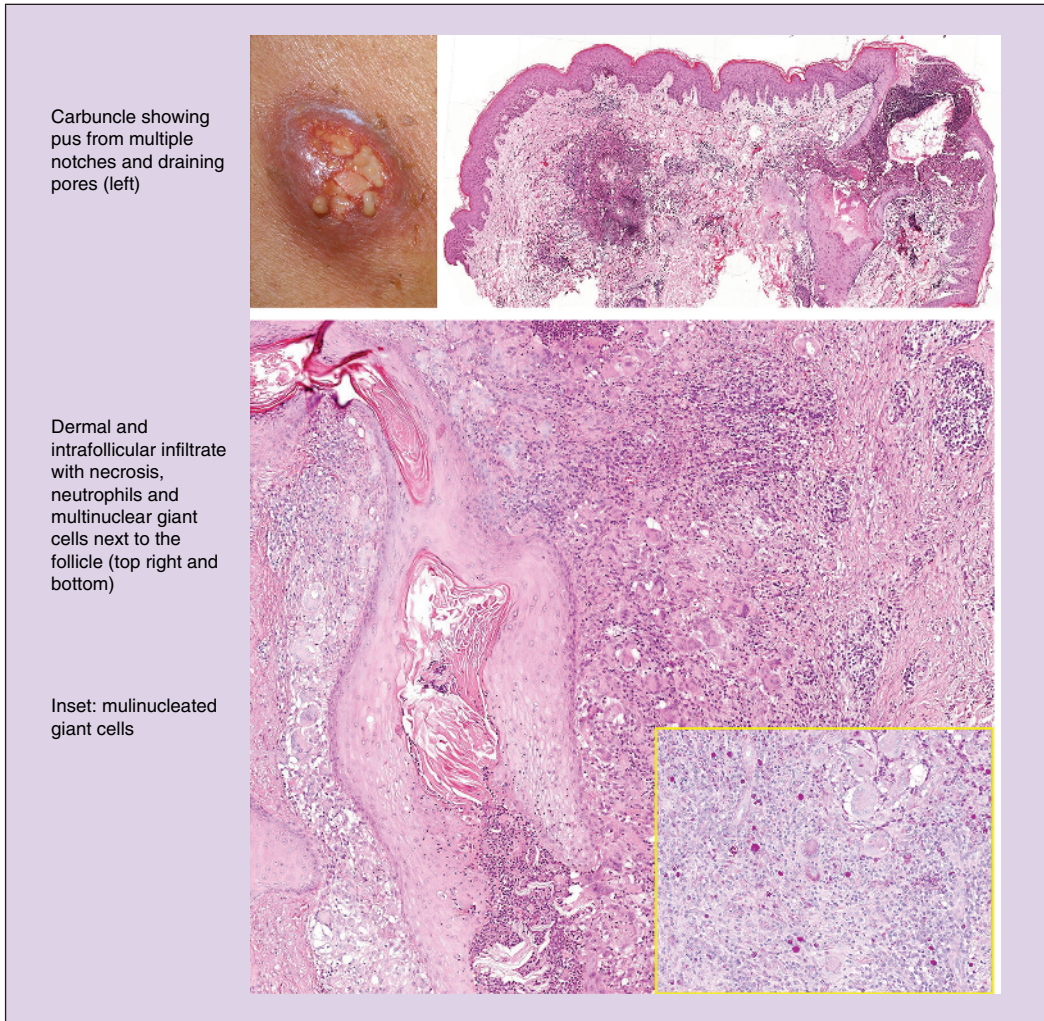


Figure 1.1.10 Carbuncle.

CF: A carbuncle comprises a large nodular furunculoid coalescing purulent lesion involving multiple follicles producing a circumscribed highly inflamed soft nodule, which extrudes pus from multiple notches and openings. Preferential localization is the trunk.

HF:

- Damage of dermal and adnexal structures

- Abscess formation and necrosis
- Granuloma formation with multinucleated giant cells
- Clusters of bacilli (Gram)
- Granulomatous reaction with multinucleated giant cells
- Resolves with scarring

1.1.11 Erysipelas (Cellulitis)

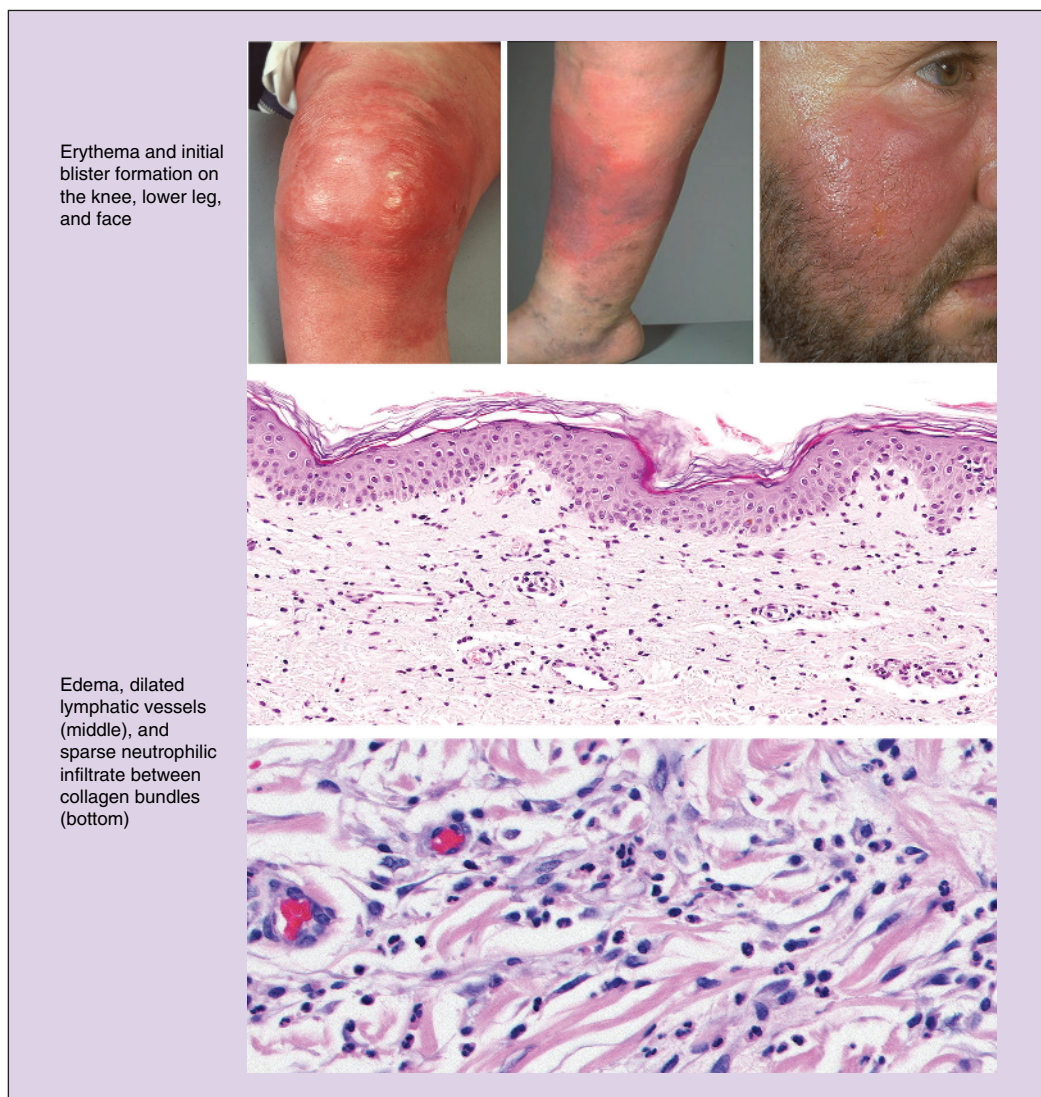


Figure 1.1.11.1 Erysipelas (Cellulitis).

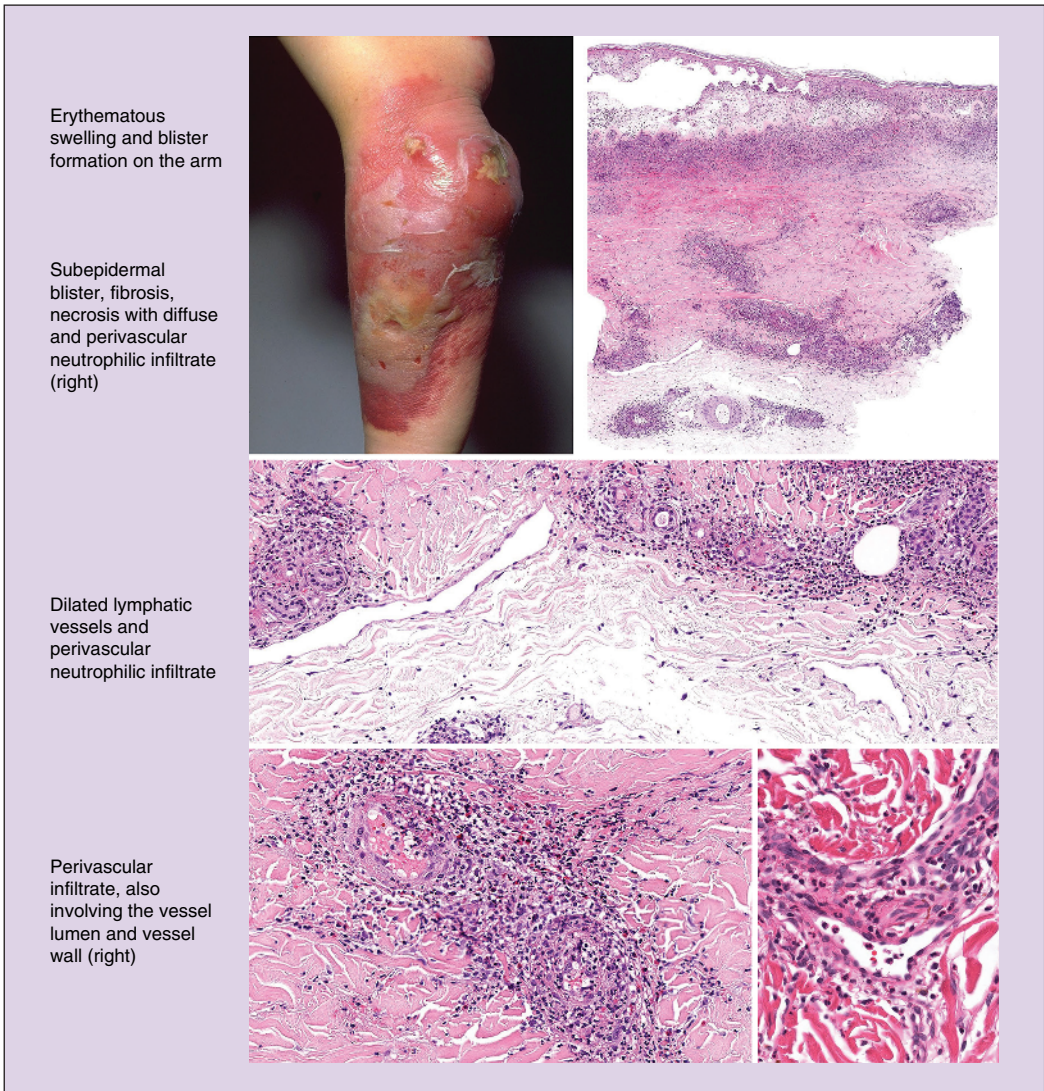


Figure 1.1.11.2 Erysipelas (Cellulitis), bullous.

CF: Following infection with streptococci type A via interdigital maceration or small defects, sharply demarcated peripherally spreading warm and painful erythema develops along superficial lymph vessels, preferentially on the lower legs, arms, or face. Lymphedema is a predisposing factor. Nosologic relationship exists to phlegmon and necrotizing cellulitis. Cellulitis is a maximal variant of erysipelas with dermal and subcutaneous

involvement, necrosis and blister formation, which may be hemorrhagic.

Associated general symptoms are fever, chills, and swelling of the regional lymph nodes. Erysipelas has a tendency to recur.

HF:

- Dermal edema
- Dilated capillaries and lymphatic vessels
- Sparse mixed interstitial and perivascular infiltrate with neutrophils and eosinophils

- Neutrophils in vessel walls and dilated lymphatic vessels
- Occasionally subepidermal blister formation
- Fibrosis in recurrent cases

DD: Contact dermatitis, rosacea, lupus erythematosus, seborrheic dermatitis: in these conditions, fever and chills are characteristically lacking.

1.1.12 Phlegmon

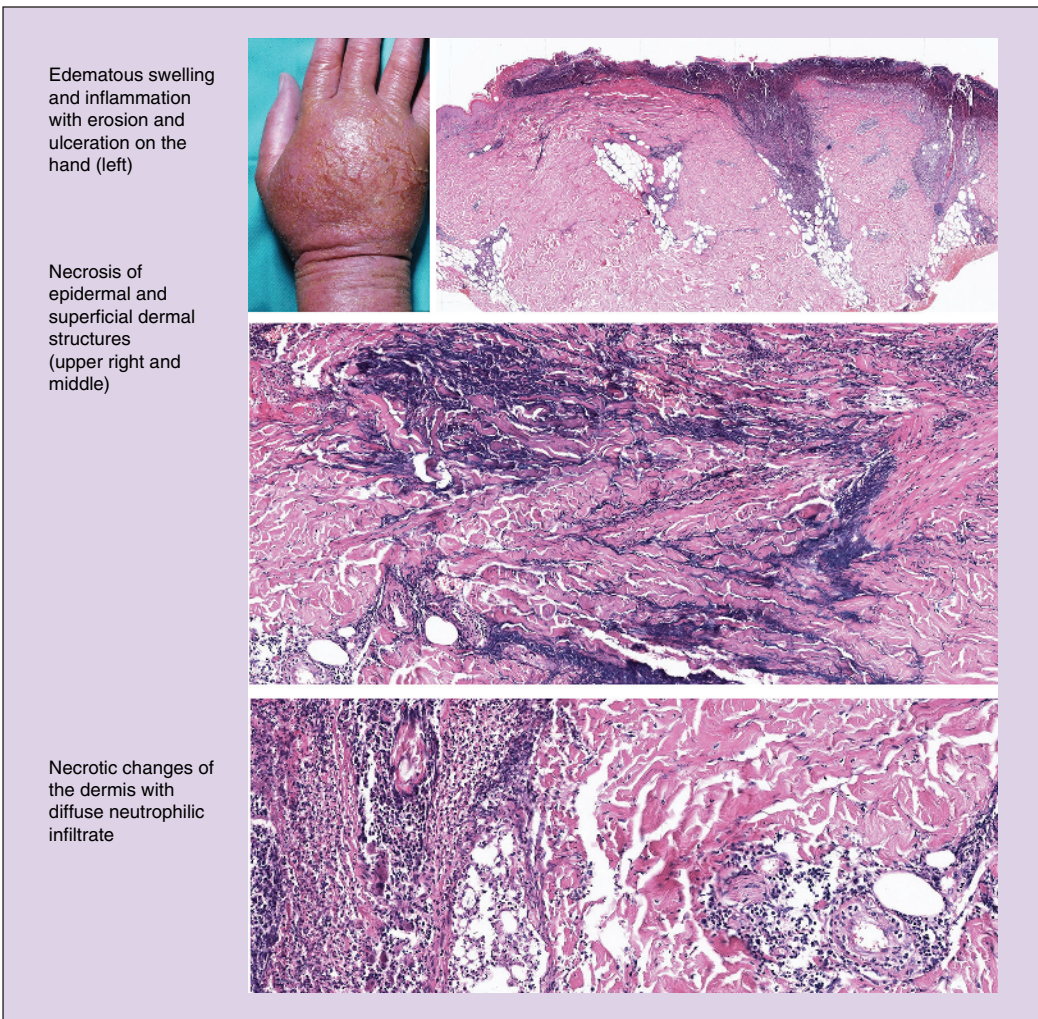


Figure 1.1.12.1 Phlegmon.

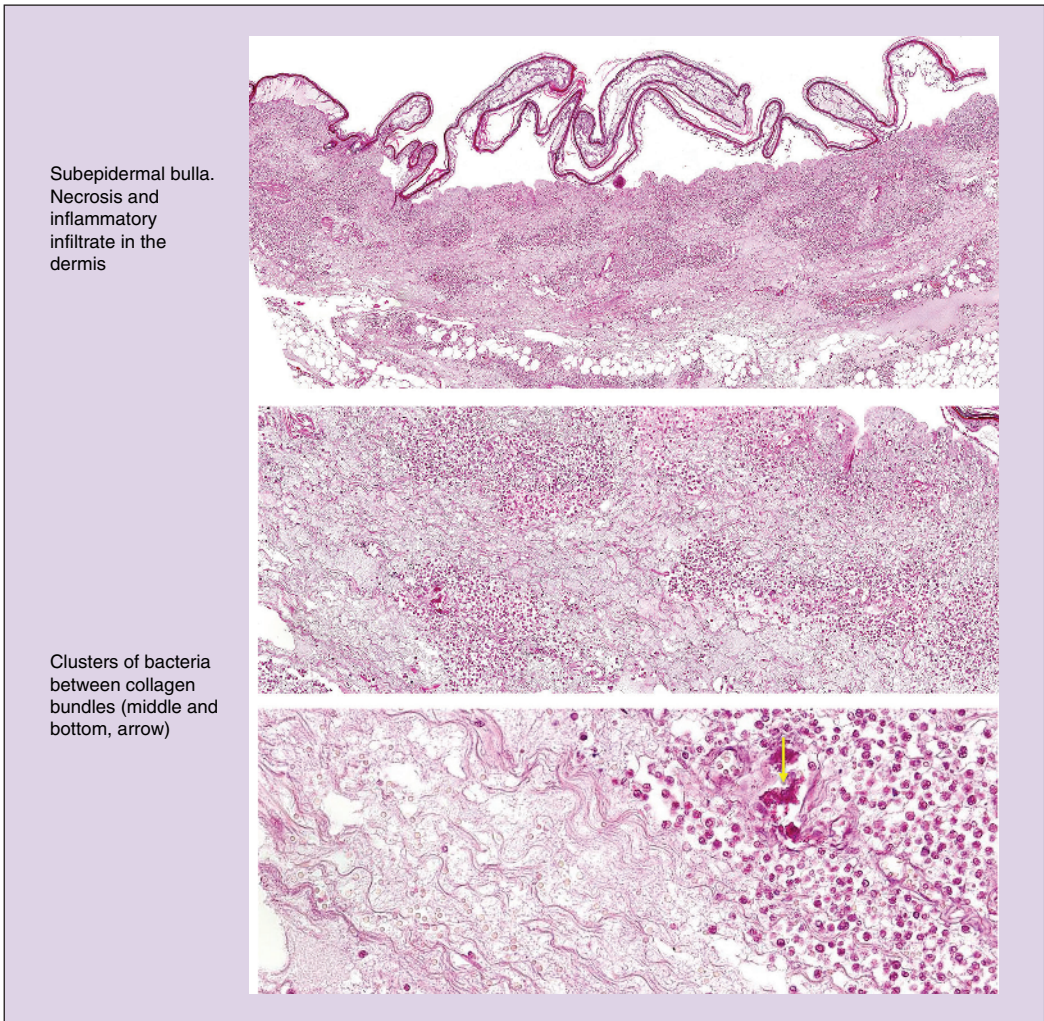


Figure 1.1.12.2 Phlegmon, bullous.

CF: In immunodeficient patients, superficial bacterial infections (staphylococci, streptococci, and others) can rapidly spread within soft tissue, preferentially along fasciae, without respecting natural tissue compartments, and eventually evolve into necrosis of connective tissue, muscles, and fasciae.

HF:

- Epidermis partially or completely necrotic
- Subepidermal blisters and bullae
- Dermal edema, neutrophilic infiltrate, and bacteria
- Blood vessels may be thrombosed

DD: Erysipelas.

1.1.13 Necrotizing Fasciitis (Streptococcal Gangrene)°

This is a fulminant necrotizing process due to infection mostly with group A β -hemolytic streptococci. Impaired health condition and immunodeficiency are predisposing factors in this rapidly developing and often fatal disease, which may follow minor trauma or surgery.

CF: Painful erythema develops rapidly into blister formation, necrosis, and deep ulceration with subsequent gangrene.

HF:

- Blistering
- Diffuse infiltration of the dermis with neutrophils and lymphocytes
- Necrosis of soft tissue
- Involvement of fasciae and muscles
- Thrombosis with occlusion of vessels

DD: Phlegmon; panniculitis.

1.1.14 Hidradenitis Suppurativa (Acne Inversa)

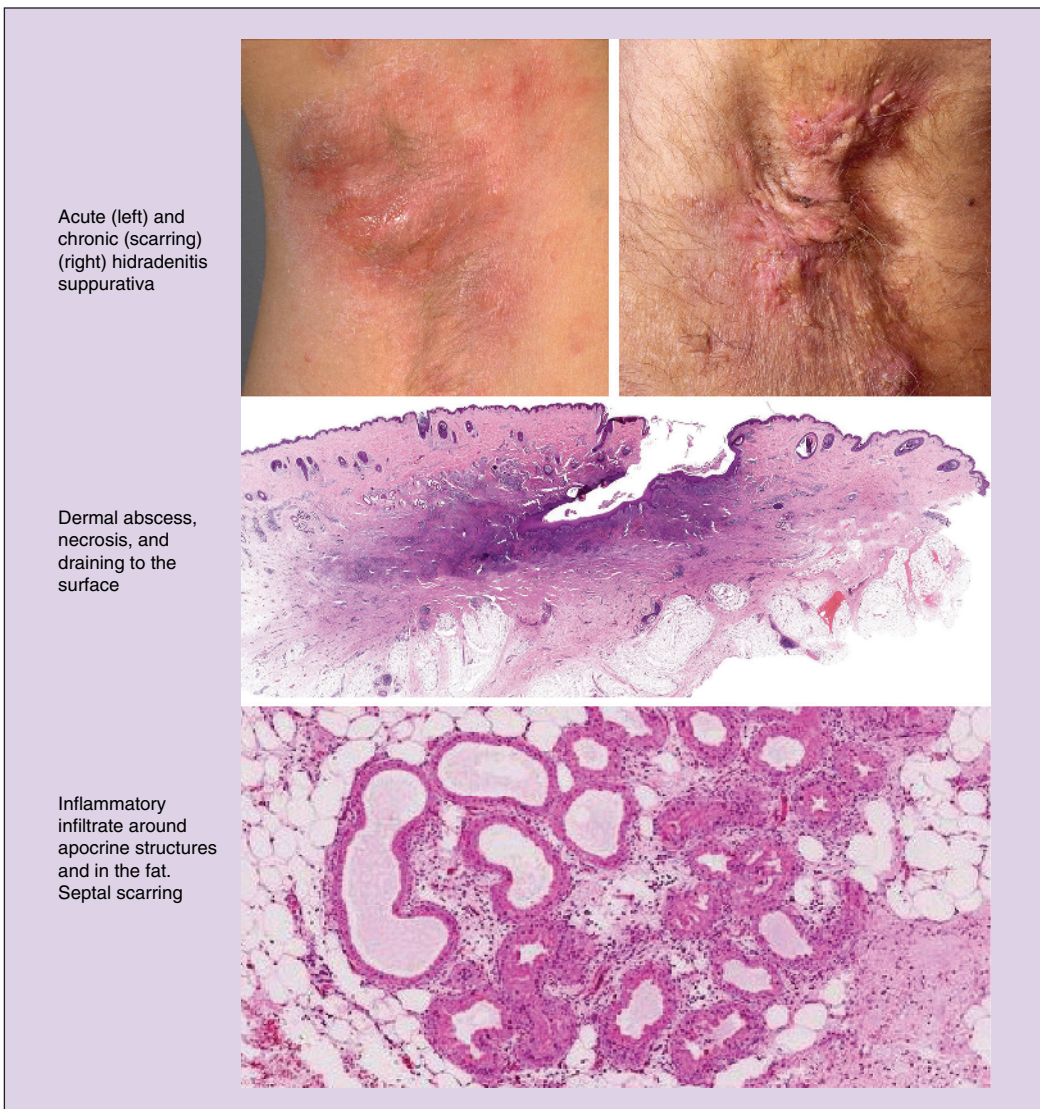


Figure 1.1.14 Hidradenitis Suppurativa (Acne Inversa).

CF: Areas rich in apocrine glands, such as axillae, groin, or buttocks, are preferentially involved, showing painful purulent, furunculoid nodules and scarring with sinuses and fistulas. The disease is associated with acne conglobata.

HF:

- Dermal abscesses, draining to the surface
- Mixed inflammatory infiltrate
- Neutrophils predominate
- Lymphocytes, plasma cells, eosinophils, and fibrosis in later stages
- Granulomatous reactions with multinucleated giant cells
- Scarring fibrosis and destruction of adnexal structures

DD: Granuloma inguinale; Crohn's disease; Pemphigus benignus familiaris (Hailey-Hailey); Actinomycosis; chronic fungal infection; Langerhans cell histiocytosis.

Reference

- Jemec, G. B., & Hansen, U. (1996). Histology of hidradenitis suppurativa. *J Am Acad Dermatol*, **34**(6), 994–999.
- Kalen, J. E., Shokeen, D., Mislankar, M., Wangia, M., & Motaparathi, K. (2018). Langerhans cell histiocytosis with clinical and histologic features of hidradenitis suppurativa: Brief report and review. *Am J Dermatopathol*, **40**(7), 502–505.
- Prens, E., & Deckers, I. (2015). Pathophysiology of hidradenitis suppurativa: An update. *J Am Acad Dermatol*, **73**(5 Suppl 1), S8–11.

1.2 Other Bacterial Infections: Corynebacteria

1.2.1 Erythrasma

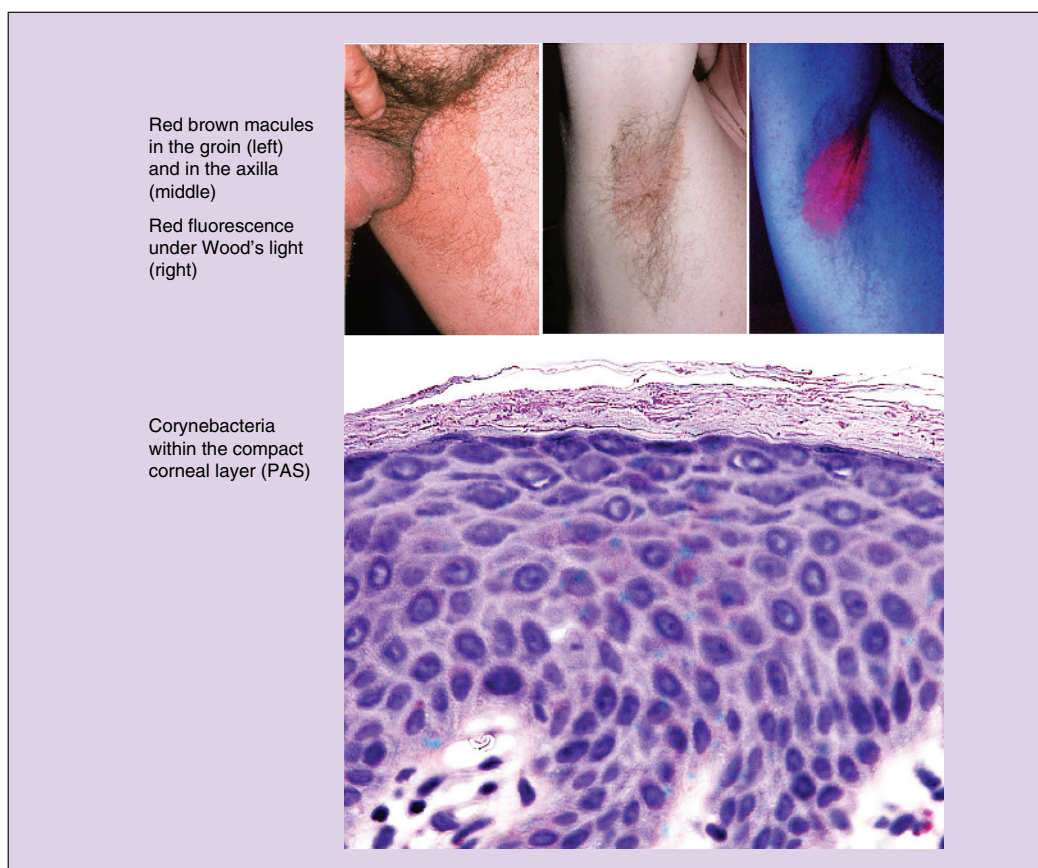


Figure 1.2.1 Erythrasma.

CF: Reddish brown macules in moist intertriginous areas (groin, axillae) due to infection with bacteria *Corynebacterium minutissimum*. Coral red fluorescence under UVA light (Wood lamp).

HF:

- “Invisible” dermatosis (i.e. distinct clinical findings correlating with inconspicuous histopathological setting)

- Tiny filamentous gram-positive, PAS-positive (slightly) rods within the cornified layer
- Sparse dermal perivascular infiltrate may be present

DD: Intertrigo, trichophytia, candidiasis, toxic or allergic contact dermatitis.

1.2.2 Pitted Keratolysis (Keratoma Sulcatum)

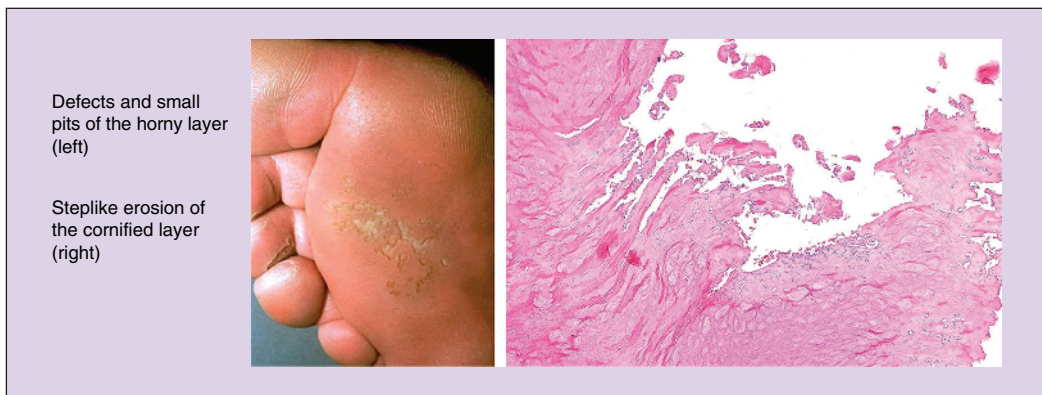


Figure 1.2.2 Pitted Keratolysis (Keratoma Sulcatum).

CF: Mostly in association with hyperhidrosis (occlusive footwear), small pits are seen within the thickened macerated corneal layer of the soles, or occasionally of the palms, due to keratolytic enzymes produced by *Corynebacterium* spp. or other gram-positive bacteria.

HF: Clefts and elongated spaces within the corneal layer, containing bacteria. Missing or sparse inflammation.

Reference

de Almeida, H. L., Jr., Siqueira, R. N., Meireles Rda, S., Rampon, G., de Castro, L. A., & Silva, R. M. (2016). Pitted keratolysis. *An Bras Dermatol*, **91**(1), 106–108.

1.2.3 Trichobacteriosis (Trichomycosis) Palmellina

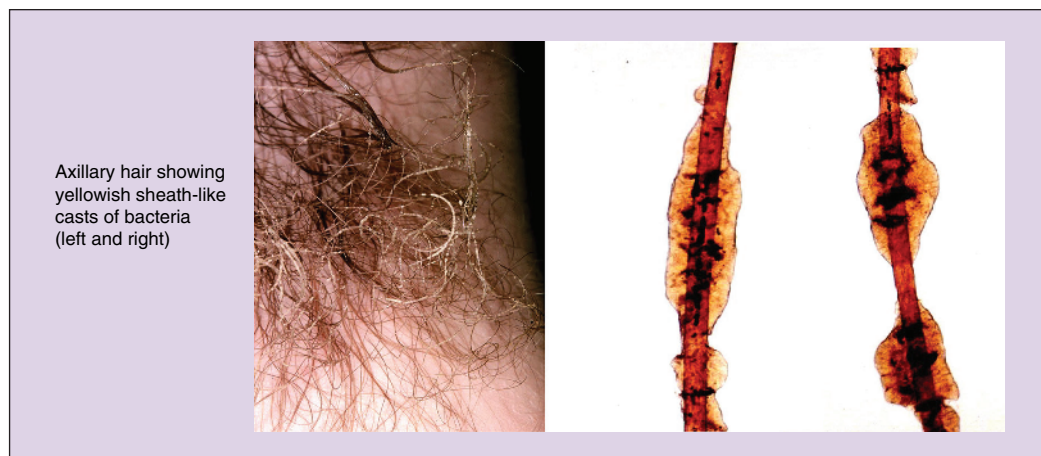


Figure 1.2.3 Trichobacteriosis (Trichomycosis) Palmellina.

CF: This disorder, which formerly was considered to be a fungal infection, in truth is caused by corynebacteria (*Corynebacterium tenuis*), forming white-yellow, red or black, difficult-to-remove, compact deposits along the hair shafts, preferentially in the axillae, where hyperhidrosis is a predisposing factor.

HF: The diagnosis is made clinically, or by microscopic examination of plucked hair shafts, or preferentially with Wood's lamp

(UVA light), revealing red fluorescence due to bacterial protoporphyrin.

DD: Piedra; hair casts; taenia amiantacea.

Reference

Rho, N. K., & Kim, B. J. (2008). A corynebacterial triad: Prevalence of erythrasma and trichomycosis axillaris in soldiers with pitted keratolysis. *J Am Acad Dermatol*, **58**(2 Suppl), S57–58.

1.2.4 Erysipeloid

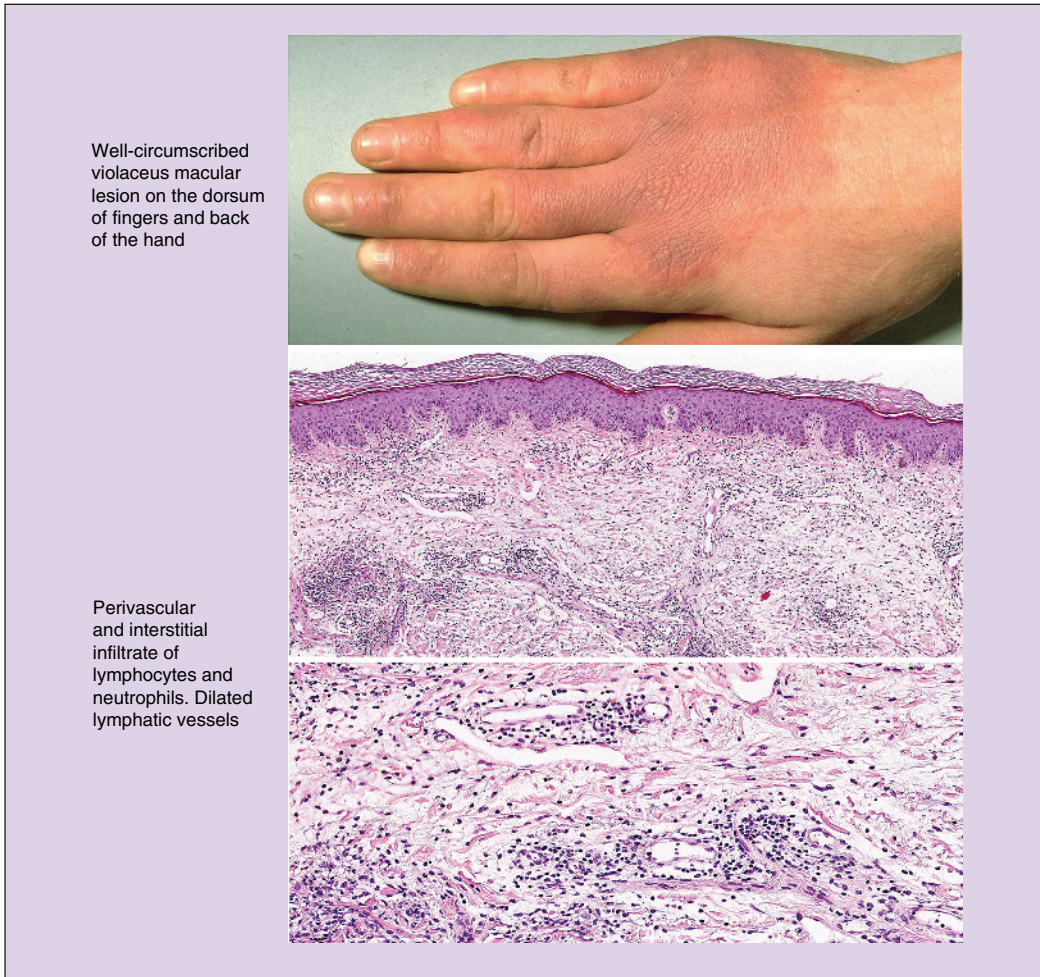


Figure 1.2.4 Erysipeloid.

This rare, acute, mostly self-limited infection, resembling erysipelas, is caused by the gram-positive bacillus *Erysipelothrix rhusiopathiae*. Infections result from direct contact with swine or contaminated animal material. Systemic symptoms, which are commonly encountered in erysipelas, as well as lymphangitis and lymphadenitis, are lacking.

CF: The painful violaceous, macular, well-circumscribed lesion usually evolves from pinpoint injuries on the hands or fingers and slowly spreads peripherally with central clearing. There may be slight diffuse swelling.

HF:

- Dermal edema
- Dilatation of lymphatic vessels

- Diffuse superficial and deep polymorphous inflammatory infiltrate showing lymphocytes, neutrophils, eosinophils, and plasma cells
- Organisms in most cases cannot be detected with histological staining
- Microbiology/molecular pathology from skin specimens reveals infectious organisms

DD: Erysipelas; erythema migrans; contact dermatitis.

Reference

Varela, T. C., & Nico, M. M. (2005). Erysipeloid. *Int J Dermatol*, **44**(6), 497–498.

1.2.5 Anthrax

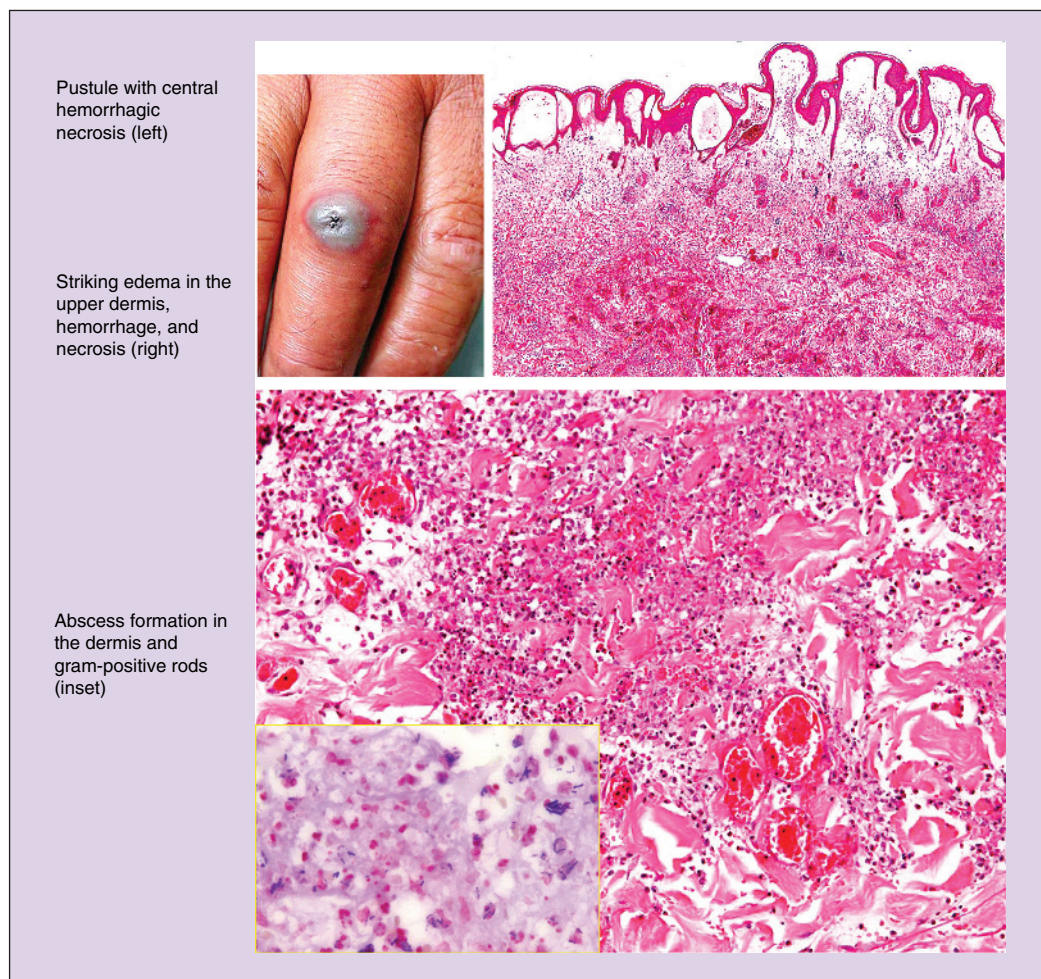


Figure 1.2.5 Anthrax.

The gram-positive *Bacillus anthracis* spawns permanent spores that are resistant in harsh environment, thrive in tissue, and produce exotoxins. Farmers, veterinarians, butchers, and slaughterhouse workers are especially vulnerable to infection. Remarkably, anthrax spores have been misused as biological weapons (respiratory infection).

CF: In cutaneous anthrax infection, striking edema develops at the inoculation site. A pustule forms, which becomes hemorrhagic, necrotic, and

finally turns black in the center (“pustula maligna”).

HF:

- Striking edema in the upper dermis
- Hemorrhage
- Necrosis
- Diffuse lymphocytic and neutrophilic infiltrate in the dermis
- Abscess formation
- Gram-positive, markedly elongated bacterial rods

DD: Sporotrichosis; orf; arthropod bite reaction; staphylococcal infection; tularemia.

Reference

- Dixon, T. C., Meselson, M., Guillemin, J., & Hanna, P. C. (1999). Anthrax. *N Engl J Med*, **341**(11), 815–826.
- Mallon, E., & McKee, P. H. (1997). Extraordinary case report: Cutaneous anthrax. *Am J Dermatopathol*, **19**(1), 79–82.

- Tutrone, W. D., Scheinfeld, N. S., & Weinberg, J. M. (2002). Cutaneous anthrax: A concise review. *Cutis*, **69**(1), 27–33.

1.2.6 Nocardiosis

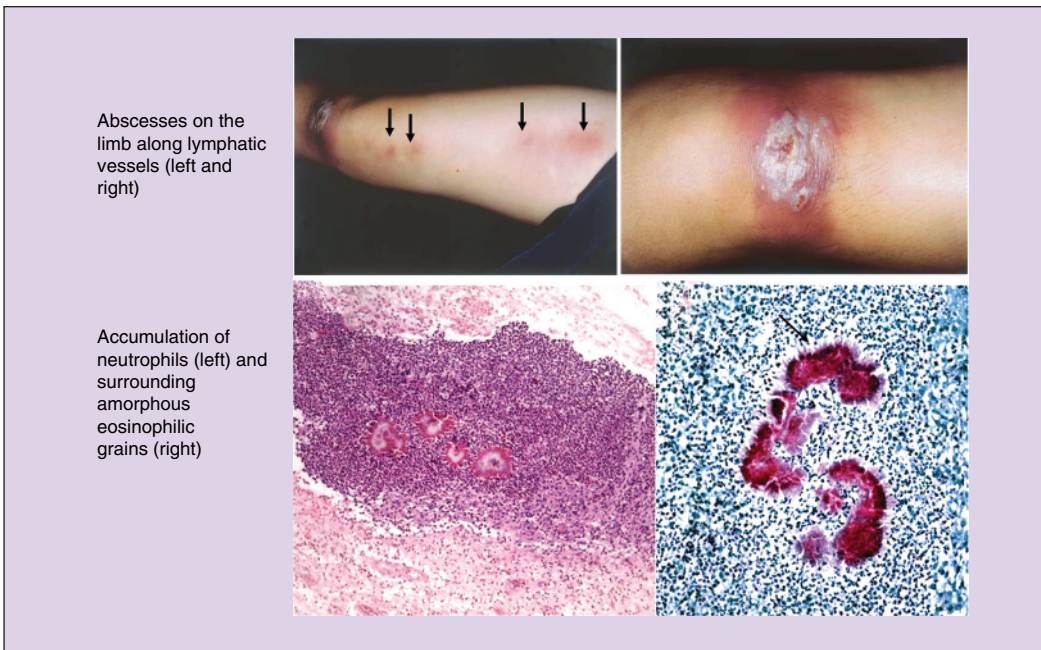


Figure 1.2.6 Nocardiosis. *Source:* The images top left and right is modified from Fukuda et al. (2008). Lymphocutaneous type of nocardiosis caused by *Nocardia brasiliensis*: a case report and review of primary cutaneous nocardiosis caused by *N. brasiliensis* reported in Japan. *J Dermatol*, 35(6), 346-353. The images bottom left and right is modified from Bandeira et al. (2019). Primary cutaneous nocardiosis. *J Dtsch Dermatol Ges*. doi:10.1111/ddg.13770.

Nocardia species comprises a group of gram-positive bacteria with low or moderate virulence, which branch with filaments, and occur worldwide in soil, plants, and organic material. Cutaneous nocardiosis in most cases is caused by infection with *Nocardia brasiliensis*, mostly in immunocompromised patients.

CF: In sporotrichoid nocardiosis, abscesses develop on the limbs along lymphatic vessels.

HF:

- Suppurative infiltrate resembling actinomycosis
- Large superficial neutrophilic abscesses
- Granulomatous reaction at the periphery
- Grains with pale center, surrounded by amorphous eosinophilic (pseudoactinomycotic) bodies (Splendore–Hoepli phenomenon)

DD: Actinomycosis; sporotrichosis; deep fungal and atypical mycobacterial infections.

Reference

Bandeira, I. D., Guimaraes-Silva, P., Cedro-Filho, R. L., de Almeida, V. R. P., Bittencourt, A. L., & Brites, C. (2019). Primary cutaneous nocardiosis. *J Dtsch Dermatol Ges*, **17**(3), 327–329.

Naka, W., Miyakawa, S., Niizeki, H., Fukuda, T., Mikami, Y., & Nishikawa, T. (1995). Unusually located lymphocutaneous nocardiosis caused by *Nocardia brasiliensis*. *Br J Dermatol*, **132**(4), 609–613.

Warren, N. G. (1996). Actinomycosis, nocardiosis, and actinomycetoma. *Dermatol Clin*, **14**(1), 85–95.

1.2.7 Rhinoscleroma

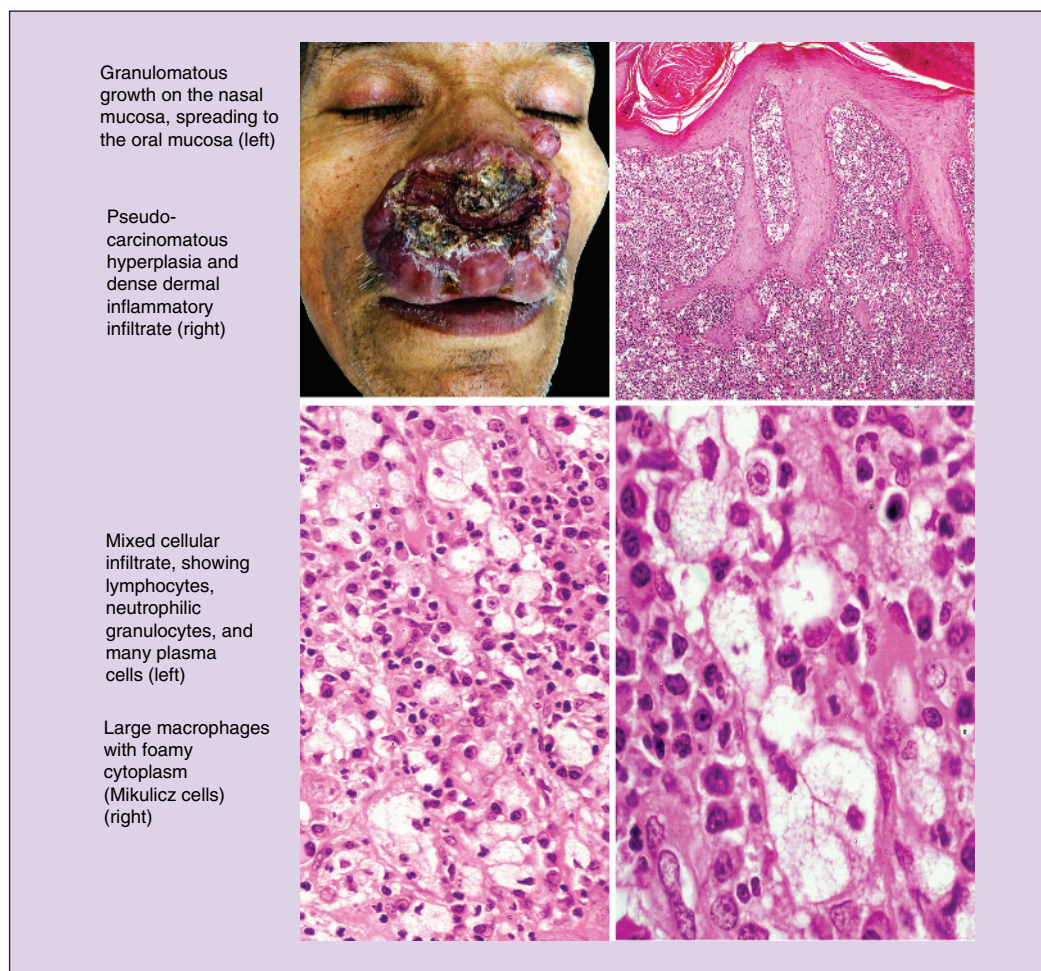


Figure 1.2.7 Rhinoscleroma.

Rare infection by the gram-negative *Klebsiella pneumoniae rhinoscleromatis*.

CF: The nasal mucosa is preferentially affected. Initially chronic rhinitis, followed by granulomatous growth on the nasal mucosa, spreading to the oral mucosa. Lesions resolve by scarring and permanent tissue destruction.

HF:

- Pseudocarcinomatous hyperplasia of the mucosa
- Mixed diffuse and dense infiltrate of the upper and lower propria
- Lymphocytes, neutrophils, and many plasma cells with Russell bodies (cytoplasmic deposits of immunoglobulin)

- Large macrophages with foamy cytoplasm and bacilli (Mikulicz cells)
- Special stains: silver, Gram, Giemsa, PAS (Russell bodies)

DD: Leishmaniasis, NK/T-cell lymphoma.

Reference

- Ahmed, A. R., El-Badawy, Z. H., Mohamed, I. R., & Abdelhameed, W. A. (2015). Rhinoscleroma: A detailed histopathological diagnostic insight. *Int J Clin Exp Pathol*, **8**(7), 8438–8445.
- Castanedo Cazares, J. P., & Martinez Rosales, K. I. (2015). Images in clinical medicine. Rhinoscleroma. *N Engl J Med*, **372**(25), e33.

Efared, B., Hammas, N., Gabrielle, A. E., Ben Mansour, N., El Fatemi, H., & Chbani, L. (2018). Rhinoscleroma: A chronic infectious disease of poor areas with characteristic histological features – report of a series of six cases. *Trop Doct*, **48**(1), 33–35.

1.3 Rochalimaea/Bartonellae

Gram-negative bacteria (*Bartonella henselae* or *Bartonella quintana*; formerly Rochalimaea) are the causative agent in bacillary angiomatosis, cat scratch disease, and in verruga peruana.

1.3.1 Bacillary Angiomatosis and Cat Scratch Disease



Figure 1.3.1 Bacillary Angiomatosis and Cat Scratch Disease (top right).

*Source: Burg et al. (2019). *Atlas of Dermatopathology: Tumors, Nevi, and Cysts* (p. 273). Oxford: Wiley.

Immunodeficient patients suffering from AIDS are most commonly affected.

CF: Pyogenic granuloma-like, mostly multiple red hemorrhagic nodules or plaques. Granulomatous swelling of the draining lymph node in cat scratch disease. Concomitant internal manifestation may occur (peliosis hepatica).

HF:

- Vascular proliferation resembling pyogenic granuloma or granulation tissue
- Blood vessels with large, activated epithelioid endothelia, high mitotic activity
- Conspicuous lack of fibrous septa between capillary lobules
- Edematous stroma
- Neutrophil-rich inflammatory infiltrate with karyorrhexis
- Causative bacteria can be demonstrated by Warthin–Starry stain or immunostains, preferentially in close proximity to vessels

DD: Pyogenic granuloma (lobular capillary hemangioma); epithelioid hemangioma

(angiolympoid hyperplasia with eosinophilia); Kaposi's sarcoma; verruga peruana.

Reference

- Amsbaugh, S., Huiras, E., Wang, N. S., Wever, A., & Warren, S. (2006). Bacillary angiomatosis associated with pseudoepitheliomatous hyperplasia. *Am J Dermatopathol*, **28**(1), 32–35.
- Kempf, V. A., Lebiedziejewski, M., Alitalo, K., Walzlein, J. H., Eहेhalt, U., Fiebig, J., . . . Autenrieth, I. B. (2005). Activation of hypoxia-inducible factor-1 in bacillary angiomatosis: Evidence for a role of hypoxia-inducible factor-1 in bacterial infections. *Circulation*, **111**(8), 1054–1062.
- Perez-Piteira, J., Ariza, A., Mate, J. L., Ojanguren, I., & Navas-Palacios, J. J. (1995). Bacillary angiomatosis: A gross mimicker of malignancy. *Histopathology*, **26**(5), 476–478.
- Tsang, W. Y., Chan, J. K., & Wong, C. S. (1992). Giemsa stain for histological diagnosis of bacillary angiomatosis. *Histopathology*, **21**(3): 299.

1.3.2 Verruga Peruana

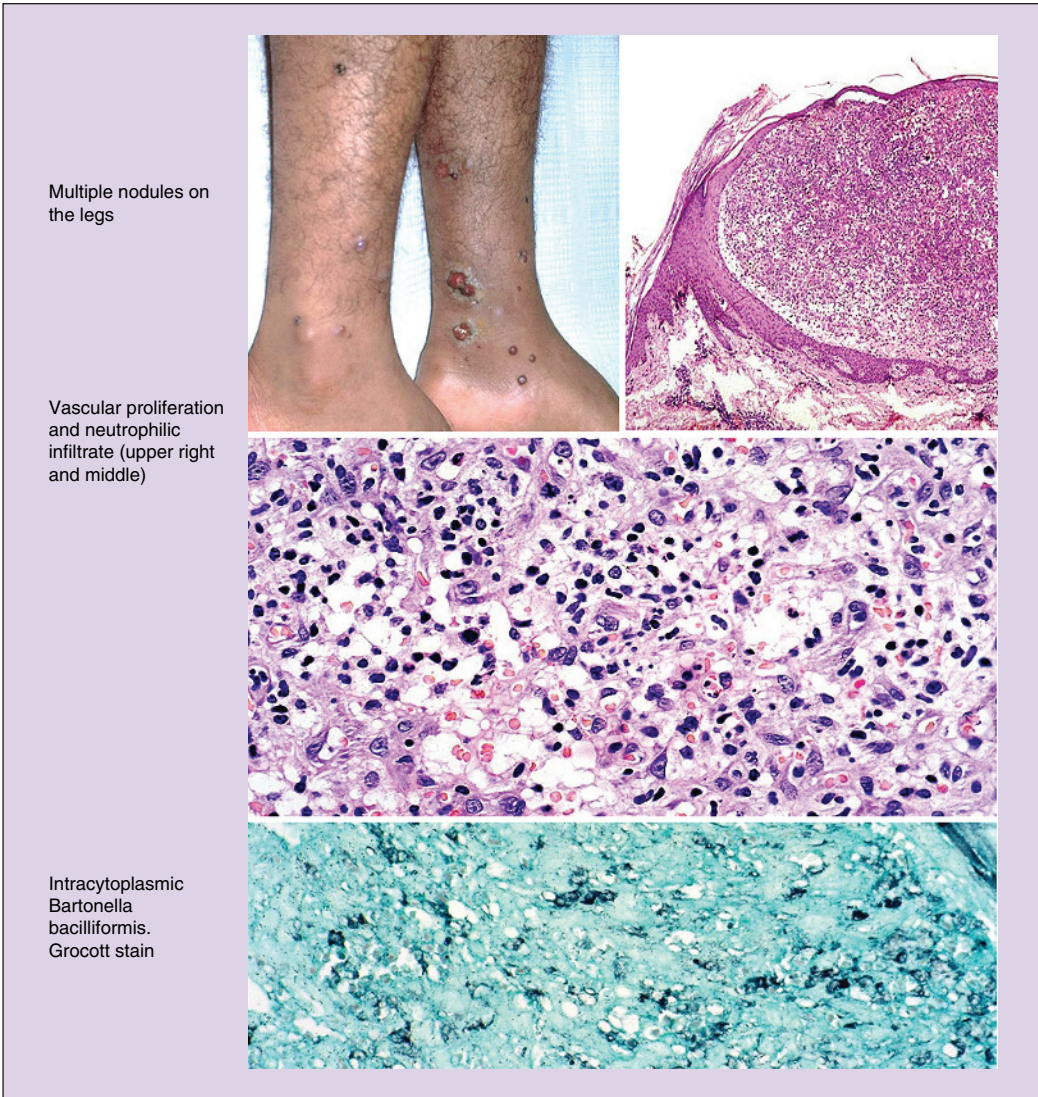


Figure 1.3.2 Verruga Peruana.

Source: Burg et al. (2019). *Atlas of Dermatopathology: Tumors, Nevi, and Cysts* (p. 274). Oxford: Wiley.

CF: Dermal papules and nodules, pedunculated, eroded or verrucous, resembling bacillary angiomatosis. Verruga peruana is the late stage of Oroya fever that is caused by *Bartonella bacilliformis*, almost exclusively in the Andes Mountains (Peru). Infectious vectors are sandflies.

HF: Corresponds to bacillary angiomatosis, albeit with exclusively intracytoplasmic bacteria (Rocha–Lima bodies), while in bacillary angiomatosis infectious organisms thrive purely extracellularly.

DD: See bacillary angiomatosis.

Reference

- Arias-Stella, J., Lieberman, P. H., Garcia-Caceres, U., Erlandson, R. A., Kruger, H., & Arias-Stella, J., Jr. (1987). Verruga peruana mimicking malignant neoplasms. *Am J Dermatopathol*, **9**(4), 279–291.
- Bhutto, A. M., Nonaka, S., Hashiguchi, Y., & Gomez, E. A. (1994). Histopathological and electron microscopical features of skin lesions in a patient with bartonellosis (verruca peruana). *J Dermatol*, **21**(3), 178–184.
- Jimenez-Lucho, V. (1998). Images in clinical medicine. Verruga peruana. *N Engl J Med*, **339**(7), 450.

1.3.3 Differential Diagnosis: Pyogenic Granuloma (Lobular Capillary Hemangioma; Botryomycosis)

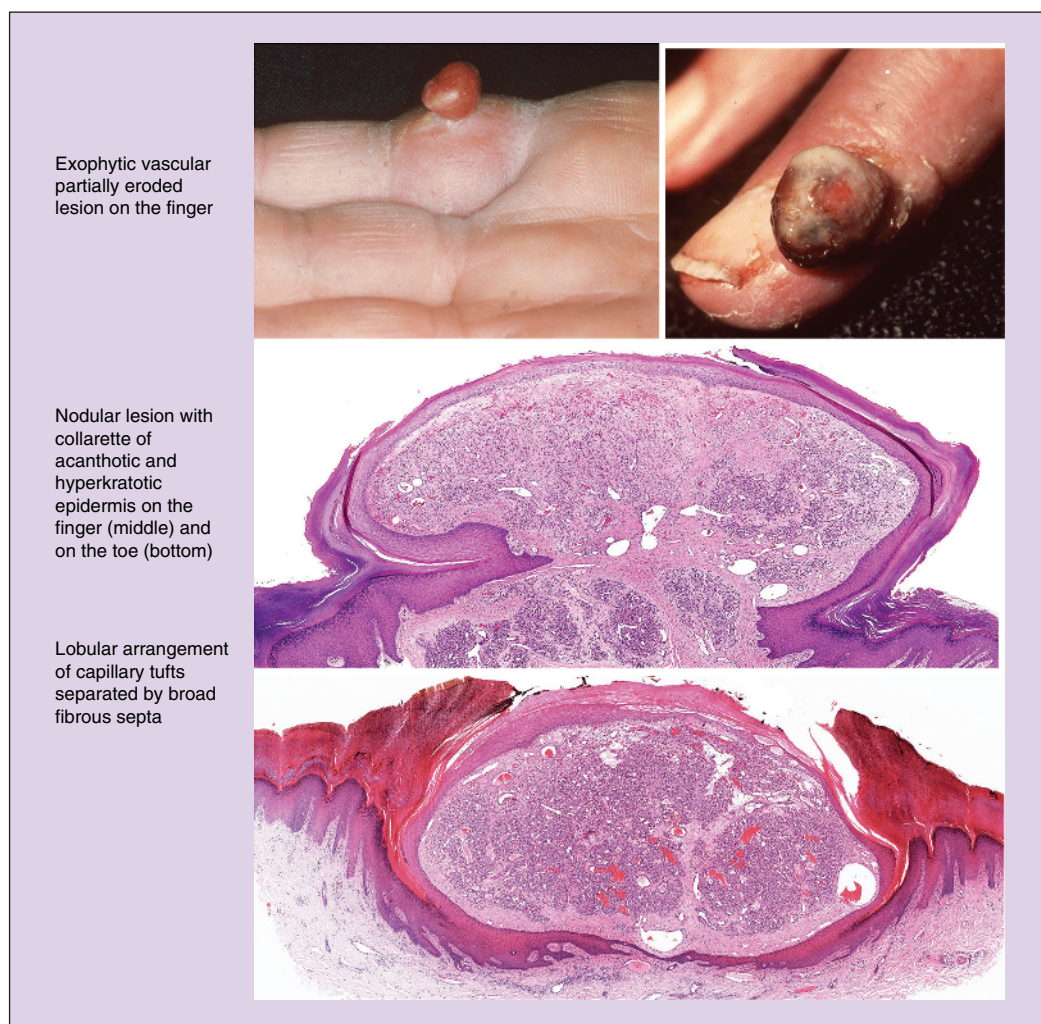


Figure 1.3.3 Differential Diagnosis: Pyogenic Granuloma (Lobular Capillary Hemangioma; Botryomycosis).

Source: Burg et al. (2019). *Atlas of Dermatopathology: Tumors, Nevi, and Cysts* (p. 270). Oxford: Wiley.

Benign vascular hyperplasia, histologically showing a lobular structure with fibrous septa and accompanied by variable inflammatory infiltrate.

CF: Soft, friable, easily vulnerable and bleeding, pedunculated exophytic nodular lesion. The lesion is surrounded by an epithelial collarette. Fingers, palms, face, and scalp are preferential sites. Pyogenic granuloma, however, may occur on any other part of the body, including oral mucosa. Superficial trauma is considered the most common cause. The growth of the lesion can be fostered by hormonal (pregnancy) and other factors (tretinoin).

HF:

- Dome-shaped lesion
- Epithelial collarette at the borders
- Flat epidermis; superficial ulceration and crust formation with bacteria are common
- Multilobular architecture with fibrous septa between vascular lobules
- Proliferation of capillaries (CD31; CD34); central “feeder vessel”
- Mitoses of endothelial cells without cellular atypia
- Variable inflammatory neutrophil-rich infiltrate and edema; predominant fibrosis in advanced lesions
- Remarkably, bacteria never occur within the center of the lesion

DD: Granulation tissue; amelanotic malignant melanoma; infantile/congenital hemangioma; nodular Kaposi sarcoma; angiosarcoma; acquired tufted angioma.

Reference

- Fortna, R. R., & Junkins-Hopkins, J. M. (2007). A case of lobular capillary hemangioma (pyogenic granuloma), localized to the subcutaneous tissue, and a review of the literature. *Am J Dermatopathol*, **29**(4), 408–411.
- Fukunaga, M. (2000). Kaposi’s sarcoma-like pyogenic granuloma. *Histopathology*, **37**(2), 192–193.
- McClain, C. M., Haws, A. L., Galfione, S. K., Rapini, R. P., & Hafeez Diwan, A. (2016).

Pyogenic granuloma-like Kaposi’s sarcoma. *J Cutan Pathol*, **43**(6), 549–551.

- Vega Harring, S. M., Niyaz, M., Okada, S., & Kudo, M. (2004). Extramedullary hematopoiesis in a pyogenic granuloma: A case report and review. *J Cutan Pathol*, **31**(8), 555–557.

1.4 Mycobacterial Infections

Mycobacteria that cause tuberculosis and leprosy are subsumed under the heading of “typical” mycobacteria, while infections caused by *M. marinum* (swimming pool or fish tank mycobacteriosis), *M. ulcerans* (Buruli ulcer), and *M. kansasii* are commonly referred to as “atypical” mycobacterioses. Histopathologically, all mycobacteria can be detected by Ziehl–Neelsen stain (acid-fast bacilli), immunohistochemistry, or by PCR.

1.4.1 Tuberculosis Cutis

Depending on the immune status of the patient, various forms of cutaneous and subcutaneous tuberculosis of the skin occur.

Reference

- Kannan, S., Simpson, G. L., Sheehan, D. J., & Leshner, J. L., Jr. (2009). Giant verrucous nodules in a patient with tuberculosis. *Am J Dermatopathol*, **31**(6), 591–593.
- Maldonado-Bernal, C., Ramos-Garibay, A., Rios-Sarabia, N., Serrano, H., Carrera, M., Navarrete-Franco, G., . . . Isibasi, A. (2019). Nested Polymerase Chain Reaction and Cutaneous Tuberculosis. *Am J Dermatopathol*, **41**(6), 428–435.
- Massi, D., Trotta, M., Franchi, A., Pimpinelli, N., & Santucci, M. (2004). Atypical CD30+ cutaneous lymphoid proliferation in a patient with tuberculosis infection. *Am J Dermatopathol*, **26**(3), 234–236.
- Sharma, S., Sehgal, V. N., Bhattacharya, S. N., Mahajan, G., & Gupta, R. (2015). Clinicopathologic spectrum of cutaneous tuberculosis: A retrospective analysis of 165 Indians. *Am J Dermatopathol*, **37**(6), 444–450.

1.4.1.1 Primary Tuberculosis of the Skin

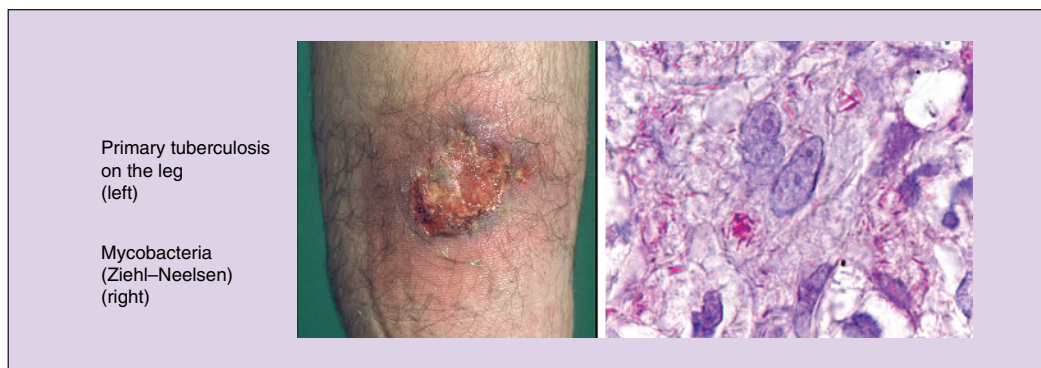


Figure 1.4.1.1 Primary Tuberculosis of the Skin.

Primary tuberculosis of the skin, caused by *Mycobacterium tuberculosis* inoculation via superficial skin ulceration, is very rare and mostly occurs in children without previous mycobacterial contact or without Bacille Calmette-Guerin (BCG) vaccination. The immune status is anergic and the tuberculin test negative; high numbers of mycobacteria are present in the tissue.

CF: Papule or ulceration. Swelling of the draining lymph node.

HF:

- Abscess
- Necrosis
- Many mycobacteria (Ziehl-Neelsen stain)
- Granulomatous reaction occurs many weeks later

DD: Other primary mycobacterioses; foreign body granuloma; actinomycosis; sporotrichosis; tularemia.

1.4.1.2 BCG Vaccination Granuloma



Figure 1.4.1.2 BCG Vaccination Granuloma.

CF: Papulopustular reaction with erythema.

HF: Granulomatous inflammation with predominant epithelioid granulomas at the site of previous BCG vaccination.

DD: Insect bite; furuncle.

Reference

Keijsers, R. R., Bovenschen, H. J., & Seyger, M. M. (2011). Cutaneous complication after

BCG vaccination: Case report and review of the literature. *J Dermatolog Treat*, **22**(6), 315–318.

Lyu, S. M., Choi, Y. W., Oh, C. W., Choi, H. Y., & Byun, J. Y. (2013). Granulomatous reaction after BCG vaccination histologically mimicking reticulohistiocytoma. *Eur J Dermatol*, **23**(4), 527–528.

1.4.1.3 Differential Diagnosis: Lupus Miliaris Disseminatus Faciei (LMDF)

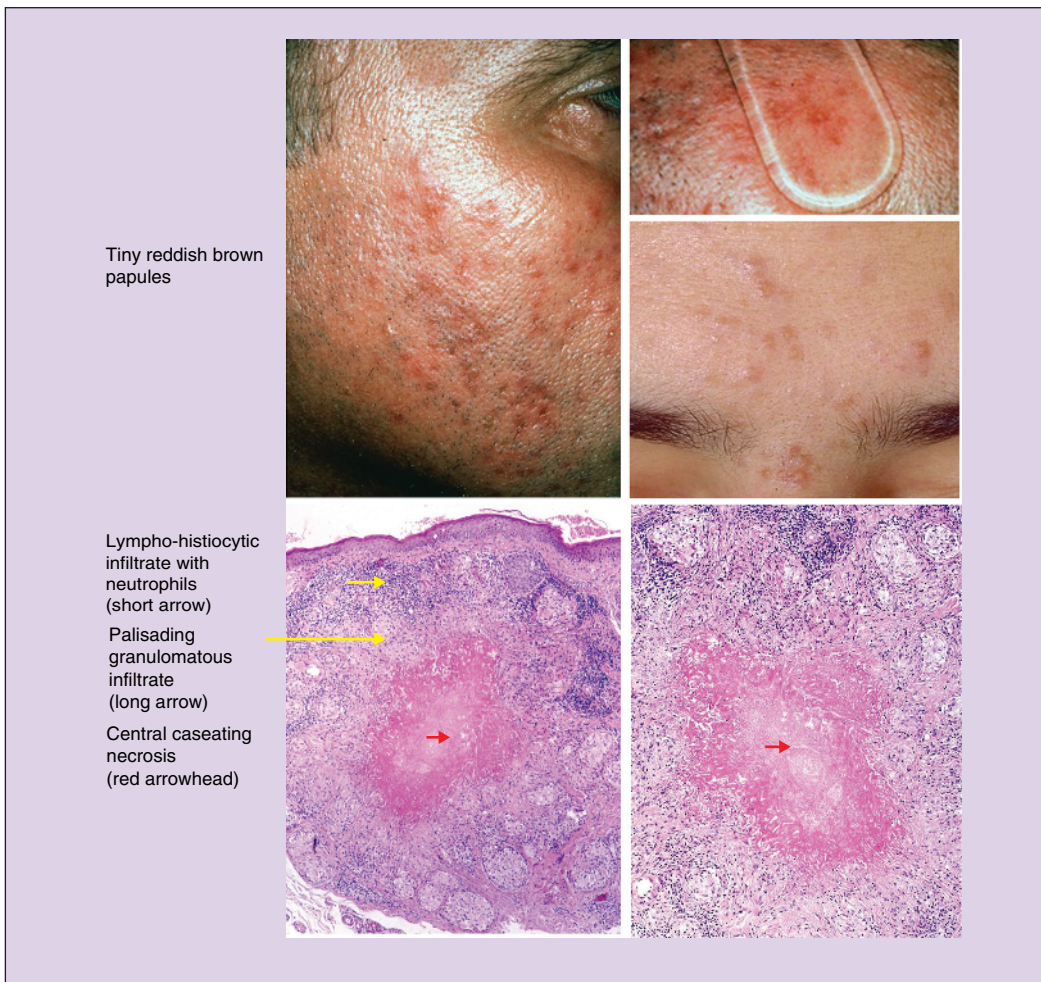


Figure 1.4.1.3 Differential Diagnosis: Lupus Miliaris Disseminatus Faciei.

Source: Burg et al. (2015). *Atlas of Dermatopathology: Practical Differential Diagnosis by Clinicopathologic Pattern* (p. 184). Oxford: Wiley.

LMDF originally was considered to be a tuberculid, but eventually was subsumed under the spectrum of granulomatous rosacea or acne agminata. However, the disease occurs also in extrafacial areas.

CF: Tiny reddish brown papules, simulating acne (syn. Acne agminata and acnitis).

HF:

- Small well-circumscribed interfollicular superficial granulomas in the upper dermis
- Admixture of neutrophils
- Marked central caseating necrosis devoid of any organisms
- Peripheral wreath of densely packed histiocytes and multinucleate giant cells

- All special stains and PCR for infectious organisms are negative

DD: Acne; rosacea; verrucae planae.

Reference

- Chougule, A., Chatterjee, D., Yadav, R., Sethi, S., De, D., & Saikia, U. N. (2018). Granulomatous rosacea versus lupus miliaris disseminatus faciei-2 faces of facial granulomatous disorder: A clinicohistological and molecular study. *Am J Dermatopathol*, **40**(11), 819–823.
- Schaarschmidt, M. L., Schlich, M., Staub, J., Schmieder, A., Goerdts, S., & Peitsch, W. K. (2017). Lupus miliaris disseminatus faciei: Not only a facial dermatosis. *Acta Derm Venereol*, **97**(5), 655–656.

1.4.1.4 Lupus Vulgaris (LV)

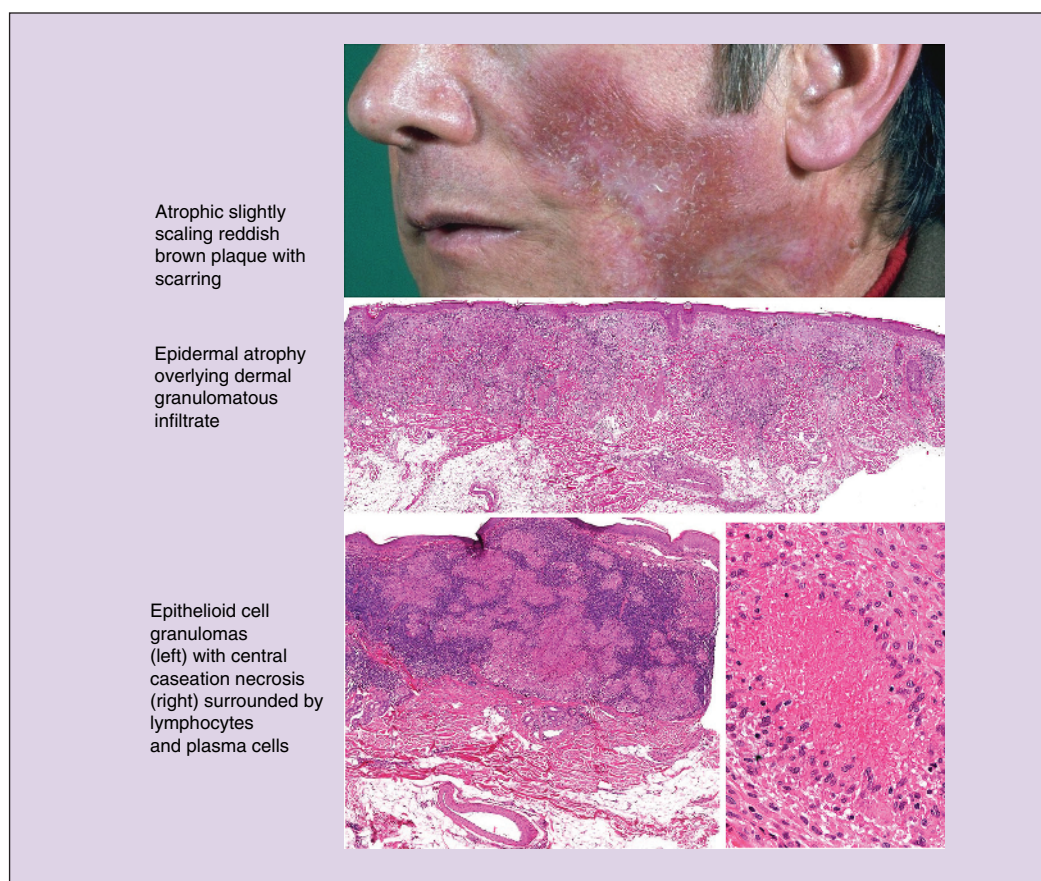


Figure 1.4.1.4 Lupus Vulgaris.

Source: Burg et al. (2015). *Atlas of Dermatopathology: Practical Differential Diagnosis by Clinicopathologic Pattern* (p. 179). Oxford: Wiley.

Patients with LV have a positive Mantoux test, which indicates a normergic immune response following post-primary endogenous reactivation or secondary external inoculation.

CF: Slowly growing lesions are found mostly at acral sites, for example, ears, nose, cheeks, and peripheral parts of limbs. Tiny apple-jelly-colored reddish brown «lupoid» nodules are highly characteristic, and correlate to the granulomatous infiltrate with macrophages and multinucleate giant cells, which can be demonstrated easily by dermoscopy. Lesions resolve with atrophic and mutilating scars; recurrences are common. LV may progress to various clinical variants: verrucous, hypertrophic, ulcerating, vegetating, mutilating types of LV. Tuberculosis cutis colliquative and scrofuloderma are subcutaneous (lymph node) variants of LV.

HF:

- Epidermis is mostly atrophic, but in the verrucosus variant of LV may show pseudocarcinomatous hyperplasia

- Caseating tuberculous granulomas, composed of central necrosis, epithelioid cells, lymphocytes, multinuclear giant cells (Langhans type), plasma cells, and some neutrophils
- Fibrosis
- Infectious organisms (*M. tuberculosis*) are present in exceedingly low numbers and can almost never be detected microscopically
- Confirmation by PCR (biopsy) is difficult; conventional microbiological methods (culture) are preferred

DD: Other granulomatous infiltrates; sarcoidosis, tuberculoid leprosy; granuloma annulare; necrobiosis lipoidica; rheumatoid papule; rosacea; perioral dermatitis; deep mycosis; leishmaniasis; tertiary syphilis.

Reference

- Motswaledi, M. H., & Doman, C. (2007). Lupus vulgaris with squamous cell carcinoma. *J Cutan Pathol*, **34**(12), 939–941.

1.4.1.5 Variant: Tuberculosis (Lupus) Cutis Verrucosa

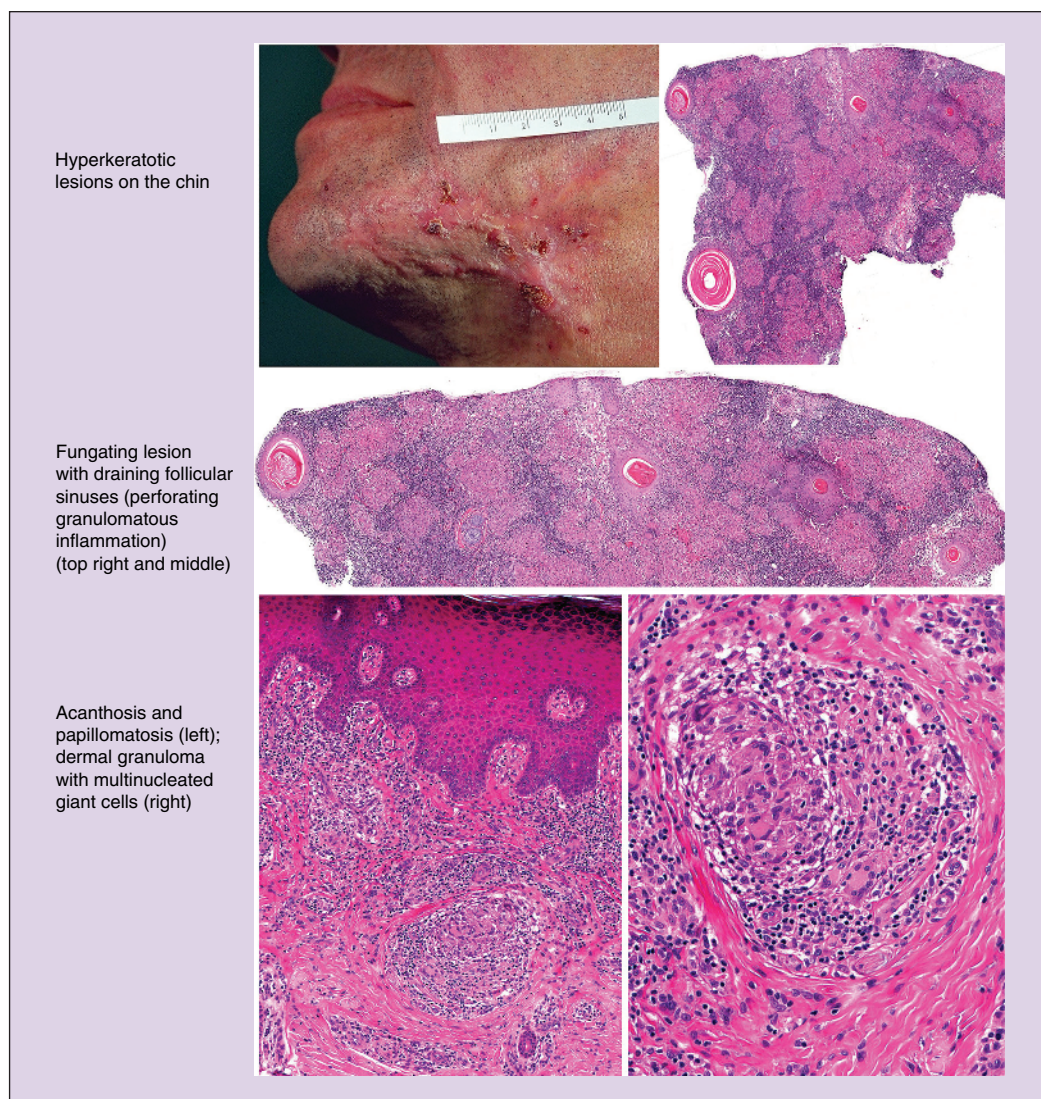


Figure 1.4.1.5 Variant: Tuberculosis (Lupus) Cutis Verrucosa.

Variant of lupus vulgaris with overlying verrucous (pseudocarcinomatous) epidermis.

Reference

- Chahar, M., Dhali, T. K., & D'Souza, P. (2015). Multifocal tuberculosis verrucosa cutis. *Dermatol Online J*, **21**(1).
- Lim, J. A., Tan, W. C., Khor, B. T., Hukam Gopal Chand, S. D., & Palanivelu, T. (2017). Early onset of squamous cell carcinoma arising from tuberculosis verrucosa cutis. *J Am Coll Clin Wound Spec*, **9**(1–3), 35–38.

1.4.1.6 Variant: Tuberculosis Cutis Colliquativa (Scrofuloderma)

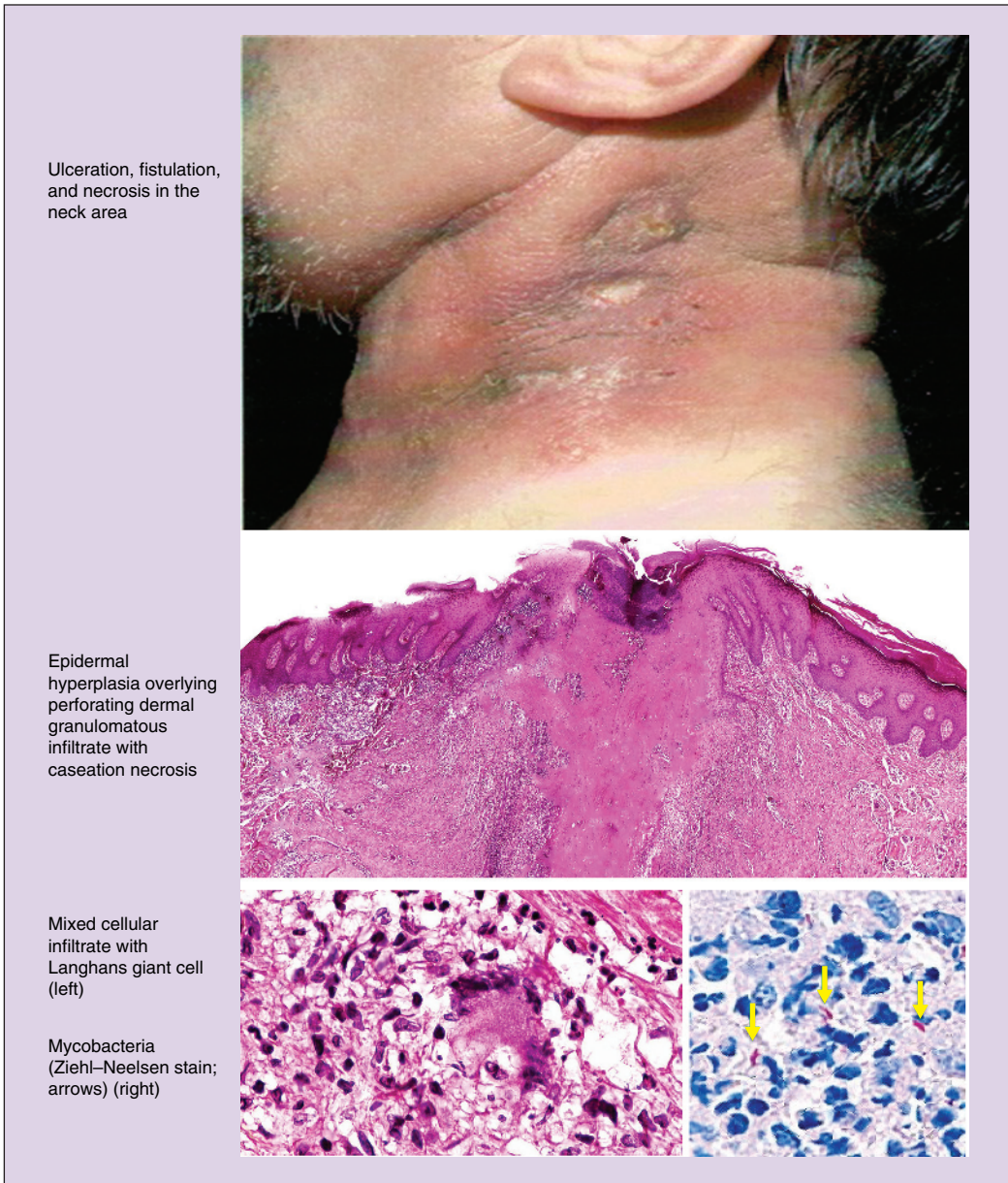


Figure 1.4.1.6 Variant: Tuberculosis Cutis Colliquativa (Scrofuloderma).

Chronic subcutaneous variant of tuberculosis with underlying normergic immune status.

CF: Skin involvement may result from per continuitatem draining infected lymph

nodes in the head and neck area. Typical are painless swelling and ulceration with necrosis and fistulation, leading to adherence of the overlying skin and finally scar formation.

HF:

- Nonspecific epidermal hyperplasia
- Massive necrosis
- Tuberculoid granulomas with Langhans giant cells
- Mixed inflammatory infiltrate with lymphocytes, plasma cells, and neutrophils
- Tuberculous pus

DD: Actinomycosis; deep fungal infections; lymphogranuloma; tertiary syphilis (gumma).

Reference

- Gupta, M., Gupta, M., & Kaur, R. (2013). Tuberculosis colliquativa cutis of the cheek: An extremely uncommon manifestation of primary extrapulmonary tuberculosis. *BMJ Case Rep*, 2013.
- Tur, E., Brenner, S., & Meiron, Y. (1996). Scrofuloderma (tuberculosis colliquativa cutis). *Br J Dermatol*, **134**(2), 350–352.

1.4.1.7 Lichen Scrofulosorum (Tuberculosis Cutis Lichenoides)

Figure 1.4.1.7 Lichen Scrofulosorum (Tuberculosis Cutis Lichenoides).

Hyperergic immune status, showing strongly positive tuberculin test. *Mycobacteria* usually cannot be detected in the tissue, although they may be present in very low numbers.

CF: Tiny reddish brown follicular or perifollicular papules clustered (“lichenoid”) in a circumscribed area of the trunk or extremities. Remarkable morphological overlap with lichen nitidus.

HF:

- Follicular or perifollicular granulomatous infiltrate
- Epithelioid cell infiltrate with some Langhans giant cells

- Lymphocytes and histiocytes between tuberculoid nodules
- Rarely, mycobacteria may be detectable in some cases by special stains (Ziehl–Neelsen) or by PCR

DD: Lichen (ruber) planus; lichen nitidus; lichen syphiliticus; lichen trichophyticus

Reference

- Ben Jazia, E., Hachfi, W., Trimech, M., Hmissa, S., Jeddi, C. H., & Omezzine-Letaief, A. (2006). Detection of mycobacterial tuberculosis DNA in lichen scrofulosorum. *J Am Acad Dermatol*, **55**(2 Suppl), S54–55.

Camacho, D., Pielasinski, U., Revelles, J. M., Gorgolas, M., Manzarbeitia, F., Kutzner, H., & Requena, L. (2011). Lichen scrofulosorum

mimicking lichen planus. *Am J Dermatopathol*, **33**(2), 186–191.

1.4.1.8 Papulonecrotic Tuberculid



Figure 1.4.1.8 Papulonecrotic Tuberculid.

*Source: Burg et al. (2015). *Atlas of Dermatopathology. Practical Differential Diagnosis by Clinicopathologic Pattern* (p. 182). Oxford: Wiley.

Immune status as in lichen scrofulosorum, that is, hyperergic with strongly positive tuberculin test.

CF: Symmetric disseminated erythematous papulonecrotic and ulcerated lesions, mostly in acral localization; resolving with scar formation.

HF:

- Wedge-shaped infiltrate in the dermis
- Granulomatous infiltrate with caseous necrosis
- Giant multinuclear cells (Langhans giant cells)
- Concomitant lymphocytic vasculitis
- Thrombosed blood vessels
- Mycobacteria completely lacking (negative Ziehl–Neelsen stain)

- PCR/culture for mycobacteria may be positive

DD: Pityriasis lichenoides et varioliformis acuta (PLEVA); leukocytoclastic vasculitis; prurigo.

Reference

- Jordaan, H. F., Van Niekerk, D. J., & Louw, M. (1994). Papulonecrotic tuberculid. A clinical, histopathological, and immunohistochemical study of 15 patients. *Am J Dermatopathol*, **16**(5), 474–485.
- Victor, T., Jordaan, H. F., Van Niekerk, D. J., Louw, M., Jordaan, A., & Van Helden, P. D. (1992). Papulonecrotic tuberculid. Identification of *Mycobacterium tuberculosis* DNA by polymerase chain reaction. *Am J Dermatopathol*, **14**(6), 491–495.

1.4.1.9 Erythema Induratum Bazin

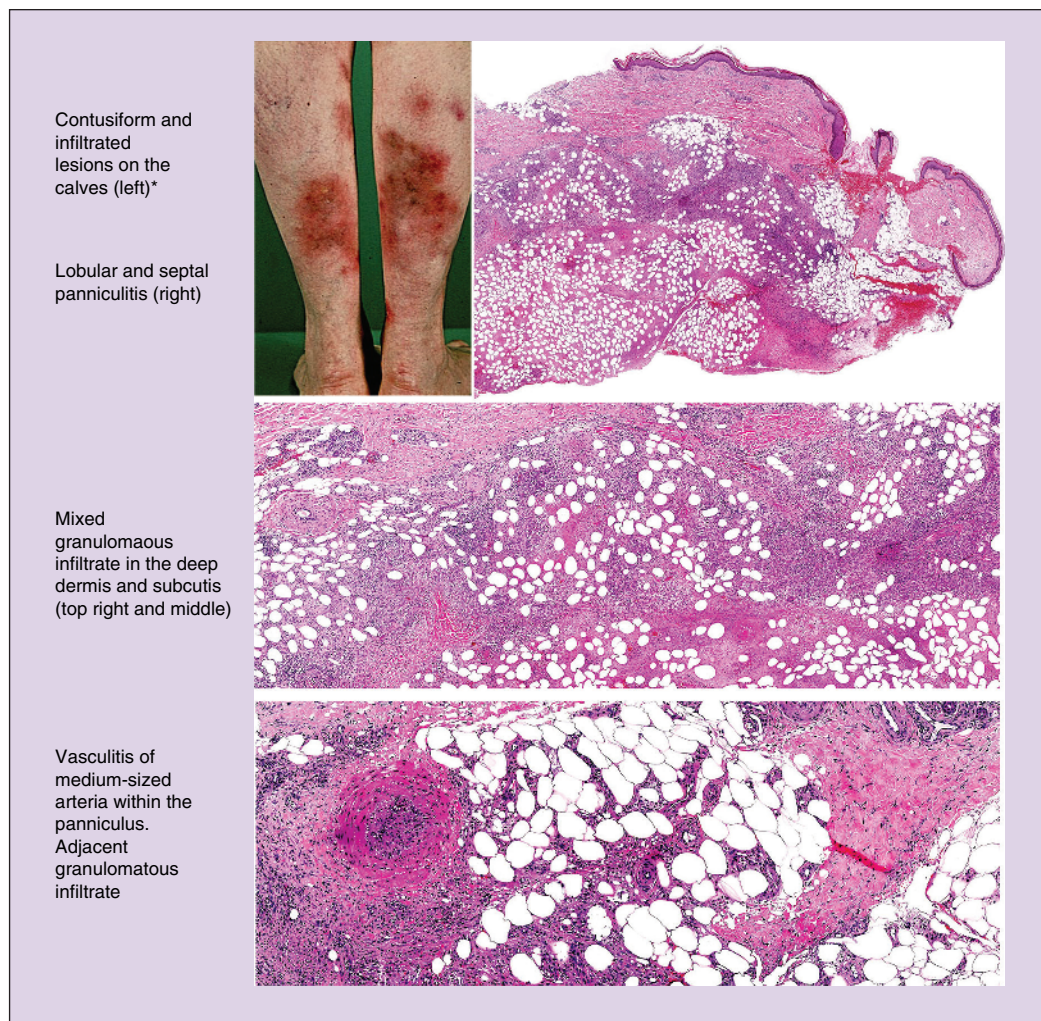


Figure 1.4.1.9 Erythema Induratum (Bazin).

*Source: Burg et al. (2015). *Atlas of Dermatopathology: Practical Differential Diagnosis by Clinicopathologic Pattern* (p. 183). Oxford: Wiley.

“Classic” EIB is a subcutaneous variant of hyperergic reaction in patients who have or have had tuberculosis. The tuberculin test is strongly positive. Non-tuberculous variants of EIB may occur, clinically and histopathologically often overlapping with nodular vasculitis.

CF: Contusiform plaques and intradermal nodular infiltration, often located on the

calves, simulating vasculitis or thrombophlebitis. Ulceration is rare, but may occur at advanced stages.

HF:

- Lobular panniculitis, occasionally evolving into suppurative panniculitis
- Granulomatous perivascular infiltrates, mostly in the deep dermal plexus
- Lipophagic granulomas in advanced lesions

- Nodular arterial subcutaneous vasculitis is not an inherent part of “classic” EIB

DD: Nodular vasculitis, erythema nodosum; sarcoidosis; pernio

Reference

Roblin, D., Kelly, R., Wansbrough-Jones, M., & Harwood, C. (1994). Papulonecrotic tuberculide and erythema induratum as presenting

manifestations of tuberculosis. *J Infect*, **28**(2), 193–197.

Wang, T. C., Tzen, C. Y., & Su, H. Y. (2000). Erythema induratum associated with tuberculous lymphadenitis: Analysis of a case using polymerase chain reactions with different primer pairs to differentiate bacille Calmette-Guerin (BCG) from virulent strains of *Mycobacterium tuberculosis* complex. *J Dermatol*, **27**(11), 717–723.

1.4.2 Atypical Mycobacteriosis: Fish Tank (Swimming Pool) Granuloma

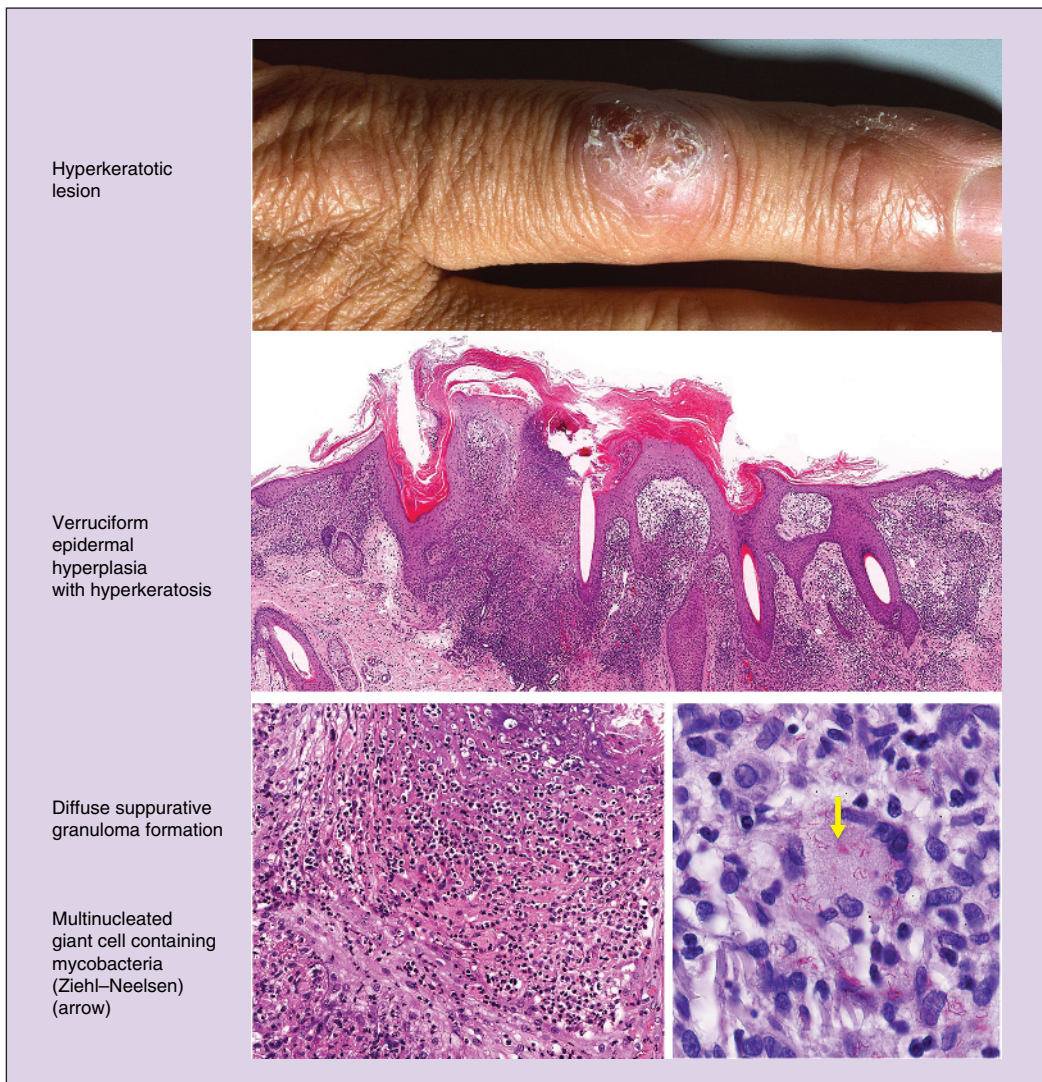


Figure 1.4.2 Fish Tank (Swimming Pool) Granuloma.

Inoculation with *Mycobacterium marinum* occurs via local trauma and exposure to infested water, mostly in fish tanks or swimming pools.

CF: Hyperkeratotic lichenoid and granulomatous lesion with superficial ulceration and crust formation.

HF:

- Acanthosis and hyperkeratosis of overlying epidermis
- Tuberculoid granulomas
 - Central necrosis often present
 - Macrophages and multinucleated Langhans giant cells
 - Mixed adjacent inflammatory infiltrate, with neutrophils and lymphocytes
 - Ziehl–Neelsen stain often positive showing few microorganisms
- Fibrosis

DD: Other chronic infections and diseases associated with granulomas and mixed inflammatory dermal infiltrates.

Reference

- Boyd, A. S., & Robbins, J. (2005). Cutaneous *Mycobacterium avium* intracellulare infection in an HIV+ patient mimicking histoid leprosy. *Am J Dermatopathol*, **27**(1), 39–41.
- Breza T, J., & Magro, C. M. (2006). Lichenoid and granulomatous dermatitis associated with atypical mycobacterium infections. *J Cutan Pathol*, **33**(7), 512–515.
- Redbord, K. P., Shearer, D. A., Gloster, H., Younger, B., Connelly, B. L., Kindel, S. E., & Lucky, A. W. (2006). Atypical *Mycobacterium* furunculosis occurring after pedicures. *J Am Acad Dermatol*, **54**(3), 520–524.

1.4.3 Leprosy (Hansen Disease)¹

Leprosy is caused by the acid-fast *Mycobacterium leprae*, which was identified by the Norwegian physician

Gerhard Armauer Hansen (1874). The armadillo is a natural carrier and serves as a vector, without becoming ill. Culturing of *M. leprae* has not been successful.

Leprosy predominantly affects the skin and preferentially the sensory nerves (pain and temperature) and is still considered a serious health concern in many tropical and subtropical countries. The incubation period is very long (3–5 years). The Ridley–Jopling (R-J) classification of leprosy is widely used.

The early stage is called “indeterminate leprosy” and shows hypopigmented (dark-skinned people) or slightly red (fair skin) spots. Histologically there may be minimal inflammation with a few bacteria present. Depending on the patient’s immune status, tuberculoid, borderline, lepromatous leprosy and intermediate forms may evolve. For monitoring therapy, the bacterial index (1–6; depending on the number of bacteria found in the skin) and the morphologic index (percentage of solid staining bacteria) are applied. For the demonstration of leprosy bacilli in the tissue, the Fite–Faraco stain is more suitable than the Ziehl–Neelsen method. In situ hybridization and PCR analysis of specimens are more sensitive.

Reference

- Jerath, V. P., & Desai, S. R. (1998). Diversities in clinical and histopathological classification of leprosy. *Lepr India*, **54**, 130–134.
- Walkar, S. L., & Lockwood, D. N. (2006). The clinical and immunological features of leprosy. *Br Med Bull*, **78**, 174–176.

¹ This chapter was prepared in cooperation with Ram Chandra Adhikari MD, Consultant Dermatopathologist, DISHARC Hospital, Kathmandu/Nepal

1.4.3.1 Tuberculoid Leprosy

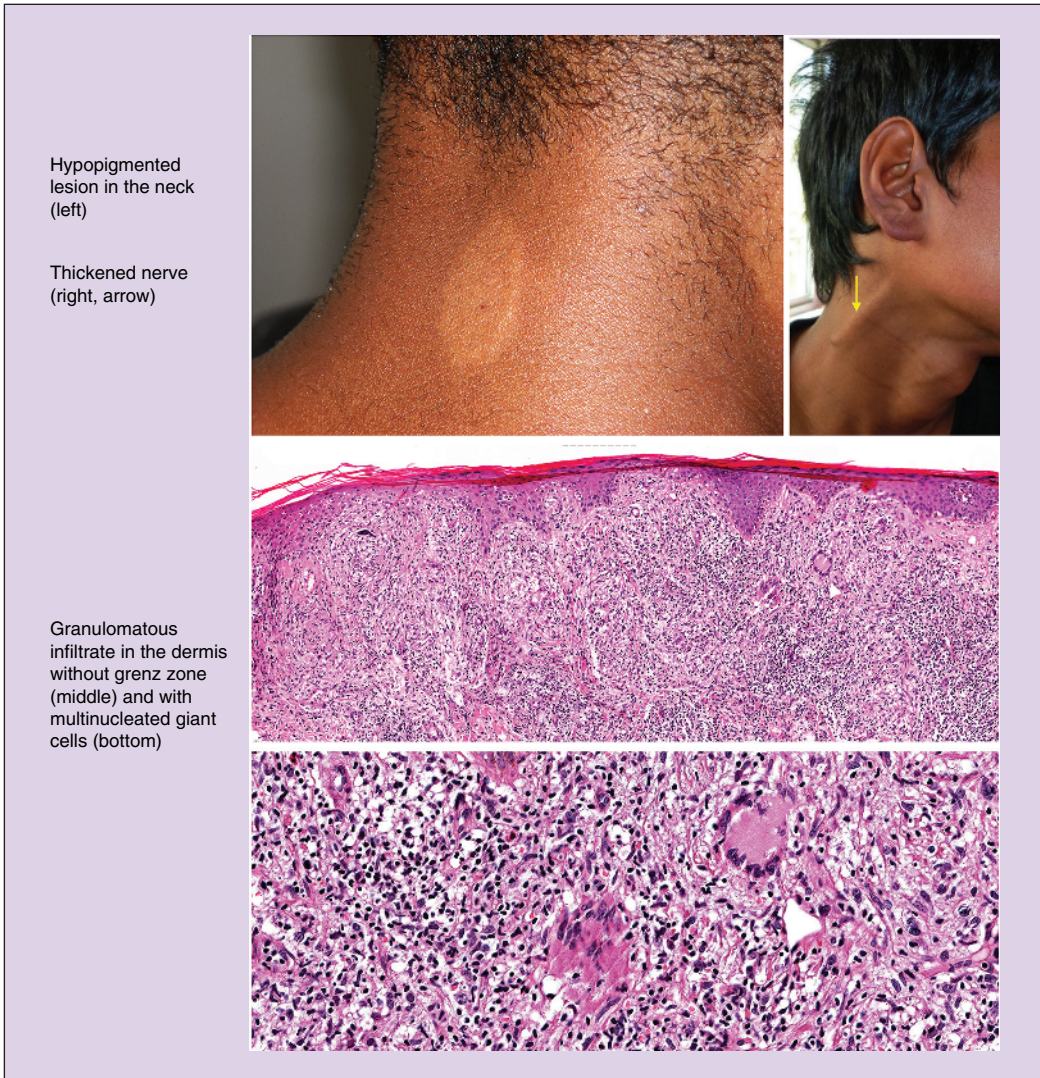


Figure 1.4.3.1 Leprosy, Tuberculoid (Paucibacillary) (TT).

Tuberculoid leprosy is seen in individuals with intact cell-mediated immunity and is associated with high resistance to the lepra bacilli. The lepromin test is strongly positive.

CF: Preferentially on the trunk and limbs there are single or few asymmetrically distributed anesthetic, anhidrotic macules or plaques with a sharply defined border. The skin is dry, scaly, erythematous, or

hypopigmented. One or two nerves near the skin lesion may be thickened. Internal organs are not involved. Loss of pain and sensory functions may lead to injuries and mutilations on the acra.

HF:

- Epithelioid granulomas with Langhans multinucleated giant cells and many lymphocytes, a few plasma cells, and eosinophils

- Infiltrates sometimes along nerves
 - No grenz zone
 - No caseous necrosis
 - Partly destroyed dermal nerves by granulomas are diagnostic for leprosy
 - Granulomas may erode the epidermis
 - Acid-fast bacilli are rare or absent
- DD:** Lupus vulgaris; sarcoidosis; leishmaniasis; xanthomas; granular cell tumor.

1.4.3.2 Borderline Leprosy

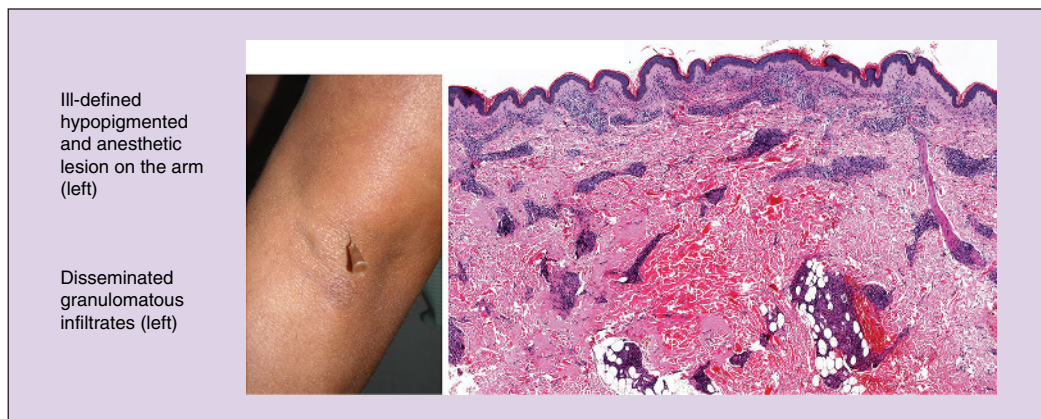


Figure 1.4.3.2.1 Leprosy: Borderline Tuberculoid (BT).

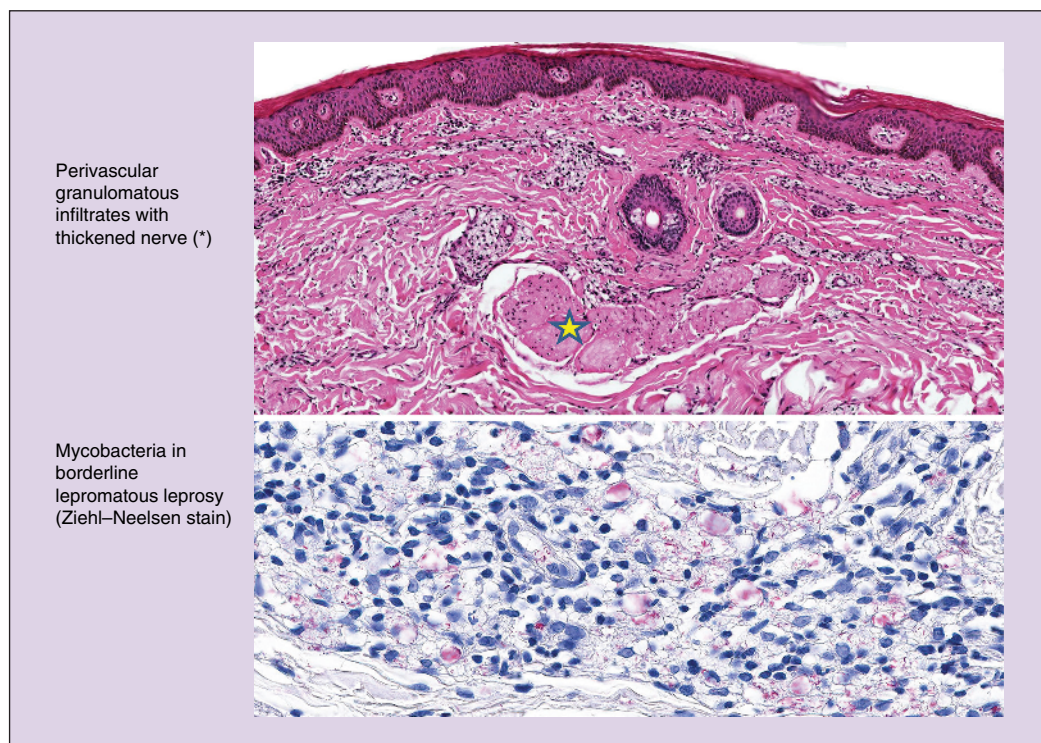


Figure 1.4.3.2.2 Leprosy, Borderline Lepromatous.

Borderline leprosy is an unstable form, constituting 10–15% of cases of leprosy and can progress to either pole (tuberculoid or lepromatous), depending on the immune status. The lepromin test is positive or negative.

CF: Variable lesions between lepromatous and tuberculoid leprosy. Multiple erythematous copper-colored patches of various size and shape with punched-out center and ill-defined border are seen. These

lesions tend to be symmetrical. Nerves may be irregularly thickened.

HF:

- Ill-defined granulomas with unbalanced mixture of epithelioid cells, lymphocytes, and macrophages
- Langhans multinucleated giant cells are usually absent
- Mycobacteria may be present, especially in the BL-variant

DD: Lupus vulgaris; Leishmaniasis.

1.4.3.3 Lepromatous Leprosy



Figure 1.4.3.3 Leprosy, Lepromatous (LL).

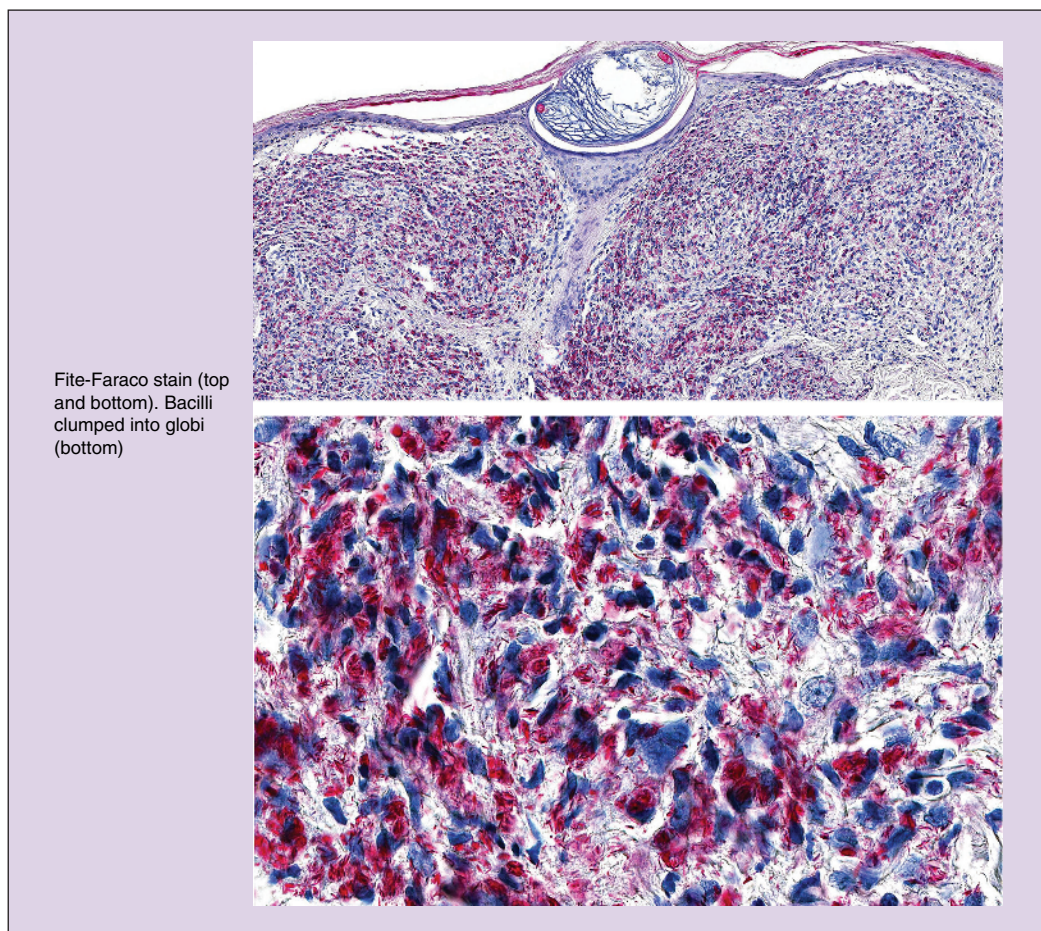


Figure 1.4.3.3 (Continued)

Lepromatous leprosy occurs in individuals with poor cell-mediated immunity to *M. leprae*. The lepromin test is negative. Sensation may be intact.

CF: Numerous hypopigmented or erythematous partly confluent macules, plaques, nodules, or diffusely infiltrating lesions (leonine facies) occur. They are symmetrically distributed on the face, trunk, and extremities and show ill-defined borders. Nerves are symmetrically enlarged. Internal organs may become involved.

HF:

- Thin atrophic epidermis with grenz zone
- Dermis shows numerous foamy bluish-gray macrophages with vacuoles, loaded

with *M. leprae* (Virchow cells), diffusely arranged or in large sheets, replacing skin adnexal structures

- Lymphocytes are very few in number; however, there may be perineural and intraneural infiltration of nerves by lymphocytes
- Numerous *M. leprae* are seen with Fite-Faraco stain

DD: Atypical mycobacterial infections; xanthoma; molluscum contagiosum.

Reference

Santos-Arroyo, A. E., Nevares-Pomales, O. W., Almodovar, P. I., & Sanchez, J. L. (2014). Molluscum-like lesions in a 12-year-old boy: Challenge. Lepromatous leprosy. *Am J Dermatopathol*, **36**(12), 984, 992.

1.4.3.4 Variant: Histoid Lepromatous

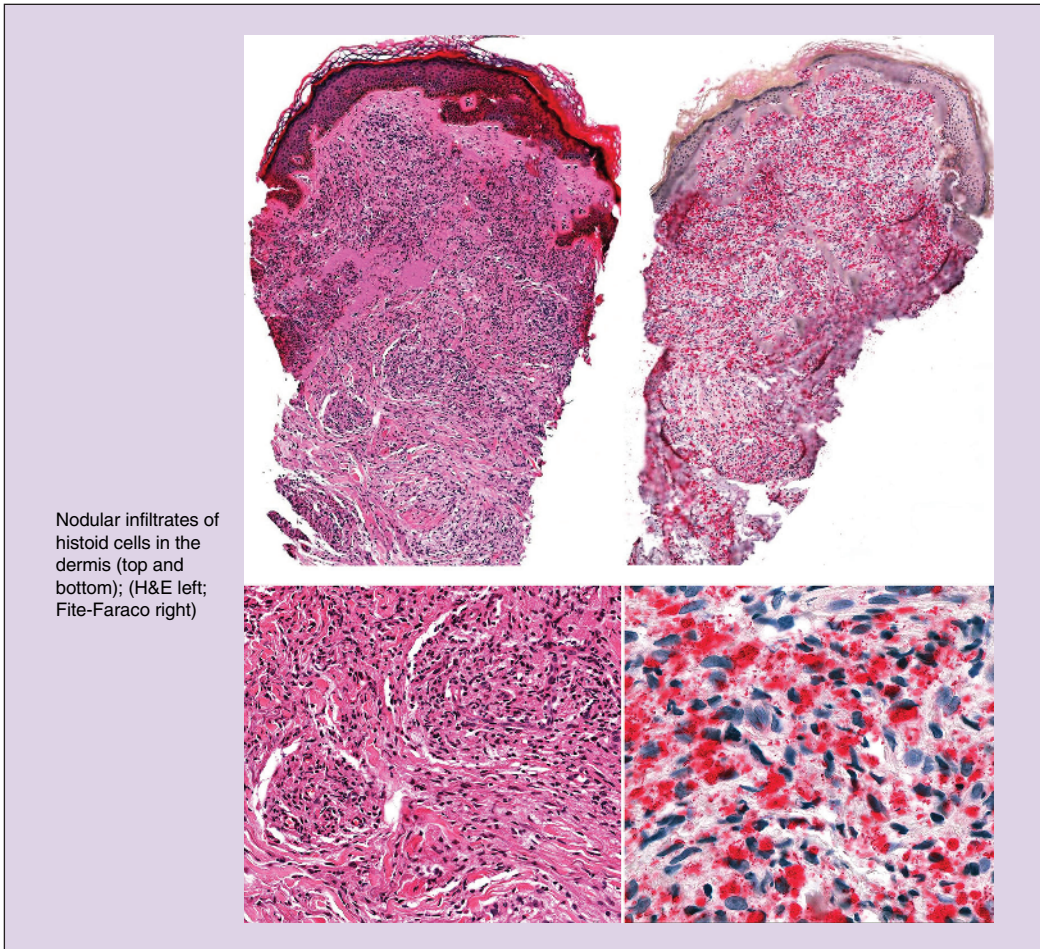


Figure 1.4.3.4 Leprosy, Histoid Lepromatous (HL).

This is an uncommon variant of lepromatous leprosy occurring in patients with lepromatous leprosy and inadequate or irregular therapy.

CF: Single or multiple well demarcated dermatofibroma-like cutaneous and subcutaneous deep-seating nodules arising on normal skin.

HF:

- Atrophy of the epidermis
- Subepidermal grenz zone
- Interlacing bundles of spindle-shaped fusiform histiocytes in the dermis arranged in storiform or crisscross pattern

- High bacillary index, without globi formation of lepra bacilli
- Histologic variants comprise pure fusocellular, fusocellular with epithelioid component, and fusocellular with vacuolated (foamy) cells

DD: Fibrous histiocytoma (dermatofibroma); keloid; erythema nodosum leprosum; sarcoidosis; reticulohistiocytosis; cutaneous metastases; atypical mycobacteriosis; molluscum.

Reference

Kalla, G., Purohit, S., & Vyas, M. C. (2000). Histoid, a clinical variant of multibacillary

leprosy: Report from so-called nonendemic areas. *Int J Lepr Other Mycobact Dis*, **68**(3), 267–271.

Punia, R. P. S., Dhingra, H., Baliyan, A., Handa, U., Mohan, H., & Thami, G. P. (2017). Clinicopathologic spectrum of histoid lepra *International Journal of Current Research*, **9**(5), 50765–50769.

Rodrigues Daxbacher, E. L., Cabrera Pereira, J. P., Ramos de Oliveira, S., Duarte Tortelly, V., Carneiro, S., & Jeunon, T. (2020). The importance of the biopsy technique in the diagnosis of histoid leprosy. *Am J Dermatopathol*, **42**(2), 125–128.

1.4.3.5 Variant: Erythema Nodosum Leprosum

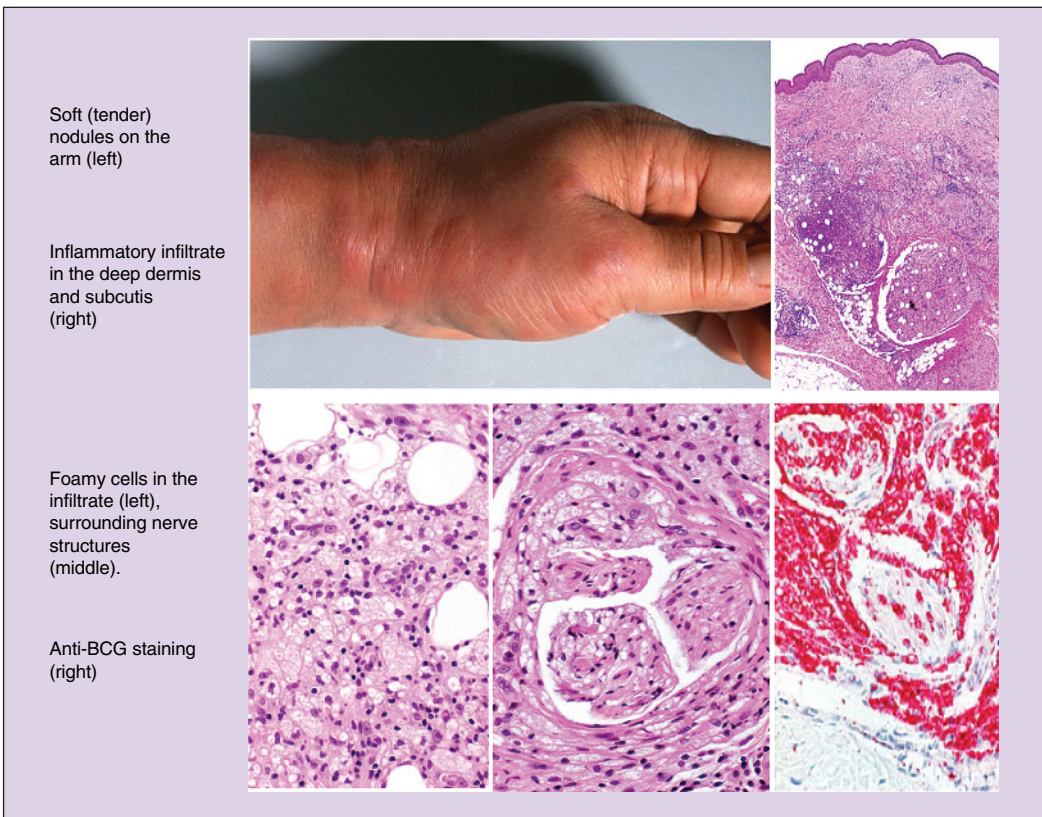


Figure 1.4.3.5 Virchow cell-rich variant of ENL with minimal vasculitis.

Various immunological reactions may be seen in conjunction with (lepromatous) leprosy. A shift toward the tuberculoid pole with better immune status under

treatment is referred to as type 1 (lepra) reaction. The Lucio phenomenon, presenting as small vessel vasculitis with hemorrhagic plaques (erythema necroticans),

is called type 3 reaction and is seen in patients with diffuse lepromatous leprosy. Erythema nodosum leprosum, referred to as a type 2 inflammatory reaction, shows a shift of the immune status toward the lepromatous pole with a high bacterial index.

CF: Erythema nodosum leprosum (type 2 reaction) presents as multiple, tender, contusiform red or violaceous swelling and nodules, preferentially on the extremities. Bullous variants have been reported.

HF: ENL is an immune complex-mediated necrotizing vasculitis involving capillaries, arterioles, arteries, venules, and veins.

- Dermis and subcutaneous tissue are involved
- Small vessel vasculitis with endothelial swelling and fibrinoid necrosis
- Fibrin in vessel walls
- Focal necrosis
- Perivascular lymphocytic and neutrophilic infiltrates and nuclear debris
- Foamy macrophages containing numerous bacilli

DD: Other forms of nodular erythema.

Reference

- Bakshi, N., Rao, S., & Batra, R. (2017). Bullous erythema nodosum leprosum as the first manifestation of multibacillary leprosy: A rare phenomenon. *Am J Dermatopathol*, **39**(11), 857–859.
- Kutzner, H., Argenyi, Z. B., Requena, L., Rutten, A., & Hugel, H. (1998). A new application of BCG antibody for rapid screening of various tissue microorganisms. *J Am Acad Dermatol*, **38**(1), 56–60.
- ### 1.4.4 Buruli Ulcer
- CF:** Even minor injury may be followed by infection with *Mycobacterium ulcerans*. Characteristically infections occur in tropical areas (Australia, Africa: Buruli is a district of Uganda) and slowly evolve into papules or nodules followed by painless ulceration with subsequent mutilation of local tissue.
- HF:**
- Marked necrosis with complete destruction of local tissue
 - Very sparse inflammation, starting in the septal portion of the subcutaneous fat
 - Giant cells
 - Organisms at the borders of the ulcer (Ziehl–Neelsen)
- DD:** Ecthyma; squamous cell carcinoma; melanoma.
- ## Reference
- Portaels, F., Silva, M. T., & Meyers, W. M. (2009). Buruli ulcer. *Clin Dermatol*, **27**(3), 291–305.
- Walsh, D. S., Portaels, F., & Meyers, W. M. (2008). Buruli ulcer (*Mycobacterium ulcerans* infection). *Trans R Soc Trop Med Hyg*, **102**(10), 969–978.
- Zavattaro, E., Boccafroschi, F., Borgogna, C., Conca, A., Johnson, R. C., Sopoh, G. E., . . . Valente, G. (2012). Apoptosis in Buruli ulcer: A clinicopathological study of 45 cases. *Histopathology*, **61**(2), 224–236.

1.5 Actinomycosis

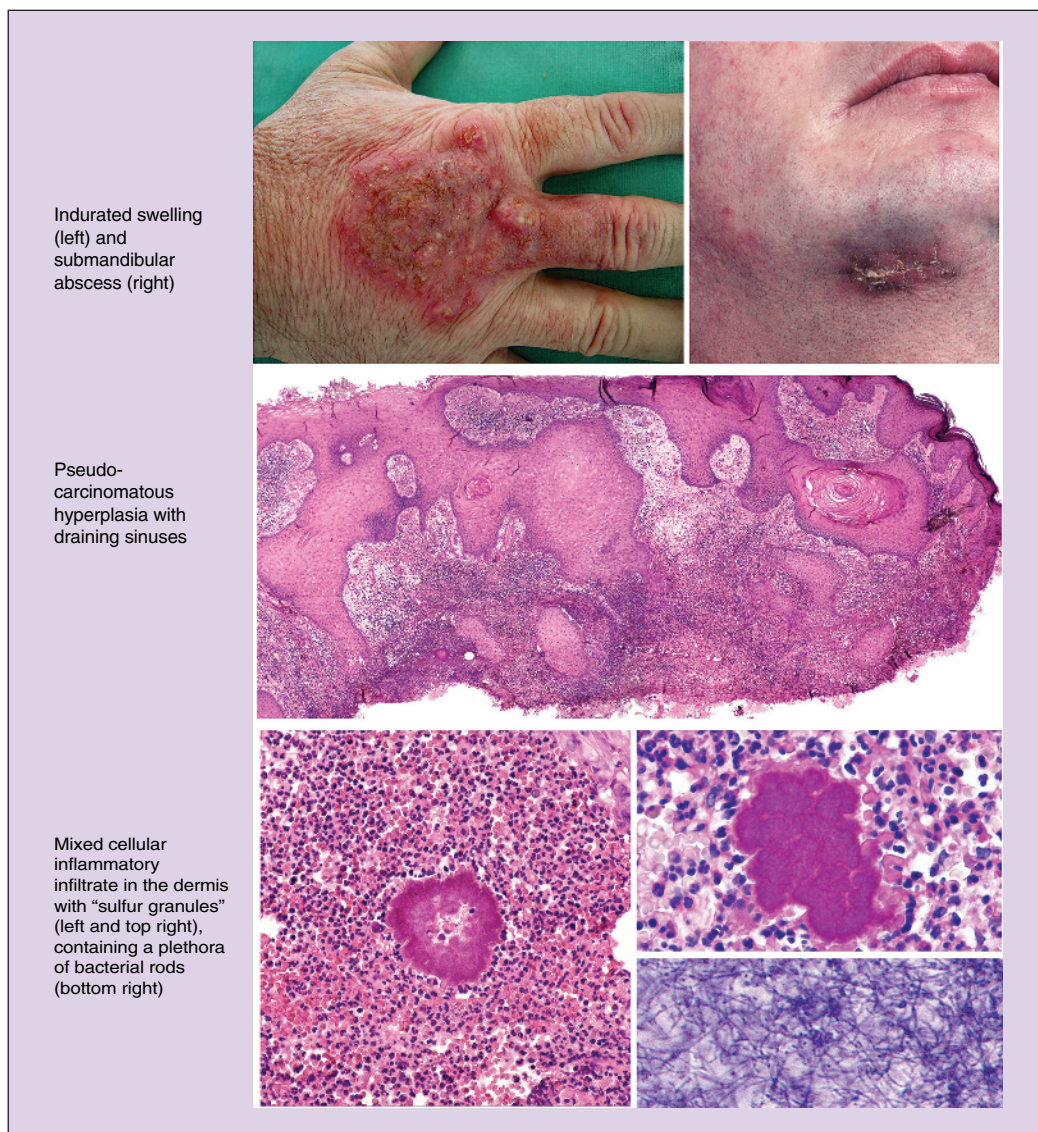


Figure 1.5 Actinomycosis.

The anaerobic saprophytic gram-positive bacterium *Actinomyces israelii* thrives in the autochthonous flora of the mouth and the gastrointestinal tract of healthy

individuals. *Actinomyces israelii* is also the most common cause of chronic suppurative infection of the mucosa, often in the course of dental or surgical procedures.

Pulmonary or gastrointestinal involvement is not unusual.

CF: Typical clinical features are erythema and concomitant indurated swelling, subsequent abscess formation, and purulent discharge with tiny granules draining through sinusoidal tracts into the cervicofacial premandibular area.

HF:

- Pseudocarcinomatous mucosal hyperplasia
- Purulent suppurative infiltrate
- Neutrophils, eosinophils, plasma cells, histiocytes
- Basophilic aggregates of *Actinomyces* organisms (“sulfur granules”)
- *Actinomyces* can be detected by Giemsa or Gomori silver stains
 - in smears
 - in histological specimens
 - by cultivation
- Fibrotic induration and scarring

DD: Scrofuloderma, gumma (tertiary syphilis), lymphogranuloma venereum, Nocardiosis, metastases

Reference

- Cirillo-Hyland, V., Herzberg, A., & Jaworsky, C. (1993). Cervicofacial actinomycosis resembling a ruptured cyst. *J Am Acad Dermatol*, **29**(2 Pt 2), 308–311.
- De, D., Dogra, S., Kanwar, A. J., & Saikia, U. N. (2011). Actinomycosis presenting as a destructive ulcerated plaque on the palate and gingiva. *J Am Acad Dermatol*, **65**(6), 1235–1236.

1.6 Borrelia Infections (Lyme Disease)

Lyme disease, named after a small town in Connecticut, is caused by the spirochete *Borrelia burgdorferi*, transmitted by the tick *Ixodes dammini* (North America) or *Ixodes ricinus* (Europe).

Early (stage I) disease presents with a slowly expanding erythema (chronicum) migrans. If not treated, systemic neurologic, cardiac, and other symptoms as well as additional skin lesions may develop (stage II) due to hematogenous spread of the bacteria. In late disease (stage III), edema eventually transforms into atrophic (wrinkled “cigarette paper-like”) skin (acrodermatitis chronica atrophicans), which may be accompanied by juxta-articular fibroid nodules and migratory monoarthritis.

Serologic tests (specific IgM antibodies) and/or detection of *Borrelia* sp. DNA by PCR confirm the diagnosis.

Reference

- Kempf, W., Kazakov, D. V., Hubscher, E., Gugerli, O., Gerbig, A. W., Schmid, R., . . . Kutzner, H. (2015). Cutaneous borreliosis associated with T cell-predominant infiltrates: A diagnostic challenge. *J Am Acad Dermatol*, **72**(4), 683–689.
- Kempf, W., Kazakov, D. V., Hubscher, E., & Tinguely, M. (2015). Cutaneous borreliosis with a T-cell-rich infiltrate and simultaneous involvement by B-cell chronic lymphocytic leukemia with t(14,18)(q32;q21). *Am J Dermatopathol*, **37**(9), 715–718.

1.6.1 Variant: Erythema (Chronicum) Migrans (ECM) (Stage I)

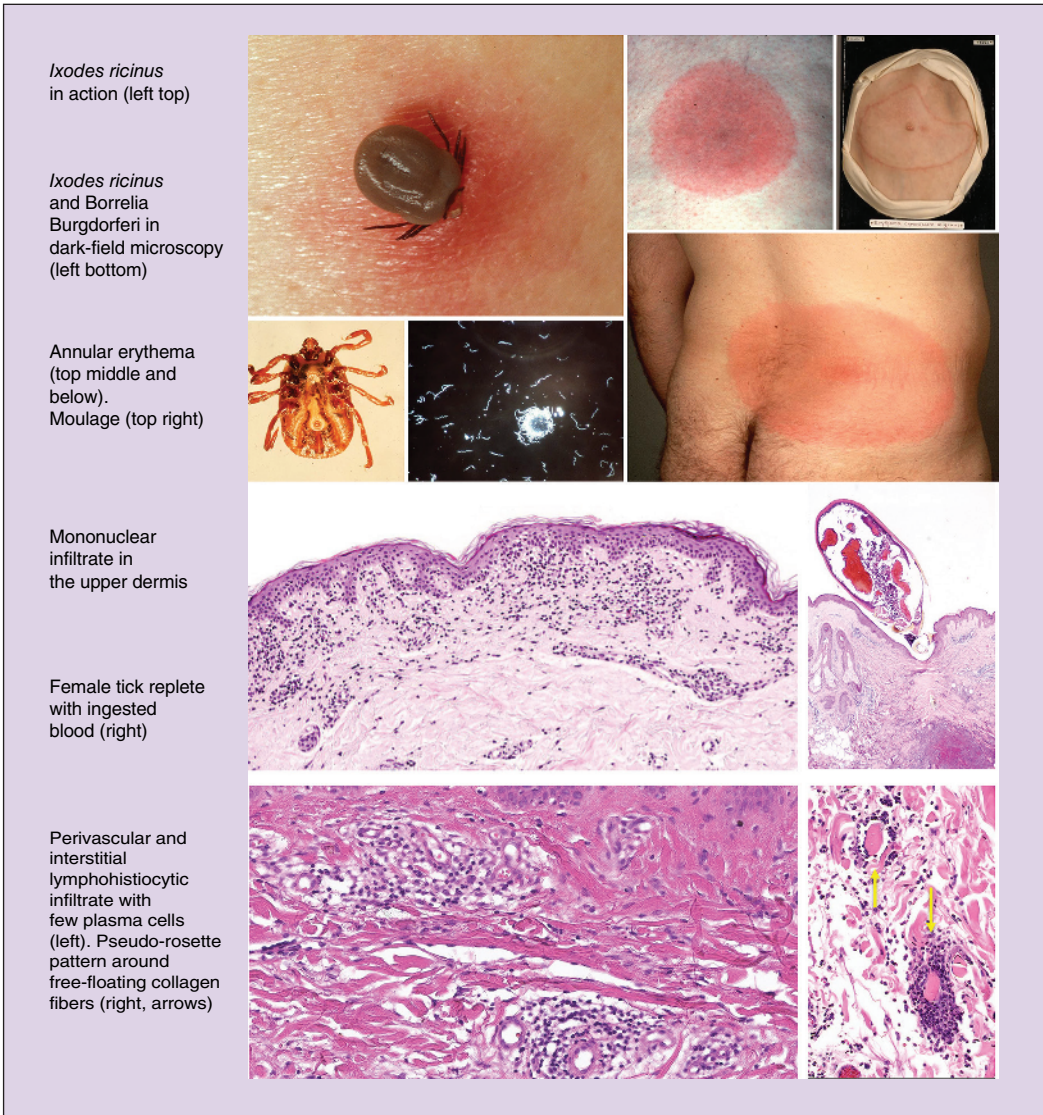


Figure 1.6.1 Variant: Erythema (Chronicum) Migrans (ECM) (Stage I).

CF: ECM, which is typically an erythematous, slowly expanding annular patch, appears at the site of a previous tick bite. A few weeks later, after the erythema has faded, a papule or a small nodule (lymphadenosis cutis benigna, lymphocytoma cutis: see below) may develop at the site of the tick bite or at a distant site, following hematogenous spread of the spirochetes (stage II).

HF: The diagnosis is based on the patient's history, clinical presentation, and serologic tests/PCR, respectively. Immunohistochemical demonstration of spirochetes is rarely feasible. In the center of the lesion, chitinous remnants of the tick (hypostome) and a neutrophil-rich inflammatory infiltrate followed by granulomatous changes may occur.

- Erythematous patch or peripheral annular rims
 - Missing or only slight spongiosis with exocytosis
 - Sparse patchy lymphoplasmacytic perivascular or interstitial (Indian file-like) infiltrate in the upper dermis
 - Eosinophils in early stages more frequent
 - Interstitial lymphohistiocytic infiltrate, sometimes in pseudo-rosette pattern around free-floating collagen fibers

- Plasma cells, with diffuse splaying in the upper dermis, may be rare
- Center of the lesion
 - Eczematous changes of the epidermis
 - Chitinous remnants of the tick (hypostome)
 - Slight edema with dilated blood vessels
 - Mixed inflammatory cell infiltrate
 - Eosinophils (early stages) and plasma cells (advanced stages) commonly occur
 - Granulomatous reaction (advanced lesions)
 - Spirochetes can be identified only in exceptional cases (immunohistochemistry)

DD: Erysipelas; insect bite; acute urticaria (hives); tinea; all other annular (allergic) erythemas.

Reference

- Celebi Cherukuri, N., Roth, C. G., Aggarwal, N., Ho, J., Gehris, R., & Akilov, O. E. (2016). Cutaneous small/medium CD4+ pleomorphic T-cell lymphoma-like nodule in a patient with erythema chronicum migrans. *Am J Dermatopathol*, **38**(6), 448–452.
- Wilson, T. C., Legler, A., Madison, K. C., Fairley, J. A., & Swick, B. L. (2012). Erythema migrans: A spectrum of histopathologic changes. *Am J Dermatopathol*, **34**(8), 834–837.

1.6.2 Variant: Lymphadenosis Cutis Benigna (Pseudolymphoma, Lymphocytoma Cutis) (Stage I)

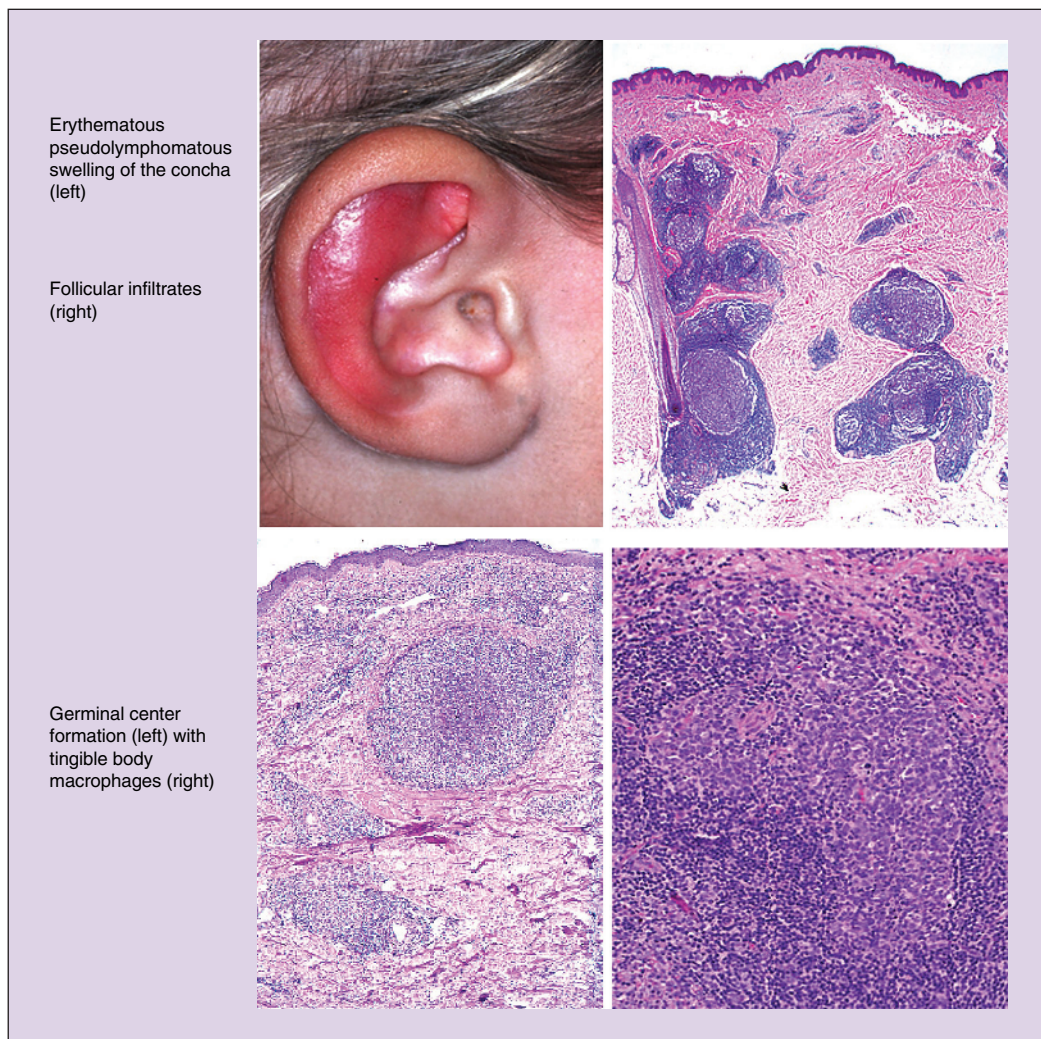


Figure 1.6.2.1 Variant: Lymphadenosis Cutis Benigna (Pseudolymphoma; Lymphocytoma Cutis) (Stage I).

Source: Burg et al. (2019). *Atlas of Dermatopathology: Tumors, Nevi, and Cysts* (p. 393). Oxford: Wiley.

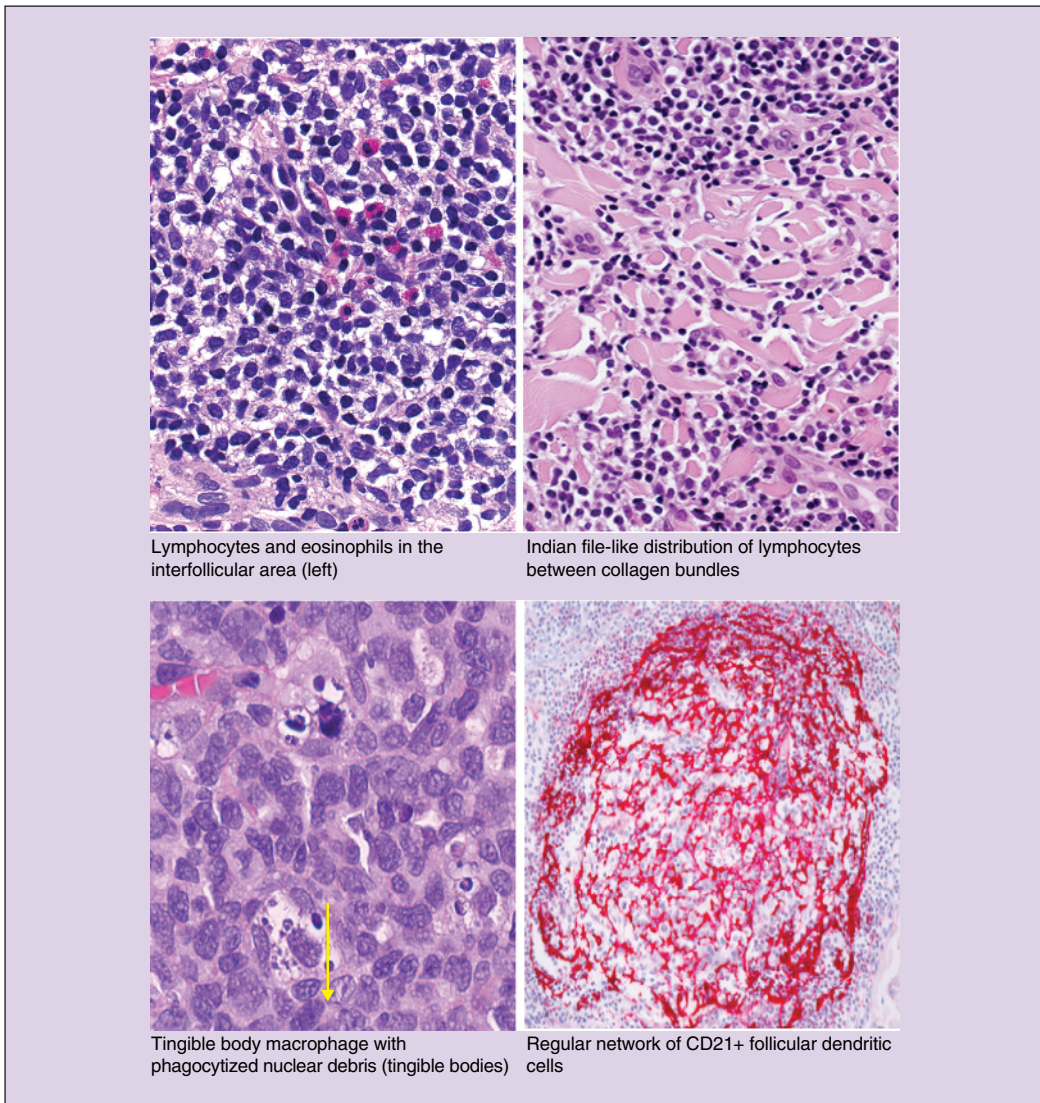


Figure 1.6.2.2 Variant: Lymphadenosis Cutis Benigna (Pseudolymphoma; Lymphocytoma Cutis) (Stage I).

Source: Burg et al. (2019). *Atlas of Dermatopathology: Tumors, Nevi, and Cysts* (p. 394). Oxford: Wiley.

In Europe, in a minority of cases pseudo-lymphomatous infiltrates most commonly occur some weeks after infection with *Borrelia burgdorferi* at the site of a previous tick bite (*Ixodes ricinus*).

CF: Mostly solitary, rarely multiple or disseminated soft red, sharply bordered nodules on the head, preferentially on the ear lobes. Other predilectional sites are the

nose, nipples, inguinal area, and the scrotum.

HF: Nodular dermal infiltrates, mainly located in the upper and mid-dermis, occasionally extending into the deep dermis.

- Preserved subepidermal grenz zone
- Dense and diffuse lymphoid infiltrates
- Reactive lymph follicles

- Follicle centers with “starry sky”-pattern: macrophages containing phagocytosed nuclear material (Fleming’s tingible body macrophages)
- Follicle centers with large (centroblasts) and small (centrocytes) follicle center cells
- Small lymphocytes around reactive lymph follicles
- Interfollicular area composed of small B-cells, diffusely splayed small T-cells, histiocytes, and a few eosinophils and plasma cells
- Characteristically, there is diffuse splaying of round cells between collagen or smooth muscle bundles (e.g. at the nipple), subsequently creating the impression of smudging borders – whereas cutaneous B-cell lymphoma typically presents with sharply demarcated borderlines
- Immunophenotype: Polyclonal B-cell infiltrate; monotypic expression of kappa or lambda chains is exceptional. Regular and sharply demarcated network of CD21+ follicular dendritic cells within the reactive lymph follicles

DD: Cutaneous B-cell lymphomas (marginal zone lymphoma; follicle center lymphoma); other pseudolymphomas caused by other microbiological, physical, or chemical agents.

Reference

- Braun-Falco, O. B., & Burg, G. (1975). [Lymphoreticular proliferations in the skin. Cytochemical and immunocytological studies in lymphadenosis benigna cutis]. *Hautarzt*, **26**(3), 124–132.
- Baefverstedt, B. (1944). Ueber lymphadenosis benigna cutis. Eine klinische pathologisch-anatomische Studie. *Acta Derm Venereol (Suppl XI) (Stockh)*, **24**, 1–102.
- Buechner, S. A., Lautenschlager, S., Itin, P., Bircher, A., & Erb, P. (1995). Lymphoproliferative responses to *Borrelia burgdorferi* in patients with erythema migrans, acrodermatitis chronica atrophicans, lymphadenosis benigna cutis, and morphea. *Arch Dermatol*, **131**(6), 673–677.
- Colli, C., Leinweber, B., Mullegger, R., Chott, A., Kerl, H., & Cerroni, L. (2004). *Borrelia burgdorferi*-associated lymphocytoma cutis: Clinicopathologic, immunophenotypic, and molecular study of 106 cases. *J Cutan Pathol*, **31**(3), 232–240.
- Grange, F., Wechsler, J., Guillaume, J. C., Tortel, J., Tortel, M. C., Audhuy, B., . . . Cerroni, L. (2002). *Borrelia burgdorferi*-associated lymphocytoma cutis simulating a primary cutaneous large B-cell lymphoma. *J Am Acad Dermatol*, **47**(4), 530–534.
- Moulouguet, I., Ghnassia, M., Molina, T., & Fraitag, S. (2012). Miliarial-type perifollicular B-cell pseudolymphoma (lymphocytoma cutis): A misleading eruption in two women. *J Cutan Pathol*, **39**(11), 1016–1021.
- Rijlaarsdam, J. U., Meijer, C. J., & Willemze, R. (1990). Differentiation between lymphadenosis benigna cutis and primary cutaneous follicular center cell lymphomas. A comparative clinicopathologic study of 57 patients. *Cancer*, **65**(10), 2301–2306.
- Watanabe, R., Nanko, H., & Fukuda, S. (2006). Lymphocytoma cutis due to pierced earrings. *J Cutan Pathol*, **33**(Suppl 2), 16–19.

1.6.3 Variant: Morphea/Scleroderma-Like Lesions (Stage II)

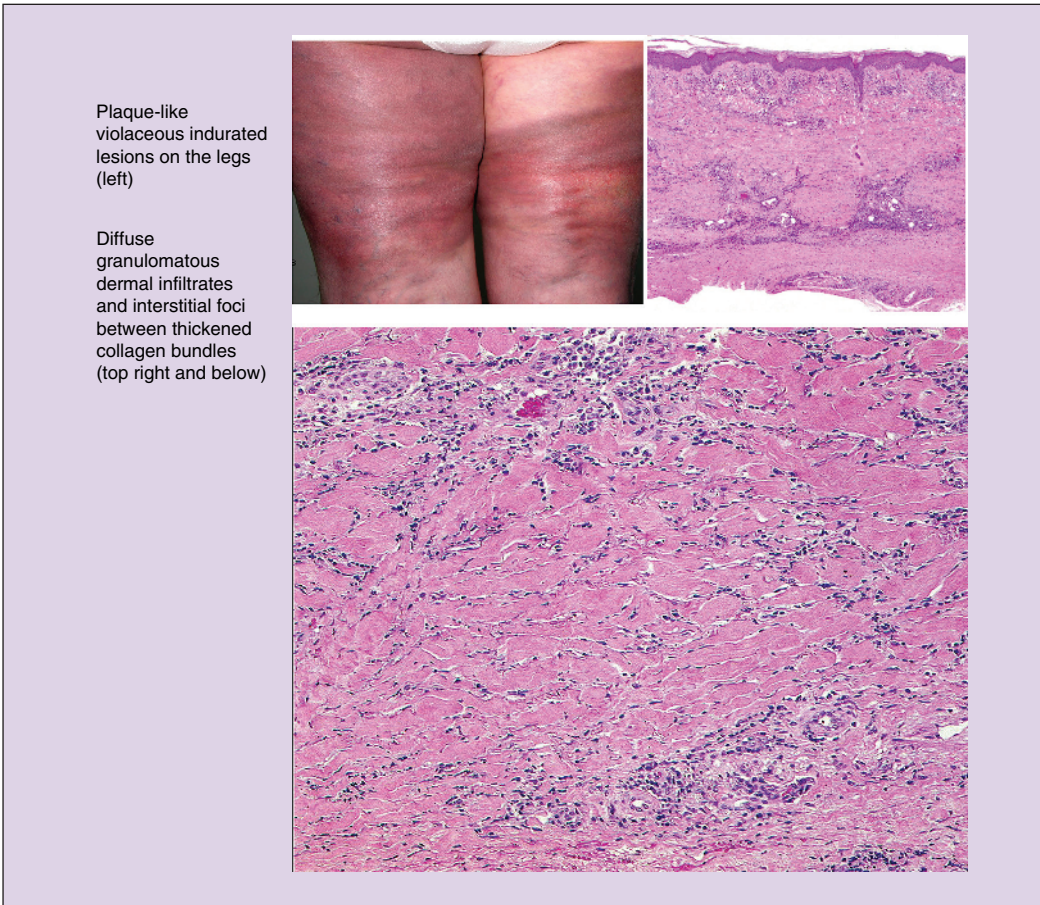


Figure 1.6.3 Variant: Morphea/Scleroderma-Like Lesions (Stage II).

Plaque-like erythematous indurations which closely resemble early morphea/scleroderma – occasionally presenting with edematous and granulomatous infiltrates (early stages).

CF: A few weeks following prior ECM manifestation, plaque-like indurated lesions develop at the site of the resolving ECM. Clinical and histopathological differential diagnoses of early stages (lilac ring) comprise interstitial granulomatous dermatitis, interstitial granulomatous drug reaction, morphea/scleroderma (lilac ring), and granuloma annulare (diffuse type).

HF:

- Diffuse granulomatous dermal infiltrates, with characteristic splaying of tiny granulomatous interstitial foci, often spilling over into the upper subcutis
- Multiple tiny wreath-like granulomas (“micro-rosettes”) with telltale free-floating thickened collagen bundles at the center and pale histiocytes at the periphery
- Additionally, throughout the entire dermis sparse diffuse mixed infiltrate, often containing histiocytes, eosinophils, and plasma cells

- Preserved elastic fiber network; no scarring

DD: Remarkably, a similar – if not identical – histopathological pattern (biopsy taken from inflamed periphery/lilac ring) may be encountered in morphea/scleroderma, interstitial granulomatous dermatitis (in conjunction with rheumatoid arthritis or with other autoimmune disorders), and interstitial granulomatous drug reactions.

Reference

Aberer, E., Klade, H., Stanek, G., & Gebhart, W. (1991). *Borrelia burgdorferi* and different types of morphea. *Dermatologica*, **182**(3), 145–154.

Breier, F., Khanakah, G., Stanek, G., Kunz, G., Aberer, E., Schmidt, B., & Tappeiner, G. (2001). Isolation and polymerase chain reaction typing of *Borrelia afzelii* from a skin lesion in a seronegative patient with generalized ulcerating bullous lichen sclerosus et atrophicus. *Br J Dermatol*, **144**(2), 387–392.

Breier, F. H., Aberer, E., Stanek, G., Khanakaha, G., Schlick, A., & Tappeiner, G. (1999). Isolation of *Borrelia afzelii* from circumscribed scleroderma. *Br J Dermatol*, **140**(5), 925–930.

Wackernagel, A., Bergmann, A. R., & Aberer, E. (2005). Acute exacerbation of systemic scleroderma in *Borrelia burgdorferi* infection. *J Eur Acad Dermatol Venereol*, **19**(1), 93–96.

1.6.4 Variant: Acrodermatitis Chronica Atrophicans (Stage III)

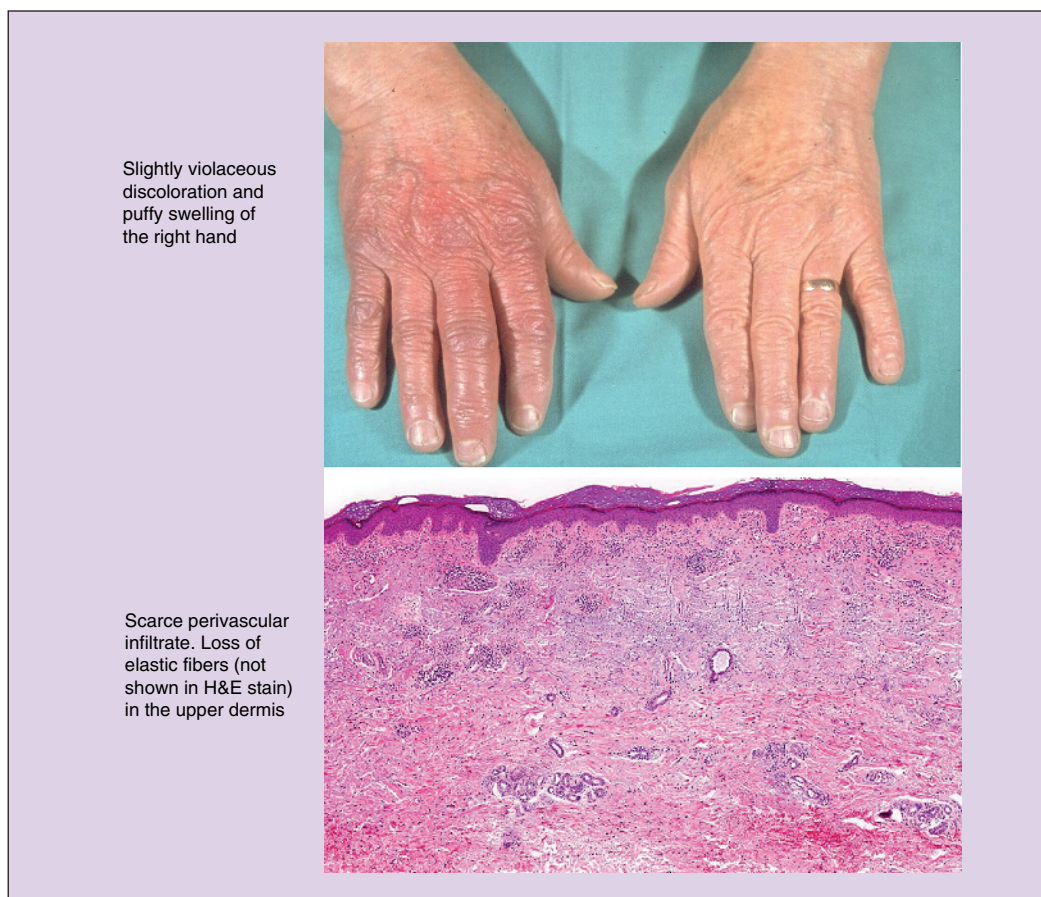


Figure 1.6.4.1 Variant: Acrodermatitis Chronica Atrophicans (Stage III).

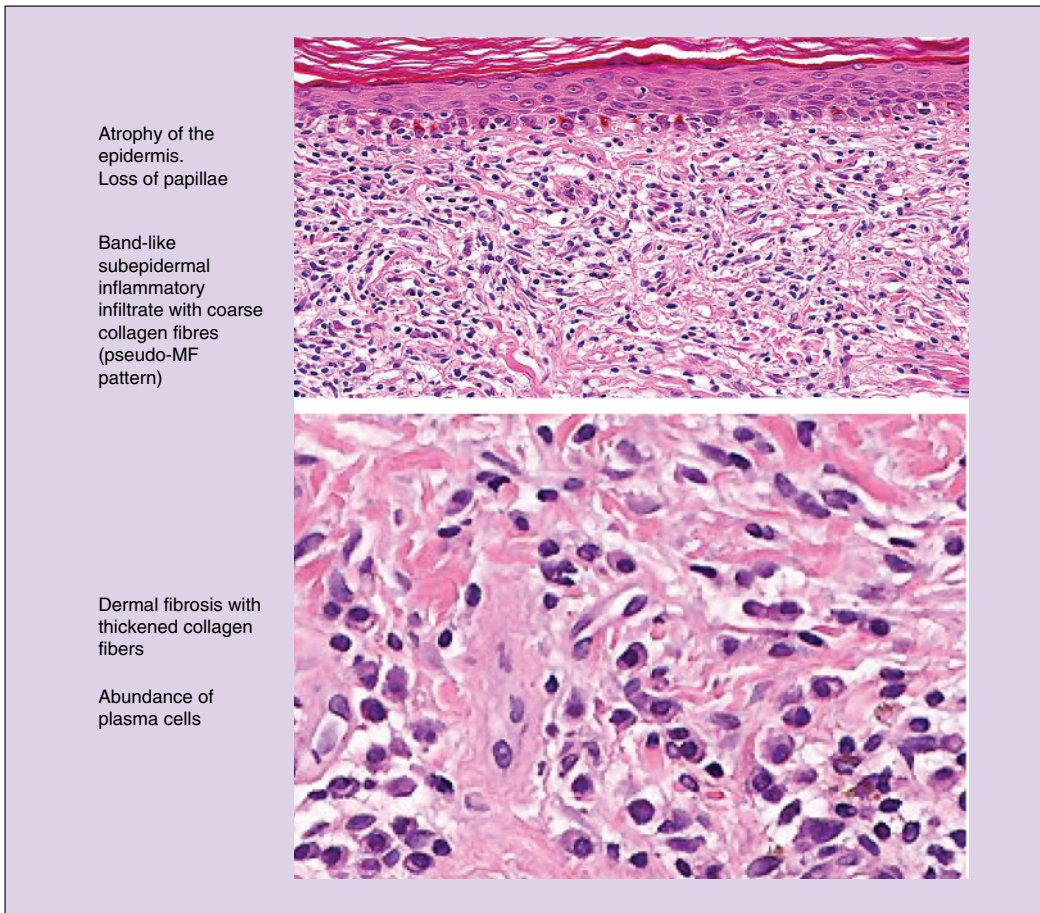


Figure 1.6.4.2 Variant: Acrodermatitis Chronica Atrophicans (Stage III).

CF: In stage II of borreliosis (usually months or years after infection) – preferentially on the limbs, mostly unilaterally, rarely bilaterally – a violaceous puffy edema appears that gradually evolves into cutaneous atrophy (“cigarette paper-type” skin, telangiectasias, red-brownish color) with characteristically translucent superficial blood vessels. Fibrosis and sclerosis with scleroderma-like collagen changes, ulnar and tibial fibro-sclerotic bands, and juxta-articular fibrous (fibroid) nodules are accompanying features of advanced acrodermatitis chronica atrophicans.

HF:

- Dermal edema and mucin deposits (early)
- Markedly thinned, atrophied epidermis (late)

- Loss of rete ridges and cutaneous adnexa (late)
- Dilated superficial blood vessels (early and late)
- Diffuse superficial round cell infiltrate, hugging the epidermis (“pseudo-MF”)
- Additional perivascular infiltrates, superficial and deep, with conspicuous plasma cells
- Dense, diffuse interstitial round cell infiltrate with abundant plasma cells (late)
- Rarely, adjacent paucicellular fibroid nodules surrounded by abundant plasma cells at periphery (late)

Remarkably, in some cases of advanced *Borrelia* infection, T-cell rich infiltrates composed of small T-cells with or without plasma cells develop that may mimic mycosis

fungoides (“Pseudo-MF” pattern of borreliosis) both clinically and histologically.

DD: Anetoderma; atrophoderma of Pasini and Pierini; varicose veins; actinic reticuloid – with histopathological morphological overlap, albeit clinically completely different.

Reference

- Gulseren, D., Cerroni, L., Hofmann-Wellenhof, R., & Arzberger, E. (2018). Correlation of reflectance confocal microscopy and dermatopathology findings in a case of Acrodermatitis chronica atrophicans. *Am J Dermatopathol*, **40**(5), 367–370.
- Kempf, W., Kazakov, D. V., Hubscher, E., Gugerli, O., Gerbig, A. W., Schmid, R., . . . Kutzner, H. (2015). Cutaneous borreliosis associated with T cell-predominant infiltrates: A diagnostic challenge. *J Am Acad Dermatol*, **72**(4), 683–689.
- Tee, S. I., Martinez-Escaname, M., Zuriel, D., Fried, I., Wolf, I., Massone, C., & Cerroni, L. (2013). Acrodermatitis chronica atrophicans with pseudolymphomatous infiltrates. *Am J Dermatopathol*, **35**(3), 338–342.
- Zalaudek, I., Leinweber, B., Kerl, H., & Mullegger, R. R. (2005). Acrodermatitis chronica atrophicans in a 15-year-old girl misdiagnosed as venous insufficiency for 6 years. *J Am Acad Dermatol*, **52**(6), 1091–1094.

1.6.5 Variant: Juxta-Articular Fibrous Nodules in Acrodermatitis Chronica Atrophicans (Stage III)

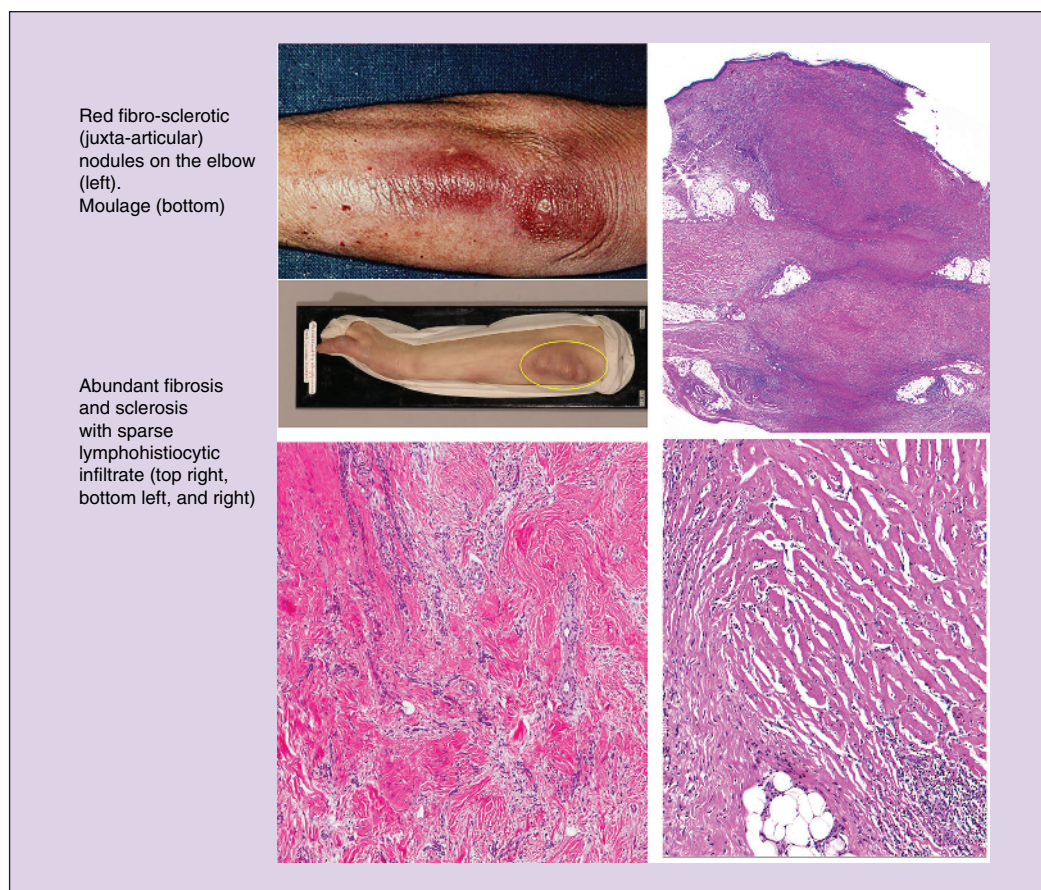


Figure 1.6.5 Variant: Juxta-Articular Fibrous Nodules in Acrodermatitis Chronica Atrophicans (Stage III).

CF: Reddish to violaceous juxta-articular subcutaneous nodules, preferentially close to the elbows, often with concomitant translucent atrophic skin. Remarkably hard consistency (“wood-hard” nodules).

HF: Lamellated compact paucicellular fibrosis and sclerosis, with abundant polyclonal plasma cells at its outer fringes.

DD: Rheumatoid nodule; dermatofibroma; keloid and hypertrophic scar; erythema elevatum diutinum (advanced stage).

Reference

- Espana, A., Torrelo, A., Guerrero, A., Suarez, J., Rocamora, A., & Ledo, A. (1991). Periarticular fibrous nodules in Lyme borreliosis. *Br J Dermatol*, **125**(1), 68–70.
- Messer, L., Felten, R., Moreau, P., Freisz, M. C., & Mahe, A. (2015). Fibrous nodules over the patella revealing acrodermatitis chronica atrophicans. *Joint Bone Spine*, **82**(3), 208.
- Netherton, E. W., & Hubler, W. R. (1945). Acrodermatitis atrophicans chronica with fibrous cutaneous nodules. *Arch Derm Syphilol*, **52**, 416.

1.6.6 Differential Diagnosis: Actinic Reticuloid°

UV-light induced disorder; often idiopathic or associated with sensitizing chemical agents.

CF: Clinically, there is remarkable thickening and coarse wrinkling of the skin, almost exclusively at sun-exposed sites (face).

HF: There may be slight morphological overlap with the incipient stage of borreliosis.

- Parakeratosis, acanthosis, spongiosis
- Dermal dendrocytes and multinucleated giant cells
- Lichenoid lymphocytic infiltrate, containing many plasma cells and eosinophils
- Fibrosis

DD: Borreliosis; cutaneous T-cell lymphoma; eczema, persistent light reaction; phototoxic and photoallergic dermatitis.

Reference

- Sidiropoulos, M., Deonizio, J., Martinez-Escala, M. E., Gerami, P., & Guitart, J. (2014). Chronic actinic dermatitis/actinic reticuloid: A clinicopathologic and immunohistochemical analysis of 37 cases. *Am J Dermatopathol*, **36**(11), 875–881.
- Toonstra, J., Henquet, C. J., van Weelden, H., van der Putte, S. C., & van Vloten, W. A. (1989). Actinic reticuloid. A clinical photobiologic, histopathologic, and follow-u study of 16 patients. *J Am Acad Dermatol*, **21**(2 Pt 1), 205–214.

1.7 Venereal Diseases

1.7.1 Gonorrhea



Figure 1.7.1 Gonorrhea.

CF: Burning sensation of urethra in conjunction with pus-laden discharge. Associated systemic (“benign”) gonococcal sepsis may occur in rare cases (see chapter on sepsis).

HF: Direct identification of bacteria in smears, showing intracellular gram-negative diplococci. Supportive diagnostic methods: Immunofluorescence, culture, PCR (urine, smear, biopsy).

DD: Non-gonococcal urethritis.

1.7.2 Syphilis, Chancere

Treponema pallidum infection is acquired mostly via direct sexual contact. Classically, untreated syphilis evolves through three

well-defined clinicopathological stages. Remarkably, at each stage syphilis may mimic various non-venereal diseases. Conversely, inflammatory dermatoses of various origin may show morphological overlap with *Treponema pallidum* infection, for example, pustular psoriasis and pustular stage II of syphilis.

Reference

- Borroni, G. (1988). A case of late congenital syphilis at the Metropolitan Museum of Art, New York. *Am J Dermatopathol*, **10**(5), 448–450.
- Ober, W. B. (1989). To cast a pox. The iconography of syphilis. *Am J Dermatopathol*, **11**(1), 74–86.

1.7.2.1 Stage I



Figure 1.7.2.1 Syphilis (Stage I).

CF: After an incubation period of about 2–3 weeks, *ulcus durum* (chancre) – the first visible manifestation of *T. pallidum* infection – develops at the primary site of infectious entry, typically at the penis (sulcus coronarius), vulva, cervix uteri, perianal skin, lips, or oral cavity. The ulcer is painless; there is always associated regional lymphadenitis.

At this early stage of disease, diagnosis can be established by the direct demonstration of spirochetes (smears; dark field

microscopy) and by serological tests, which become reactive/positive 2–3 weeks after primary infection (specific IgM antibodies).

HF:

- Shallow ulceration, often with serum and debris
- Accompanying edema
- Dense mixed inflammatory infiltrate
- Abundant plasma cells
- Dilated postcapillary venules with swelling of endothelial cells

- Histopathological demonstration of *Treponema pallidum* by Warthin–Starry silver stain and/or immunohistochemically

DD: Non-infectious balanitis plasmacellularis Zoon; chancroid of *Haemophilus ducreyi* infection.

Reference

Carlson, J. A., Dabiri, G., Cribier, B., & Sell, S. (2011). The immunopathobiology of syphilis: The manifestations and course of syphilis are determined by the level of delayed-type hypersensitivity. *Am J Dermatopathol*, **33**(5), 433–460.

1.7.2.2 Stage II

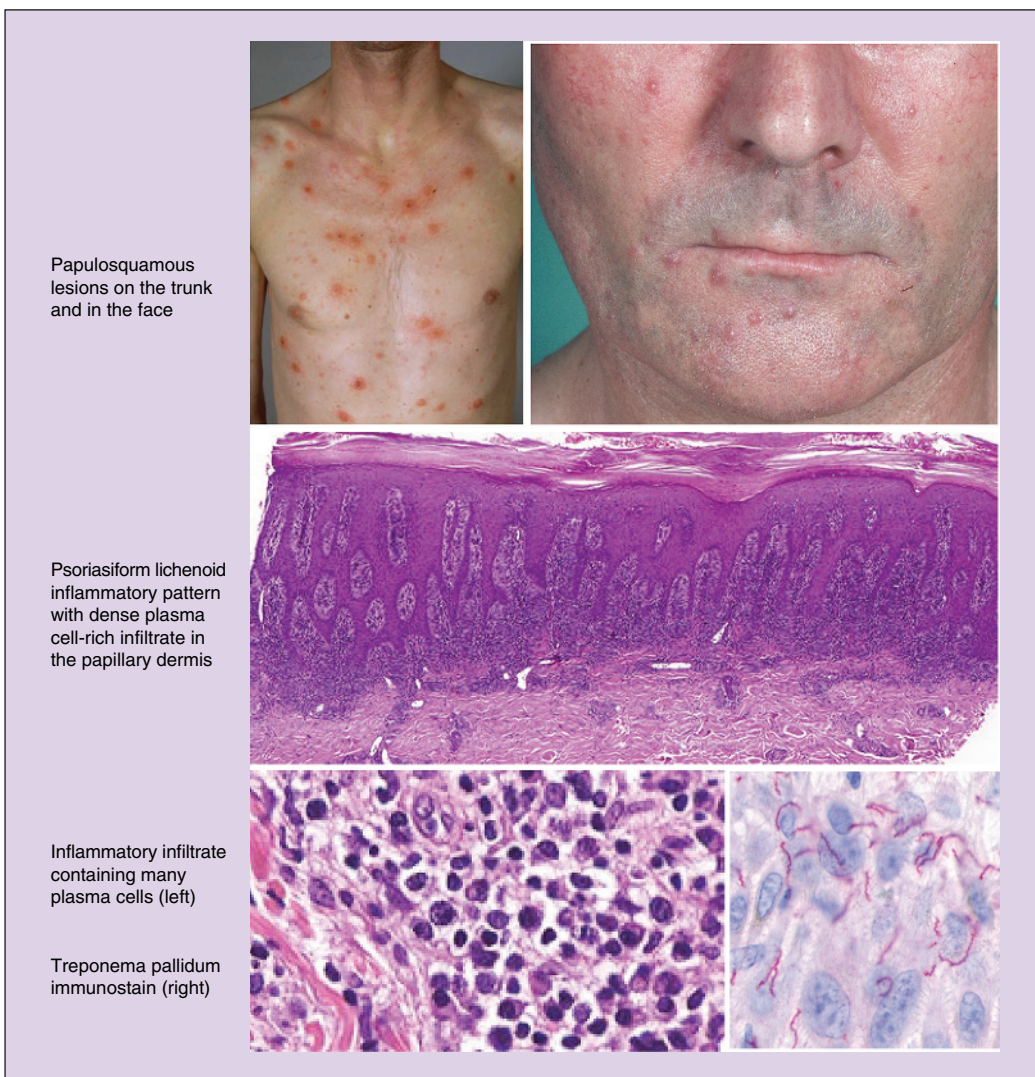


Figure 1.7.2.2 Syphilis, Papular (Stage II).

Source: Burg et al. (2019). *Atlas of Dermatopathology: Tumors, Nevi, and Cysts* (p. 398). Oxford: Wiley.

CF: In the early secondary stage of syphilis (8–12 weeks after infection), distinct tiny macules (roseola) may appear on trunk and extremities, that are easily overlooked and regress spontaneously. In the late stage of secondary syphilis (>2 years after untreated infection), disseminated small papules and papulosquamous lesions may appear on head, trunk, extremities, and on mucous membranes, presenting as plaques and patches on the palms and soles (“pustular psoriasis”) or as condyloma-like lesions in the anogenital region.

HF:

- Macular lesions: Nonspecific sparse interstitial infiltrate; few plasma cells as a telltale sign of infectious origin
- Maculopapular lesions in late secondary syphilis
 - Interface dermatitis; often associated with spongiosis with subcorneal spongiform pustulation
 - Dermal edema
 - Superficial and deep perivascular and interstitial infiltrate
 - Mixed infiltrate: lymphocytes, histiocytes, mostly scattered – occasionally numerous – eosinophils
 - Sheets or small focal clusters of plasma cells – as a clue to the diagnosis
 - Histiocyte-predominant granulomatous features at advanced stages
 - Spirochetes may be detected either by Warthin–Starry silver stain or immunohistochemically, preferentially in the upper dermis and epidermis
- Verruciform condylomata lata – with markedly spongiform pustulation – and ulcerating lues maligna – with broad shallow ulcers and massive debris – are variants of secondary syphilis at special sites, preferentially in immunocompromised patients. Spirochetes may be abundant in these conditions

DD: Pityriasis lichenoides et varioliformis acuta (PLEVA); pustular psoriasis; lymphomatoid papulosis; cutaneous lymphoma (mycosis fungoides); drug reaction; tick bites; leprosy.

Reference

- Alessi, E., Innocenti, M., & Ragusa, G. (1983). Secondary syphilis. Clinical morphology and histopathology. *Am J Dermatopathol*, **5**(1), 11–17.
- Jordaan, H. F. (1988). Secondary syphilis. A clinicopathological study. *Am J Dermatopathol*, **10**(5), 399–409.
- Pettit, C., McMurray, S., Randall, M. B., Jones, A., & Fisher, K. (2019). Highlighting a potential pitfall: Positive *Treponema pallidum* immunohistochemical stain in a patient without syphilis. *Am J Dermatopathol*, **41**(12), 924–926.
- Rosa, G., Bennett, D., & Piliang, M. P. (2015). Eosinophil-rich syphilis: A report of four cases. *J Cutan Pathol*, **42**(8), 554–558.
- Rysgaard, C., Alexander, E., & Swick, B. L. (2014). Nodular secondary syphilis with associated granulomatous inflammation: Case report and literature review. *J Cutan Pathol*, **41**(4), 370–379.

1.7.2.3 Stage III°

CF: Two years after primary infection, the course of disease – provided there was no appropriate treatment – reaches its third, latent stage. Clinical symptoms are manifold: gummatous superficial or deep ulcerating skin lesions, cardiovascular (aorta), peripheral and central neurologic symptoms (progressive paralysis, tabes dorsalis).

HF:

- Small granulomas composed of epithelioid cells and multinucleated giant cells
- Lymphohistiocytic infiltrates with plasma cells
- Dilated vessels with swollen endothelia
- Central caseating necrosis

DD: Sarcoidosis; tuberculosis; leprosy; leishmaniasis (advanced).

1.7.3 Ulcus Molle (Chancroid)

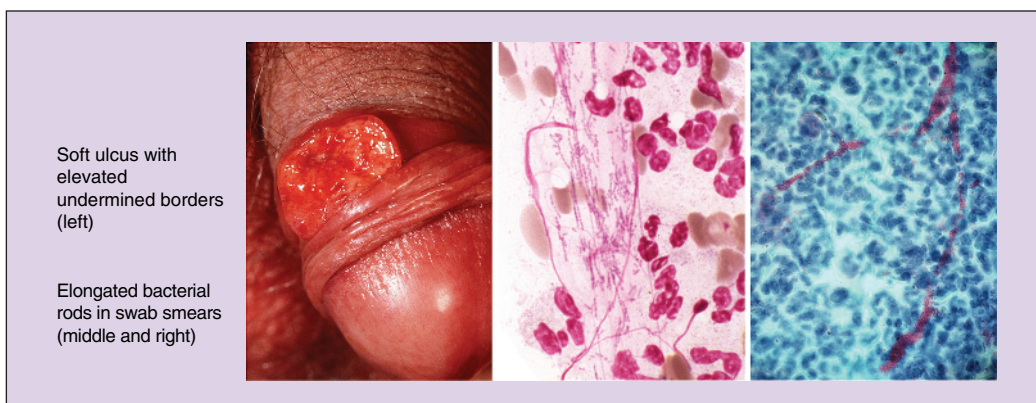


Figure 1.7.3 Ulcus Molle (Chancroid).

Haemophilus ducreyi is a gram-negative rod-like bacterium that infects the skin or mucous membranes via small superficial injuries.

CF: The most frequent sites of primary infection are the female labia majora and minora and the inner fold of the foreskin in men. The initial papule evolves into a painful ulcer with elevated undermined borders, from which a diagnostic smear may be taken for microscopic investigation.

HF: Smears taken from the base of the ulcer or its borders reveal large numbers of *Haemophilus ducreyi*, arranged in long chains.

DD: Other ulcerating venereal disease; herpes genitalis.

Reference

- Freinkel, A. L. (1987). Histological aspects of sexually transmitted genital lesions. *Histopathology*, **11**(8), 819–831.
- King, R., Gough, J., Ronald, A., Nasio, J., Ndinya-Achola, J. O., Plummer, F., & Wilkins, J. A. (1996). An immunohistochemical analysis of naturally occurring chancroid. *J Infect Dis*, **174**(2), 427–430.

1.7.4 Granuloma Inguinale (Donovanosis; Granuloma Venereum)

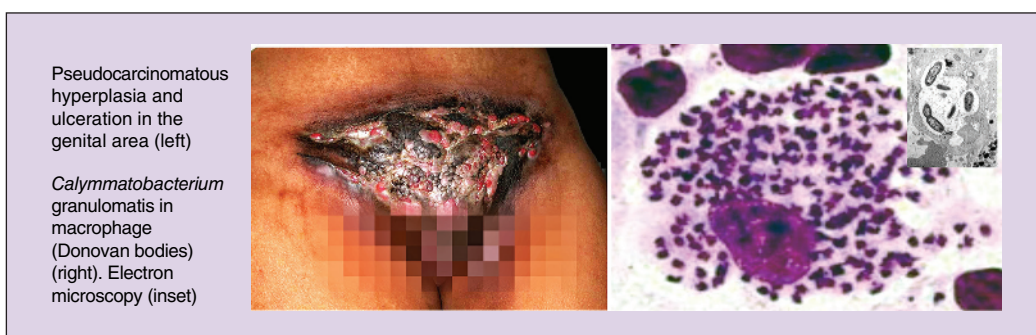


Figure 1.7.4 Granuloma Inguinale (Donovanosis; Granuloma Venereum).

Granuloma inguinale is caused by the gram-negative bacterium *Klebsiella granulomatis* (*Calymmatobacterium granulomatis*). Granuloma inguinale (syn: granuloma venereum) is not to be confused with **lymphogranuloma inguinale** (syn: **lymphogranuloma venereum**), which is a venereal infection caused by *Chlamydia trachomatis*.

CF: Small papules evolving into chronically progressive painless ulcers, preferentially at the male genitalia; mostly in tropical and subtropical regions. Ulcers with characteristically hypertrophic lateral borders. Concomitant lymphadenopathy is usually absent.

HF:

- Pseudocarcinomatous epithelial hyperplasia at the outer border of the ulcer
- Central ulceration with prominent necrosis
- Diffuse inflammatory infiltrate, containing macrophages, plasma cells, and neutrophils
- Macrophages with intracytoplasmic inclusion (Donovan bodies)
- Demonstration of bacterial rods in semithin sections (toluidine blue or Giemsa stain)

DD: Ulcus mole (chancroid); ulcus durum (syphilis); herpes simplex/genitalis.

1.7.5 Lymphogranuloma Inguinale (Lymphogranuloma Venereum; Duran-Nicolas-Favre Disease)

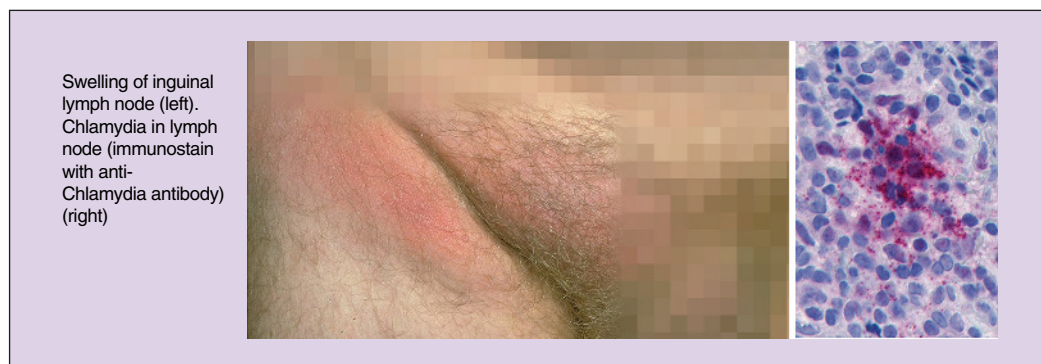


Figure 1.7.5 Lymphogranuloma Inguinale (Lymphogranuloma Venereum; Durand–Nicolas–Favre Disease).

This sexually transmitted infection caused by *Chlamydia trachomatis* should not be confused with another, sound-alike venereal infection – granuloma inguinale (syn: granuloma venereum) – which is caused by the gram-negative bacterium *Calymmatobacterium granulomatis*.

CF: Primary lesion (stage I) is an ulcerating papulopustule, usually in the genital region

or in the rectum. In stage II, the regional lymph node is involved (bubo), which shows abscess formation with ulceration and draining to the surface. Stricture and fibrosis in stage III (elephantiasis) eventually evolve into massive lymphatic edema and urethral-vaginal fistulas.

HF: Unspecific findings with ulceration and granulomatous abscess formation.

Fibrosis and scarring at later stages. The lymph nodes show granulomatous inflammation with many plasma cells and abscess formation. Chlamydia organisms preferentially are demonstrated by

immunohistochemical methods (specific monoclonal antibodies).

DD: Syphilis; granuloma inguinale; herpes simplex/genitalis; other genital ulcers.

1.8 Rickettsial Infections

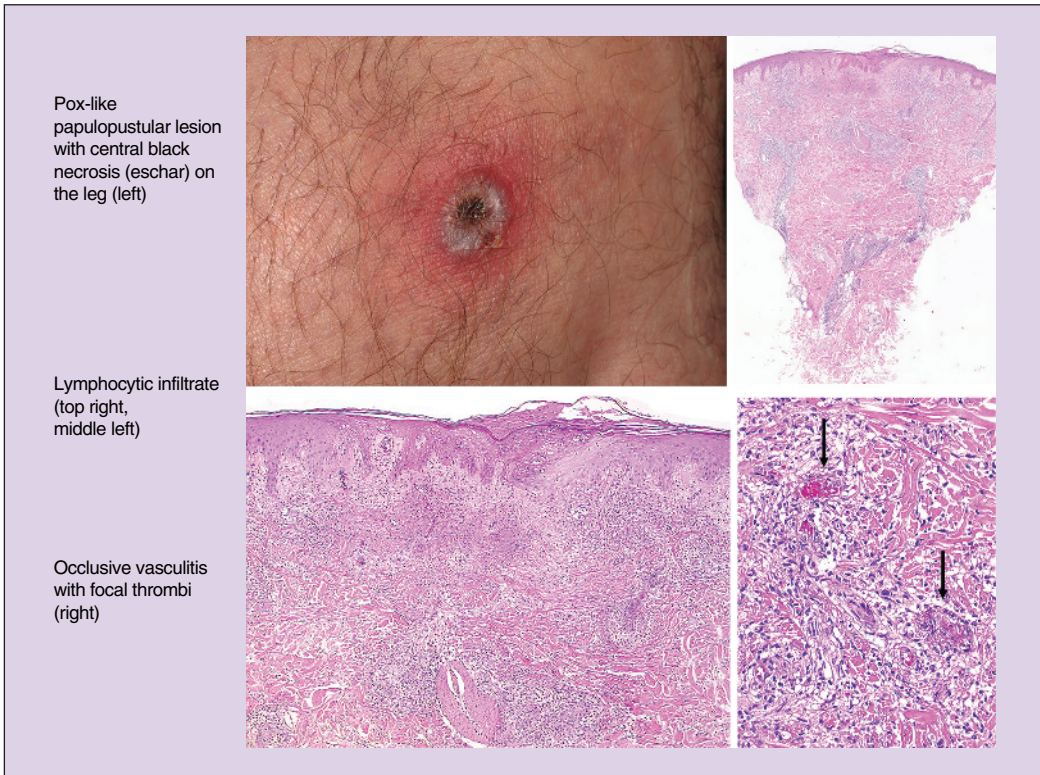


Figure 1.8 Rickettsial Infections.

Rickettsiae comprise a family of gram-negative intracellular parasites (Rickettsiaceae family), which are transmitted by various vectors (ticks, mites, flees, lice) and cause spotted fever, endemic typhus, Rocky Mountain spotted fever, Mediterranean tick fever, African tick bite fever, Rickettsial pox, and others. The different rickettsial diseases are subsumed under various groups: spotted fevers-group, typhus group, and others –

in particular, Q-fever, where the vector is not an arthropod; infectious organisms are inhaled.

CF: Diffuse exanthema – often associated with fever and chills – or solitary papulopustular lesion with marked central necrosis and hemorrhagic crust; the central eschar is highly characteristic. Occasional swelling of the draining lymph node. Milder forms may be associated with itching sensation.

HF: Histologic changes of solitary lesion, for example, in Mediterranean tick fever:

- Flat ulcer with superficial necrosis and crust formation (eschar)
- Superficial and deep perivascular infiltrate
- Focal leukocytoclastic vasculitis with small thrombi (telltale sign)
- Organisms may be demonstrated immunohistochemically or by immunofluorescence. Rickettsiae often thrive within the walls of small inflamed vessels

DD: Mosquito bite; furuncle; leishmaniasis; ecthyma; orf; anthrax (solitary lesion with eschar).

Reference

Montenegro, M. R., Mansueto, S., Hegarty, B. C., & Walker, D. H. (1983). The histology of "taches noires" of boutonneuse fever and demonstration of *Rickettsia conorii* in them by immunofluorescence. *Virchows Arch A Pathol Anat Histopathol*, **400**(3), 309–317.

1.9 Dermatoses Associated with Bacterial Infections

1.9.1 Staphylococcal Scalded Skin Syndrome (SSSS)

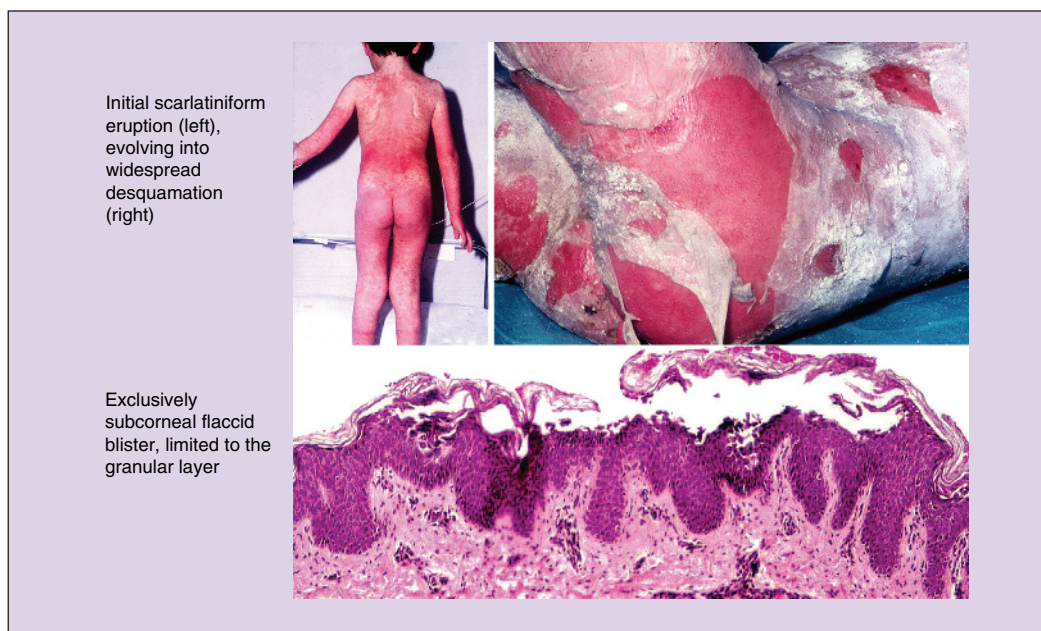


Figure 1.9.1 Staphylococcal Scalded Skin Syndrome (SSSS).

Also known as dermatitis exfoliativa neonatorum, Ritter [von Rittershain] disease, staphylococcal Lyell syndrome, Pemphigus neonatorum.

Toxin-mediated epidermolytic dermatosis, primarily in small children, characterized by erythema and widespread loss

of the superficial epidermal layers, resembling acute burn. Causative agent is the toxin-producing (exfoliative toxins A and B) *Staphylococcus aureus*, often of phage group II.

CF: Initially, there is a mild scarlatiniform rash with associated fever. Widespread

erythema evolves into marked tenderness with small unstable flaccid bullae that quickly erode and lead to burn-like loss of superficial epithelial layers. The clinical course often is acute with systemically ill patients.

HF:

- Subcorneal acantholysis and blister formation with a marked split high in the epidermis
- Blister roof composed exclusively of stratum corneum (versus blister formation in TEN, where full-thickness epidermal blister roof occurs)
- Little or no inflammatory infiltrate

- Frozen sections preferred for rapid diagnosis

DD: Toxic epidermal necrolysis (TEN) showing full-thickness epidermal detachment.

Reference

- Cribier, B., Piemont, Y., & Grosshans, E. (1994). Staphylococcal scalded skin syndrome in adults. A clinical review illustrated with a new case. *J Am Acad Dermatol*, **30**(2 Pt 2), 319–324.
- de Dobbeleer, G., & Achten, G. (1975). Staphylococcal scalded skin syndrome. *An ultrastructural study. J Cutan Pathol*, **2**(2), 91–98.
- Elston, D. M., Stratman, E. J., & Miller, S. J. (2016). Skin biopsy: Biopsy issues in specific diseases. *J Am Acad Dermatol*, **74**(1), 1–16.

1.9.2 Differential Diagnosis: Toxic Epidermal Necrolysis (TEN)

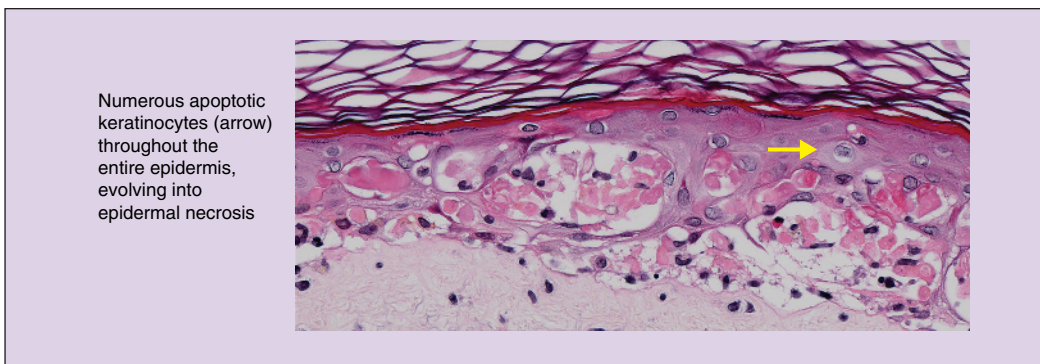


Figure 1.9.2 Differential Diagnosis: Toxic Epidermal Necrolysis (TEN).

Severe immunological drug-induced (in particular, antibiotic and antiepileptic drugs) skin reaction, characterized by complete epidermal necrosis (keratinocyte necrosis) and associated mucosal involvement.

CF: Incipient confluent maculopapular exanthem, followed by hemorrhagic blisters and widespread epidermal necrosis resulting in wide denuded areas of skin. Positive Nikolski's sign. Massive periorificial mucosal erosions are common.

HF: At early stages, scatter of necrotic keratinocytes throughout the epidermis.

Advanced lesions with full-thickness epidermal necrosis. Necrotic epidermis often completely detached from underlying cutis. The inflammatory infiltrate may be very sparse (versus erythema multiforme and fixed drug eruption with marked interface dermatitis). Frozen sections should be preferred for rapid histopathological diagnosis.

DD: Staphylococcal scaled skin syndrome (with flaccid subcorneal bullae); acute burns; erythema multiforme; fixed drug eruption; pemphigus and pemphigoid variants; linear IgA disease.

Reference

- Naik, H., Lockwood, S., & Saavedra, A. (2017). A pilot study comparing histological and immunophenotypic patterns in stage 4 skin graft vs host disease from toxic epidermal necrolysis. *J Cutan Pathol*, **44**(10), 857–860.
- Ondhia, C., Kaur, C., Mee, J., Natkunarajah, J., & Singh, M. (2019). Lichen planus pemphigoides mimicking toxic epidermal necrolysis. *Am J Dermatopathol*, **41**(11), e144–147.
- Paquet, P., & Pierard, G. E. (1997). Erythema multiforme and toxic epidermal necrolysis: A comparative study. *Am J Dermatopathol*, **19**(2), 127–132.
- Schwartz, R. A., McDonough, P. H., & Lee, B. W. (2013). Toxic epidermal necrolysis: Part I. Introduction, history, classification, clinical features, systemic manifestations, etiology, and immunopathogenesis. *J Am Acad Dermatol*, **69**(2): 173.e1–13; quiz 185–6.

1.10 Dermatoses Mimicking Bacterial Infections

1.10.1 Pyoderma Gangrenosum

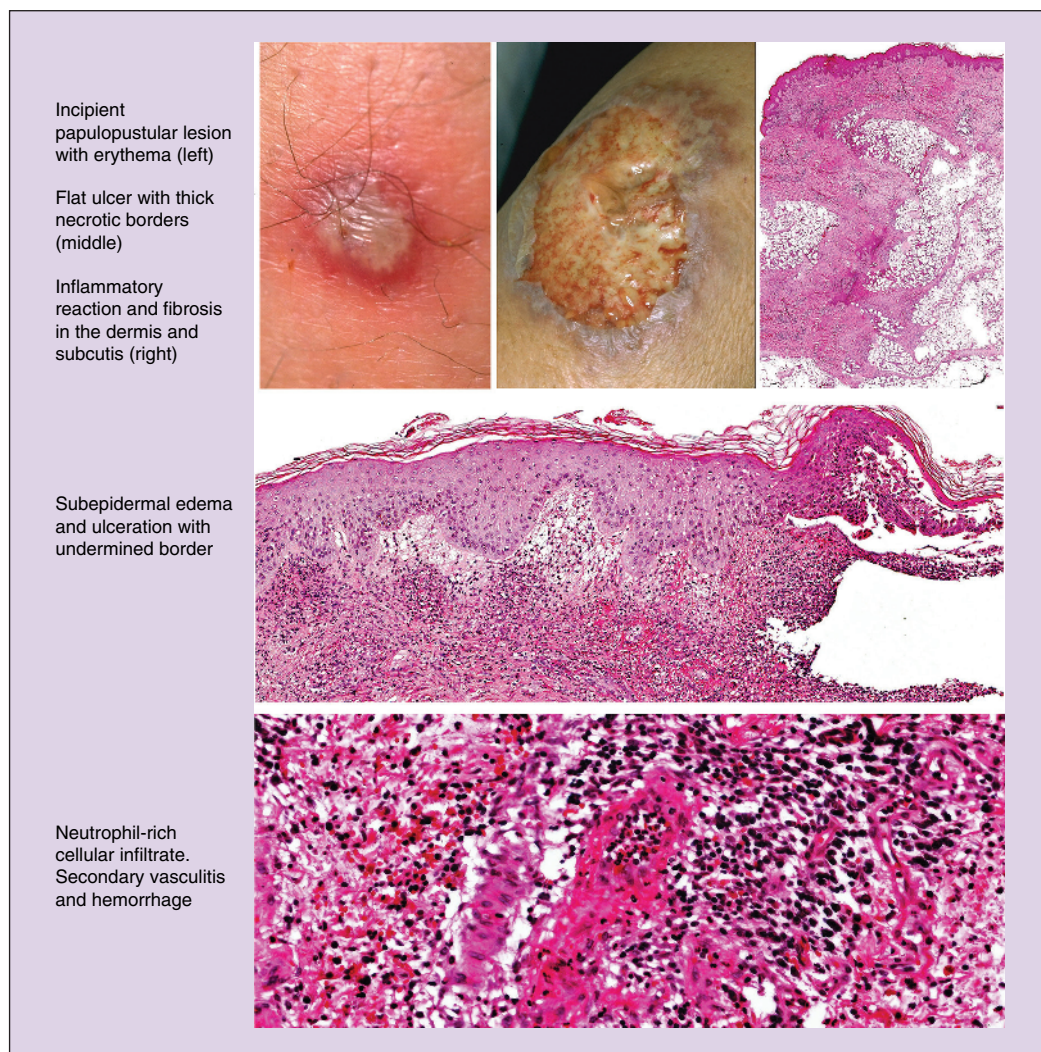


Figure 1.10.1 Pyoderma Gangrenosum.

The key pathogenetic process in the uncommon disorder bearing the misnomer “pyoderma gangrenosum” is a massive suppurative infiltration with neutrophils and associated vessel damage. PG and Sweet syndrome are paradigmatic autoinflammatory disorders and should be evaluated and treated under this particular etiopathogenetic concept. PG frequently is associated with inflammatory bowel disease (colitis ulcerosa), rheumatoid arthritis, autoinflammatory disorders, hepatitis or occurs as a sequela to traumatic or surgical wounds in patients with a distinctive predisposition to PG.

CF: Typically, banal postoperative or traumatic wounds rapidly enlarge, and evolve with centrifugally expanding erythema into a central pustular or bullous eruption with subsequent fulminant ulceration. Ulcers show pathognomonically undermined borders with necrosis and hemorrhage. The lower leg is the preferential site. Multiple lesions may coalesce. Lesions resolve from the center, leaving typical cribriform scars.

Variants of PG include bullous, superficial granulomatous, pustular vegetative, peristomal, genital, and postoperative types. Remarkably, PG may show a plethora of different histopathological patterns. Diagnosis therefore should always be based on strict clinic-pathological correlation!

HF:

- Incipient (unspecific) suppurative “folliculitis,” followed by shallow ulcer formation
- Shallow ulcer with undermined borders
- Subepidermal edema evolving into diffuse neutrophil-rich infiltrate
- Predominantly neutrophilic infiltrate, accompanied by few lymphocytes, plasma cells, and histiocytes. Morphological overlap with Sweet syndrome-like pattern
- Secondary vasculitis with intraluminal fibrin deposits and neutrophils
- End stage of PG with deep-reaching (unspecific) ulceration involving the subcutaneous fat

DD: Ecthyma; artifact; deep fungal or bacterial infection.

Reference

- Azar, M. M., Relich, R. F., Schmitt, B. H., Spech, R. W., & Hage, C. A. (2014). Cutaneous blastomycosis masquerading as pyoderma gangrenosum. *J Clin Microbiol*, **52**(4), 1298–1300.
- Saunderson, R. B., Tng, V., Watson, A., & Scurry, J. (2016). Perianal herpes simplex virus infection misdiagnosed with Pyoderma gangrenosum: Case of the month from the Case Consultation Committee of the International Society for the Study of Vulvovaginal Disease. *J Low Genit Tract Dis*, **20**(2), e14–15.

1.10.2 Infantile Acropustulosis

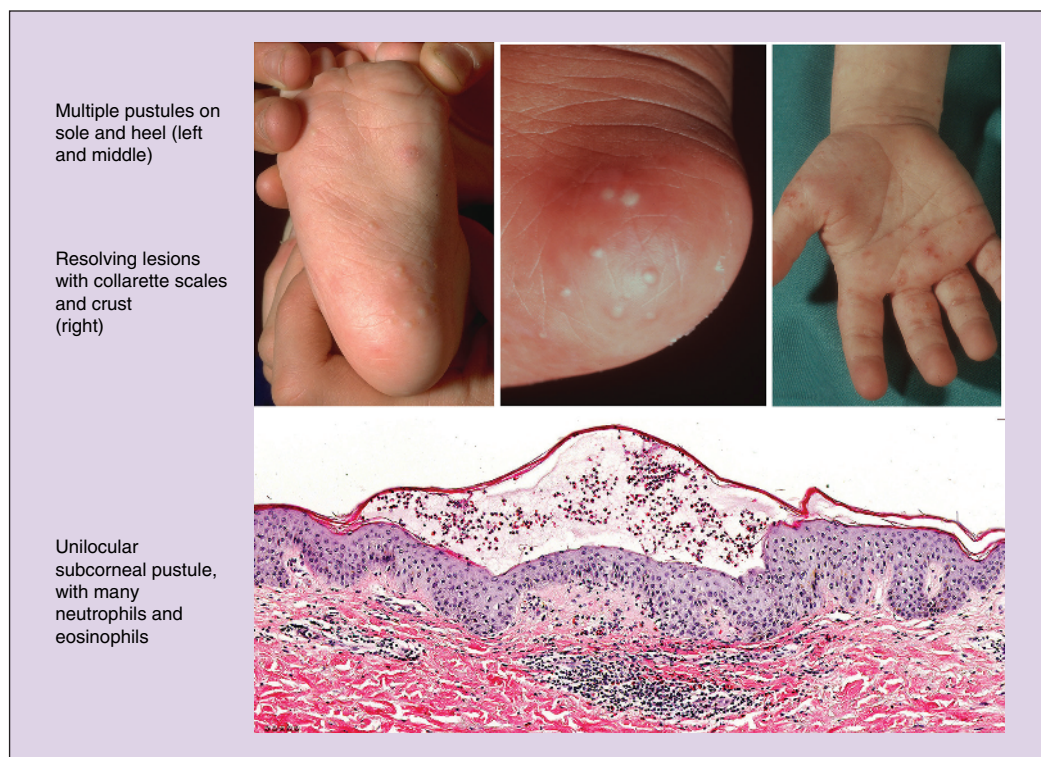


Figure 1.10.2 Infantile Acropustulosis.

CF: At birth or during the first year of life, pruritic pustules with an erythematous base occur on hands and feet, resolving with collarette-type scale-crusts, in most cases within two years. Unknown etiology.

HF:

- Unilocular, subcorneal or intraepidermal vesicle or pustule
- Sparse spongiosis at the periphery of the lesion
- Pustules contain a mixed round cell infiltrate, with predominant neutrophils and eosinophils

- Bacteria or fungi are not demonstrable with special stains

DD: Scabies; impetigo; pustular psoriasis; acrodermatitis continua suppurativa Hallopeau; IgA bullous dermatosis; IgA pemphigus.

Reference

- Hürlimann, A., Wüthrich, B., & Burg, G. (1992). Infantile Akropustulose. *Z Hautkr*, **67**(12), 1073–1079.
- Paloni, G., Berti, I., & Cutrone, M. (2013). Acropustulosis of infancy. *Arch Dis Child Fetal Neonatal Ed*, **98**(4), F340.

1.10.3 Acute Generalized Exanthematous Pustulosis (AGEP)

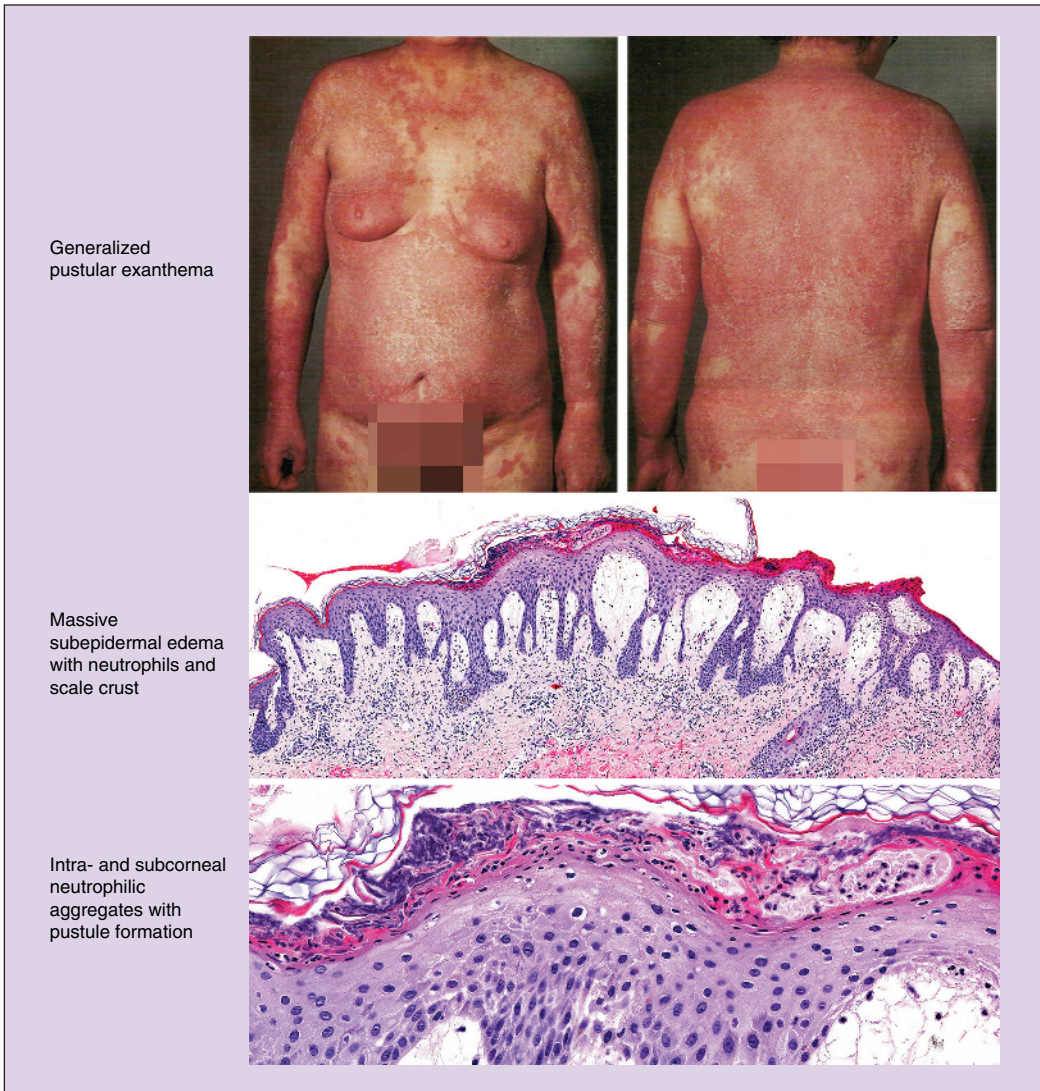


Figure 1.10.3 Acute Generalized Exanthematous Pustulosis (AGEP).

Most eruptions of AGEP are caused by antibiotic drugs. Historically, mercury has played a significant role in some cases.

CF: Sudden eruption of myriads of small pustules on erythematous ground, combined with fever and leukocytosis.

HF:

- Superficial intra- or subcorneal pustule, filled with neutrophils
- Spongiosis at the margin of the lesion
- Edema of the papillary dermis
- Sparse mixed cellular inflammatory infiltrate in the upper and deep dermis

- Almost always erythrocyte extravasation
- Leukocytoclastic vasculitis may be present (facultative)

DD: Pustular psoriasis; Sweet syndrome; Sneddon–Wilkinson syndrome; impetigo; **Drug Rash with Eosinophilia and Systemic Symptoms (DRESS);** leukocytoclastic vasculitis; incipient stage of erysipelas.

Reference

Ballmer, B. K., Widmer, M., & Burg, G. (1993). Acetylsalicylsäure-induzierte generalisierte Pustulose. *Schweiz med Wschr*, **123**, 542–546.

Poeschl, M. D., Hurley, M. Y., Goyal, S. D., & Vidal, C. I. (2014). Targetoid eruptions: Acute generalized exanthematous pustulosis. *Am J Dermatopathol*, **36**(10), 827–828, 838.

Sidoroff, A., Halevy, S., Bavinck, J. N., Vaillant, L., & Roujeau, J. C. (2001). Acute generalized exanthematous pustulosis (AGEP) – a clinical reaction pattern. *J Cutan Pathol*, **28**(3), 113–119.

Vyas, N. S., Charifa, A., Desman, G. T., & McNiff, J. M. (2019). Distinguishing pustular psoriasis and acute generalized exanthematous pustulosis on the basis of plasmacytoid dendritic cells and MxA protein. *J Cutan Pathol*, **46**(5), 317–326.

1.10.4 Psoriasis Pustulosa

Myriads of tiny pustules on erythematous ground on the back (left) and palm (right top)

Erosive pustulosis on the thumb in acrodermatitis continua suppurativa Hallopeau (right below)

Intraepidermal pustule with adjacent psoriasiform acanthosis. Sparse infiltrate in the dermis. Note characteristic spongiform pustulation at the periphery of the pustule (arrow)

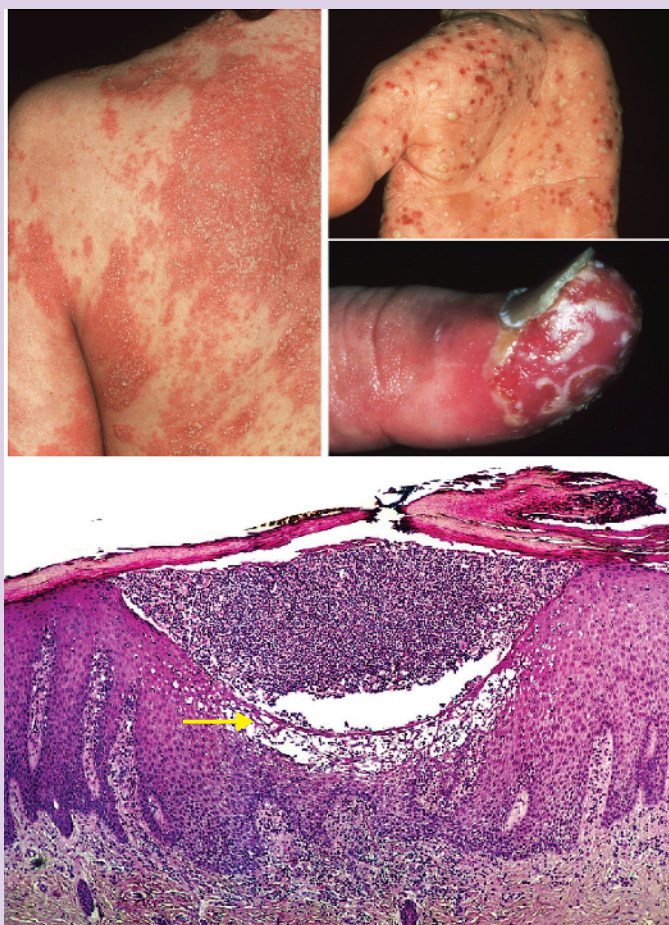


Figure 1.10.4 Psoriasis Pustulosa.

CF: Generalized pustular psoriasis (von Zumbusch type) is characterized by generalized eruption of aggregated tiny pustules, densely grouped pustular lesions on a macular erythema, and associated fever and malaise.

Acrodermatitis continua suppurativa (Hallopeau) is a localized clinical variant of psoriasis pustulosa at acral sites, mostly on the fingers and toes.

HF:

- Acanthosis and papillomatosis, slightly psoriasiform, often with accompanying scale crust
- Pathognomonic “spongiform pustulation”: Subcorneal pustules, filled with neutrophils, and neutrophil-rich spongiosis at the edges of the lesion – corresponding to Kogoj’s “unicellular pustule”
- Spongiform changes at the bottom and at the outer edges may predominate in early lesions

- Sparse to moderate predominantly neutrophilic infiltrate in the dermis
- No infectious organisms

DD: Pustular drug reaction; impetigo contagiosa.

Reference

- Kardaun, S. H., Kuiper, H., Fidler, V., & Jonkman, M. F. (2010). The histopathological spectrum of acute generalized exanthematous pustulosis (AGEP) and its differentiation from generalized pustular psoriasis. *J Cutan Pathol*, **37**(12), 1220–1229.
- Sanchez, N. P., Perry, H. O., & Muller, S. A. (1981). On the relationship between subcorneal pustular dermatosis and pustular psoriasis. *Am J Dermatopathol*, **3**(4), 385–386.
- Vyas, N. S., Charifa, A., Desman, G. T., & McNiff, J. M. (2019). Distinguishing pustular psoriasis and acute generalized exanthematous pustulosis on the basis of plasmacytoid dendritic cells and MxA protein. *J Cutan Pathol*, **46**(5), 317–326.

1.10.5 Localized Neutrophilic Eccrine Hidradenitis Associated with Mitoxantrone Treatment

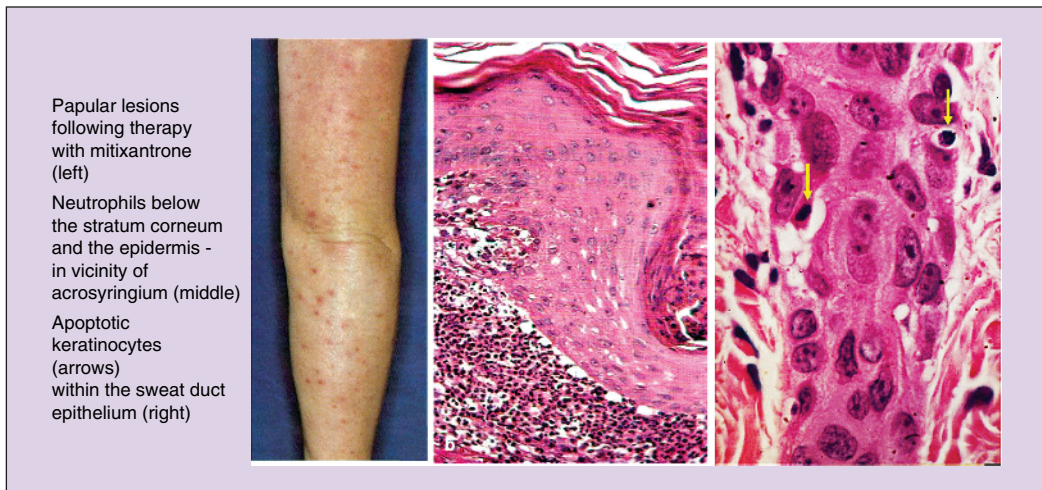


Figure 1.10.5 Localized Neutrophilic Eccrine Hidradenitis.

CF: In this self-limited disorder, which frequently is a sequela to treatment with anthracyclines, multiple small firm reddish sweat-gland-bound papules or pustules appear on the limbs or on the trunk. Underlying hematologic or other malignancies (treatment) are almost always present.

HF:

- Predominantly neutrophilic round cell infiltrate next to or within the subepidermal acrosyringeal portion of the eccrine (and apocrine) sweat ducts
- Sweat glands and duct epithelium may show only minor vacuolization and

occasional apoptosis; complete necrosis does not occur

DD: Other chemotherapy-induced drug eruptions

Reference

- Brehler, R., Reimann, S., Bonsmann, G., & Metze, D. (1997). Neutrophilic hidradenitis induced by chemotherapy involves eccrine and apocrine glands. *Am J Dermatopathol*, **19**(1), 73–78.
- Burg, G., Bieber, T., & Lanecker, P. (1988). Lokalisierte neutrophile ekrine Hidradenitis unter Mitoxantron: Eine typische Zytostatikanebenwirkung. *Hautarzt*, **39**, 233–236.

1.10.6 Erosive Pustular Dermatitis (Pustular Ulcerative Dermatitis) of the Scalp

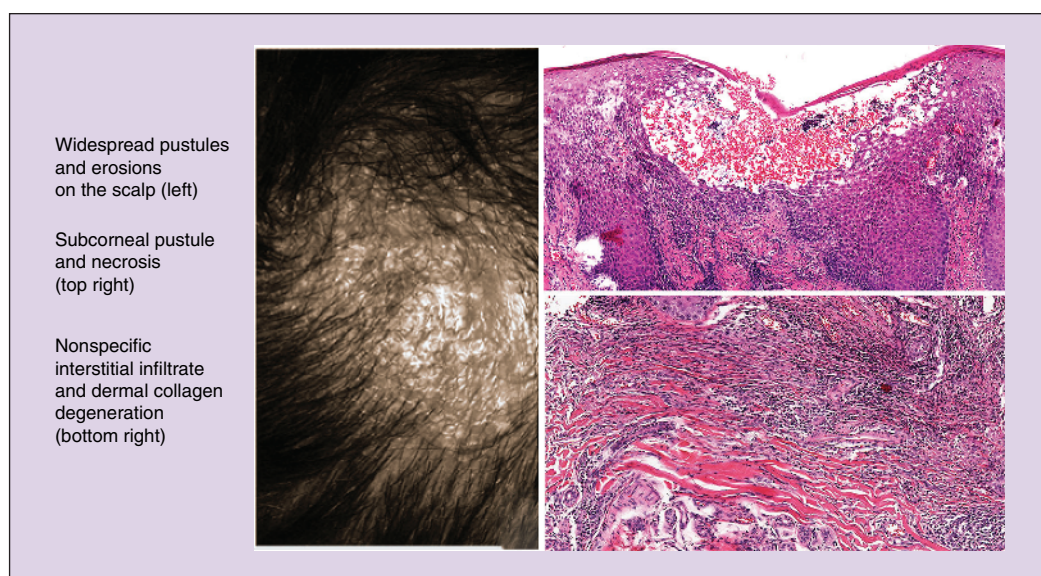


Figure 1.10.6 Erosive Pustular Dermatitis of the Scalp.

Rare disease of unknown etiology, primarily seen in elderly patients. A nosologic relationship with pyoderma gangrenosum has been suggested.

CF: Crusty erosions and pustules on the scalp.

HF: Erosive pustular dermatitis of the scalp may mimic a plethora of superficial

erosive dermatoses in sun-damaged skin. Histopathological changes are often misleading:

- Subcorneal pustules (early) – often in association with actinic keratosis
- Flat erosion evolving into shallow ulcer with slightly hyperplastic borders (late)
- Accompanying massive actinic elastosis and solar keratosis (telltale signs)
- Neutrophil-rich diffuse infiltrate without vasculitis and without demonstrable infectious organisms

DD: Subcorneal pustular dermatosis (Sneddon–Wilkinson); pyoderma gangrenosum; primary or secondary bacterial or fungal infection of the scalp; IgA pemphigus (advanced).

Reference

- Bieber, T., Ruzicka, T., & Burg, G. (1987). Erosive pustulöse Dermatitis des Kapillitiums. *Hautarzt*, **38**, 687–689.
- Starace, M., Loi, C., Bruni, F., Alessandrini, A., Misciali, C., Patrizi, A., & Piraccini, B. M. (2017). Erosive pustular dermatosis of the scalp: Clinical, trichoscopic, and histopathologic features of 20 cases. *J Am Acad Dermatol*. 2017 Jun;76(6):1109–1114.e2.
- Tomasini, C., & Michelerio, A. (2019). Erosive pustular dermatosis of the scalp: A neutrophilic folliculitis within the spectrum of neutrophilic dermatoses: A clinicopathologic study of 30 cases. *J Am Acad Dermatol*, **81**(2), 527–533.

