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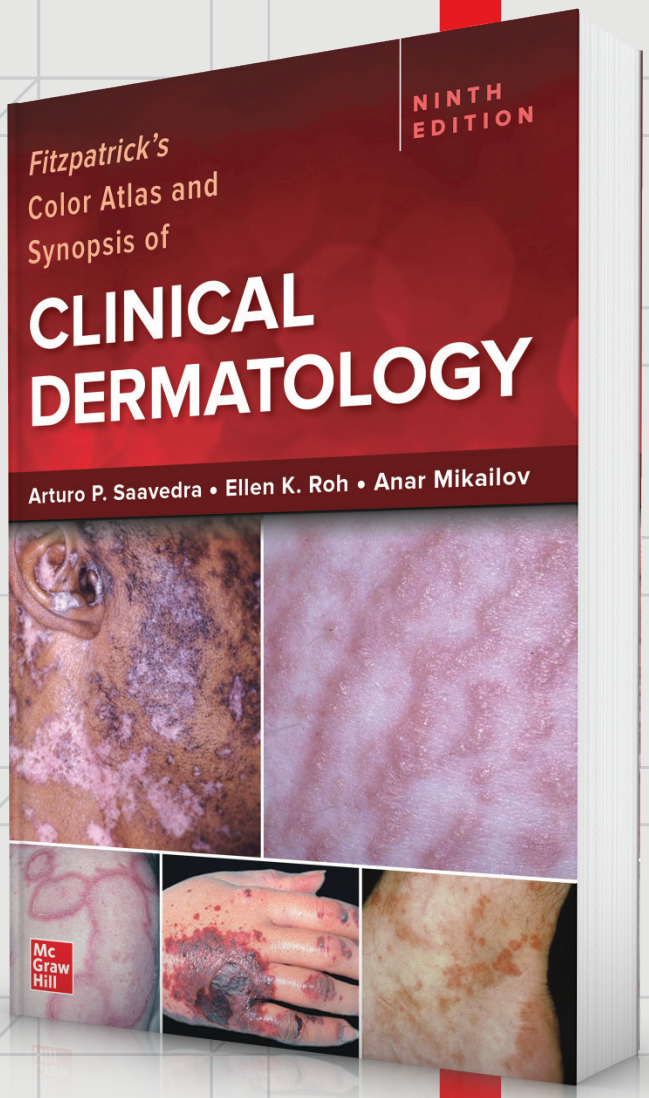
CLINICAL DERMATOLOGY

Sample Chapter

Chapter 7:
Neutrophil-Mediated Diseases



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SECTION 7

Neutrophil-Mediated Diseases

PYODERMA GANGRENOSUM (PG) ICD-10: L88

- PG is an idiopathic, either acute or chronic, severely debilitating skin disease.
- It is characterized by neutrophilic infiltration, destruction of tissue, and ulceration.
- It occurs most commonly in association with a systemic disease, especially arthritis, inflammatory bowel disease, hematologic dyscrasias, and malignancy, but may also occur alone.
- Characterized by the presence of painful, irregular, boggy, blue–red ulcers with undermined borders and purulent necrotic bases.
- It is a diagnosis of exclusion.
- The mainstays of treatment are immunosuppressive or immunomodulating agents.
- Relapses occur in most patients and there is significant morbidity.

EPIDEMIOLOGY

Rare, prevalence unknown. All age groups affected with a peak between 40 and 60 years. Slight preponderance of females.

ETIOLOGY AND PATHOGENESIS

Unknown. Although called pyoderma, it does not have a microbial etiology. Pyoderma gangrenosum (PG) is counted among the neutrophilic dermatoses because of the massive neutrophilic infiltrates within the skin. It may belong to the autoinflammatory disease spectrum.

CLINICAL MANIFESTATION

THREE TYPES ***Acute:*** Acute onset with painful hemorrhagic pustule or painful nodule either de novo or after trauma. *There is the phenomenon of pathergy,* where a needle prick, insect bite, biopsy, or other minimal trauma can trigger a lesion. **Chronic:** Slow progression with granulation and hyperkeratosis. Less painful. **Bullous:** True blisters often hemorrhagic and associated with hematologic disease.

SKIN LESIONS ***Acute:*** Superficial hemorrhagic pustule surrounded by erythematous halo; very painful (**Fig. 7-1**). Breakdown occurs with ulcer formation, whereby ulcer borders are dusky-red or purple, irregular and raised, undermined, and boggy with perforations that drain pus (**Fig. 7-2**). The base of the ulcer is purulent with hemorrhagic exudate, partially covered by necrotic eschar (**Fig. 7-3**), with or without granulation tissue. Pustules both at the advancing border and in the ulcer base; a halo of erythema spreads centrifugally at the advancing edge of the ulcer (**Fig. 7-3**). **Chronic:** Lesions may slowly progress, grazing over large areas of the body and exhibiting massive granulation within the ulcer from the outset (**Fig. 7-4**) with crusting and even hyperkeratosis on the margins (**Fig. 7-5**). Lesions are usually solitary but may be multiple and form clusters that coalesce. Most common sites: Lower extremities (**Figs. 7-2** and **7-5**) > buttocks > abdomen (**Fig. 7-3**) > face (**Fig. 7-4**). Healing of ulcers results in thin atrophic cribriform scars. **Bullous:** Blisters from the outset, often hemorrhagic, followed by ulceration.

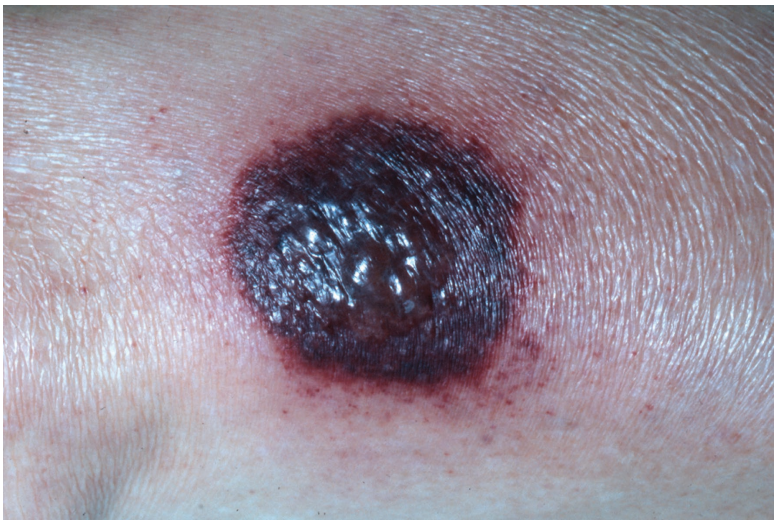

FIGURE 7-1 • Pyoderma gangrenosum The initial lesion is a rapidly enlarging hemorrhagic nonfollicular pustule surrounded by an erythematous halo and is very painful.

FIGURE 7-2 • Pyoderma gangrenosum Lesions rapidly break down in the center and become boggy, hemorrhagic, and purulent ulcers.

FIGURE 7-3 • Pyoderma gangrenosum A very large ulcer with raised bullous undermined borders covered with hemorrhagic and fibrinous exudate. There is erythema surrounding advancing borders of the lesion. When the bullae are opened, pus is drained. This lesion arose acutely and spread rapidly after laparotomy for an ovarian carcinoma.

FIGURE 7-4 • Pyoderma gangrenosum: chronic type The lesion involves the upper eyelid and represents an ulcer with elevated granulating base with multiple abscesses. The lesion later spread slowly to involve the temporal and zygomatic regions and eventually healed under systemic glucocorticoid treatment, leaving a thin cribriform scar that did not impair the function of the eyelid.

FIGURE 7-5 • Pyoderma gangrenosum: chronic type This lesion, which appears like a plaque, spread slowly but was also surrounded by an erythematous border. The lesion is crusted and hyperkeratotic and is less painful than the lesions in acute pyoderma gangrenosum.

MUCOUS MEMBRANES Rarely, aphthous stomatitis-like lesions; very rarely massive ulceration of oral mucosa and conjunctivae.

General Examination

Patient appears ill.

Associated Systemic Diseases

Up to 50% of cases occur without associated disease. The remainder of cases are associated with arthritis, large- and small-bowel disease (Crohn disease and ulcerative colitis), diverticulosis (diverticulitis), paraproteinemia and myeloma, leukemia, autoimmune hepatitis, Behçet syndrome (which is also a disease with pathergy).

LABORATORY EXAMINATIONS

There is no single diagnostic test.
ESR Variably elevated.
DERMATOPATHOLOGY Not diagnostic. Neutrophilic inflammation with abscess formation and necrosis.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Clinical findings plus history and course; confirmed by compatible dermatopathology. Differential diagnosis: Ecthyma and ecthyma gangrenosum, atypical mycobacterial infection, clostridial infection, deep mycoses, amebiasis, leishmaniasis, bromoderma, pemphigus vegetans, stasis ulcers, and granulomatous vasculitis.

COURSE AND PROGNOSIS

Untreated, course may last months to years, but spontaneous healing can occur. Ulceration may extend rapidly within a few days or slowly. Healing occurs centrally with peripheral extension. New ulcers may appear as older lesions resolve. Pathergy.

MANAGEMENT

WITH ASSOCIATED UNDERLYING DISEASE Treat underlying disease.
SYSTEMIC TREATMENT High doses of oral glucocorticoids or IV glucocorticoid pulse therapy (1 to 2 mg/kg) may be required. Cyclosporine can also be considered as a first-line treatment for severe disease. Second-line and adjunctive treatment options include TNF-alpha inhibitors, mycophenolate mofetil, methotrexate, azathioprine, and dapsone.
TOPICAL Local disease can be treated with topical and intralesional steroids.

BOWEL-ASSOCIATED DERMATOSIS-ARTHRITIS SYNDROME ICD-10: L98.2

- Associated with bowel surgery or inflammatory bowel disease.
- Serum sickness-like manifestations. Erythematous that evolve central papules/vesicles, subcutaneous nodules.
- Associated with polyarthritis and tenosynovitis.

SWEET SYNDROME (SS) ICD-10: L98.2

- An uncommon, acute, and recurrent, cytokine-induced skin reaction associated with various etiologies.
- Painful plaque-forming inflammatory papules, often with massive exudations giving the appearance of vesiculation (pseudovesiculation).
- Accompanied by fever, arthralgia, and peripheral leukocytosis.
- Associated with infection, malignancy, or drugs.
- Treatment: Systemic glucocorticoids, potassium iodide, dapsone, or colchicine.
- *Synonym*: Acute febrile neutrophilic dermatosis.

EPIDEMIOLOGY AND ETIOLOGY

AGE OF ONSET Most often 30 to 60 years.
SEX Women > men.
ETIOLOGY Unknown, possibly hypersensitivity reaction. It belongs to the group of neutrophilic dermatoses and possibly to the spectrum of autoinflammatory diseases.
ASSOCIATED DISORDERS Upper respiratory tract and gastrointestinal infections (usually occurs 1 to 3 weeks after infection), pregnancy, and inflammatory bowel disease. May precede, follow, or appear concurrently as malignancy (hematologic > solid tumors). Can also occur with drugs: granulocyte colony-stimulating factor (G-GSF), ipilimumab.

CLINICAL MANIFESTATION

Prodromes are febrile upper respiratory tract infections. Gastrointestinal symptoms (diarrhea), tonsillitis, influenza-like illness, 1 to 3 weeks before skin lesions. Lesions tender/painful. Fever (not always present), headache, arthralgia, and general malaise.
SKIN LESIONS Bright red, smooth, tender papules (2 to 4 mm in diameter) that coalesce to form irregular, sharply bordered, inflammatory plaques (**Fig. 7-6A**). Pseudovesiculation: Intense edema gives the appearance of vesiculation (**Figs. 7-6A** and **7-7A**). Lesions arise rapidly, and as they evolve, central clearing may lead to annular or arcuate patterns. Tiny, superficial pustules may occur. May present as a single lesion or multiple lesions, asymmetrically or symmetrically distributed. Most common on face (**Fig. 7-6A**), neck (**Fig. 7-6B**), and upper extremities but also on lower extremities, where lesions may be deep in the fat and thus mimic panniculitis. Truncal lesions are uncommon but widespread and generalized forms occur. If associated with leukemia, bullous lesions may occur (**Fig. 7-7B**) and lesions may mimic bullous PG.
MUCOUS MEMBRANES ± Conjunctivitis, episcleritis.

General Examination

Patient may appear ill. There may be involvement of cardiovascular, central nervous system, gastrointestinal, hepatic, musculoskeletal, ocular, pulmonary, renal, and splenic organs.

LABORATORY EXAMINATIONS

COMPLETE BLOOD COUNT Leukocytosis with neutrophilia (not always present).
ESR Elevated.
DERMATOPATHOLOGY Diagnostic. Epidermis usually normal, sometimes subcorneal pustulation. Massive edema of papillary body, dense leukocytic infiltrate with starburst pattern in mid-dermis, consisting of neutrophils with occasional eosinophils/lymphoid cells. Leukocytoclasia,

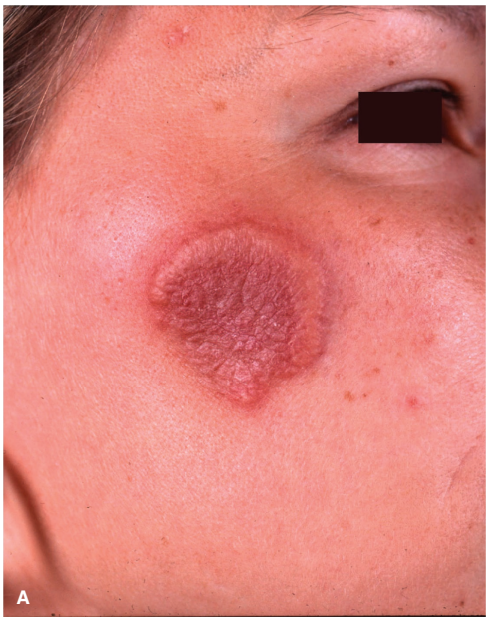

FIGURE 7-6 • Sweet syndrome (A) An erythematous, edematous plaque that has formed from coalescing papules on the right cheek. The border of the plaque looks as if composed of vesicles, but palpation reveals that it is solid (pseudovesiculation). This lesion occurred in a 26-year-old female following an upper respiratory infection, and the patient also had fever and leukocytosis. **(B)** A more exanthematic eruption in a 23-year-old female. There are multiple, coalescing, inflammatory, and very exudative papules with a wheal-like appearance on the neck. This patient also had leukocytosis and fever.

FIGURE 7-7 • Sweet syndrome **(A)** Coalescing exudative papules that look like vesicles. Upon palpation, lesions were solid. **(B)** Bullous type of Sweet syndrome. These are true bullae and pustules. The patient had myelomonocytic leukemia.

nuclear dust, but no vasculitis. ± Neutrophilic infiltrates in subcutaneous tissue.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Clinical impression and by histopathology.
DIFFERENTIAL DIAGNOSIS Erythema multiforme, erythema nodosum, prevesicular herpes simplex infection, preulcerative PG.

COURSE AND PROGNOSIS

Untreated, lesions enlarge over a period of days or weeks and eventually resolve without scarring. Recurrences occur in 30% to 69% of patients, often in previously involved sites and more often when associated with malignancy.

MANAGEMENT

Rule out sepsis.
PREDNISONE First-line treatment (0.5 to 1 mg/kg), ideally tapering over 4 to 6 weeks. Lesions typically improve within a few days.
ALTERNATIVE THERAPY Colchicine, dapsone, potassium iodide.

GRANULOMA FACIALE (GF) ICD-10: L92.2

- A rare, localized inflammatory disease of unknown etiology, clinically characterized by reddish-brown papules or small plaques primarily in the face.
- Single or multiple lesions with characteristic orange peel-like surface (**Fig. 7-8**).
- Histologically, chronic leukocytoclastic vasculitis with eosinophils, fibrin deposition, and fibrosis.
- Therapy: topical glucocorticoids; dapsone.

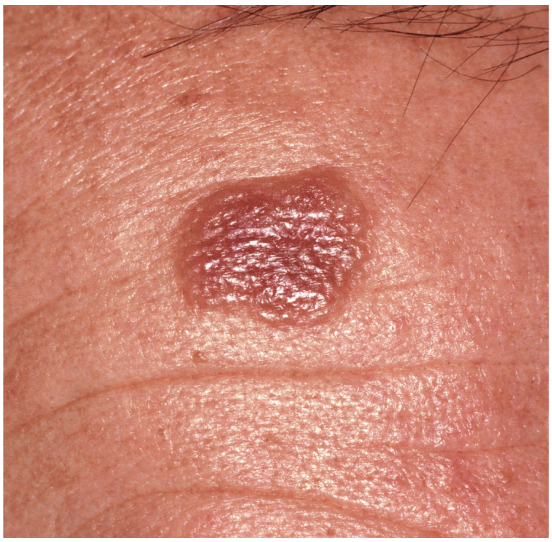

FIGURE 7-8 • Granuloma faciale: classic presentation A single, sharply defined, brown plaque with a characteristic orange peel-like surface.

ERYTHEMA NODOSUM (EN) SYNDROME ICD-10: L52

- EN is an important and common acute inflammatory/immunologic reaction pattern of the subcutaneous fat.
- Characterized by the appearance of painful nodules on bilateral shins.
- Lesions are bright red and flat but nodular upon palpation.
- Often fever and arthritis.
- Multiple and diverse etiologies.

The most common type of panniculitis, with a peak incidence at 20 to 30 years, but any age may be affected. Three to six times more common in females than in males.

ETIOLOGY Erythema nodosum (EN) is cutaneous reaction pattern to various etiologic agents. These include infections, drugs, and other inflammatory/granulomatous diseases, notably sarcoidosis (**Table 7-1**).

CLINICAL MANIFESTATION

Painful, tender lesions, usually of a few days' duration, accompanied by fever, malaise, and arthralgia (50%), most frequently of ankle joints. Other symptoms depending on etiology.

SKIN LESIONS Indurated, very tender nodules (2 to 5 cm), not sharply marginated (**Fig. 7-9**), deep seated in the subcutaneous fat, mostly on the anterior lower legs, bilateral but not symmetric. Nodules are bright to deep red and are appreciated as such only upon palpation. The term *erythema nodosum* best describes the skin lesions: *they look like erythema but feel like nodules* (**Fig. 7-9**). Lesions are oval, round, and arciform; as they age, they become violaceous, brownish, yellowish, or green, like resolving hematomas. Lesions may also occur

TABLE 7-1 Reported Etiologies of Erythema Nodosum

Bacterial Infections
- Streptococcal infections
- Tuberculosis
- *Yersinia* infections
- *Salmonella* infections
- *Campylobacter* infections
- Brucellosis
- Tularemia
- Atypical mycobacterial infections
- Chancroid
- Meningococcemia
- *Corynebacterium diphtheriae* infections
- Cat-scratch disease
- *Propionibacterium acnes*
- *Shigella* infections
- Gonorrhea
- Syphilis
- Leptospirosis
- Q fever
- Lymphogranuloma venereum
- *Chlamydophila psittaci* infections
- *Mycoplasma pneumoniae* infections
- *Helicobacter pylori* infection

Viral Infections
- Infectious mononucleosis
- Hepatitis B
- Milker nodules
- Orf (contagious ecthyma)
- Herpes simplex
- Measles
- Cytomegalovirus infections

Fungal Infections
- Dermatophytes
- Blastomycosis
- Histoplasmosis
- Coccidioidomycosis
- Sporotrichosis
- Aspergillosis

Protozoal Infections
- Toxoplasmosis
- Ancylostomiasis
- Amebiasis
- Giardiasis
- Ascariasis

Drugs
- **Sulfonamides**
- **Bromides**
- **Iodides**
- **Oral contraceptives, progesterone**
- Minocycline
- Gold salts
- **Penicillin**
- Salicylates
- Chlorothiazides
- Phenytoin
- Aminopyrine
- Arsphenamine
- Hepatitis B vaccine
- Nitrofurantoin
- Pyritinol
- D-Penicillamine
- Thalidomide
- Isotretinoin
- Interleukin-2
- Omeprazole
- Valproate
- Tdap (tetanus, diphtheria, and pertussis) vaccine
- Leukotriene-modifying agents
- Vemurafenib

Miscellaneous Conditions
- **Sarcoidosis**
- Ulcerative colitis
- Colon diverticulosis
- **Crohn disease**
- Behçet disease
- Reactive arthritis
- Sweet syndrome
- Pregnancy
- Takayasu arteritis
- Immunoglobulin A nephropathy
- Chronic active hepatitis
- Granulomatous mastitis
- Vogt–Koyanagi disease
- Sjögren syndrome
- Temporal arteritis
- Systemic lupus erythematosus
- Dental infection

Malignant Diseases
- Hodgkin disease
- Non-Hodgkin lymphoma, including mucosa-associated lymphoid tissue (MALT) lymphoma
- Leukemia
- Sarcoma
- Renal carcinoma
- Postradiotherapy for pelvic carcinoma

Source: Reproduced with permission from Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, Orringer JS, eds. *Fitzpatrick's Dermatology*. 9th ed. New York, NY: McGraw Hill; 2019, Table 73-3.

FIGURE 7-9 • Erythema nodosum Indurated, very tender, inflammatory nodules mostly in the pretibial region. Lesions are seen as red, ill-defined erythemas but palpated as deep-seated nodules, hence the designation. In this 49-year-old female, there was also fever and arthritis of the ankle joints following an upper respiratory tract infection. The throat cultures yielded β-hemolytic streptococci.

on the knees and arms but only rarely on the face and neck.

LABORATORY EXAMINATIONS

HEMATOLOGY Elevated ESR and C-reactive protein; leukocytosis.

BACTERIAL CULTURE Culture throat for group A β-hemolytic streptococcus.

IMAGING Radiologic examination of the chest is important to rule out sarcoidosis or other pulmonary disease.

DERMATOPATHOLOGY Acute (polymorphonuclear) and chronic (granulomatous) inflammation in the subcutis, around blood vessels in the septum and adjacent fat. EN is a septal panniculitis.

COURSE

Most cases spontaneously resolve in 6 weeks, though up to one-third may recur. Lesions do not ulcerate, and heal without scarring.

DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Diagnosis rests on clinical criteria and histopathology, if needed. Differential diagnosis includes all other forms of panniculitis, nodular vasculitis, pretibial myxedema, urticaria, and lymphoma.

MANAGEMENT

SYMPTOMATIC Bed rest, leg elevation, compressive bandages (lower legs).

ANTI-INFLAMMATORY TREATMENT Nonsteroidal anti-inflammatory drugs are the first line treatment. Colchicine, dapsone, and potassium iodide can also be used. Systemic glucocorticoids can provide rapid improvement in patients with severe disease.

OTHER PANNICULITIDES ICD-10: M79.3

- Panniculitis is the term used to describe diseases where the major focus of inflammation is in the subcutaneous tissue. In general, panniculitis presents as an erythematous or violaceous nodule in the subcutaneous fat that may be tender or not, may ulcerate or heal without scarring, and may be soft or hard on palpation. Thus, the term *panniculitis* describes a wide spectrum of disease manifestations.
- An accurate diagnosis requires an ample deep skin biopsy that should reach down to, or even beyond, the fascia. The panniculitides are classified histologically as lobular or septal but a clear separation is often not possible. A simplified classification of panniculitis is given in **Table 7-2.**
- Only two forms of panniculitis are briefly discussed here.[1] Other diseases in which panniculitis occurs are referred to in **Table 7-2.**
- *Pancreatic panniculitis* manifests as painful erythematous nodules and plaques that may fluctuate and occur at any site, with a predilection for abdomen, buttocks, and legs (**Fig. 7-10**). Frequently accompanied by arthritis and polyserositis. Associated with pancreatitis or pancreatic carcinoma. In middle-aged to elderly individuals, males > females. History: alcoholism, abdominal pain, weight loss, or recent-onset diabetes mellitus. Skin biopsy reveals lobular panniculitis; liquefied fat may drain from the biopsy site. General examination may reveal pleural effusion, ascites, and arthritis, particularly of the ankles. *Laboratory:* Eosinophilia, hyperlipasemia, hyperamylasemia, and increased excretion of amylase and/or lipase in the urine. The pathophysiology is probably a breakdown of subcutaneous fat caused by pancreatic enzymes released into the circulation. Course and prognosis depend on the type of pancreatic disease. Treatment is directed at the underlying pancreatic disorder.
- α_1-*Antitrypsin-deficiency panniculitis* is also characterized by recurrent tender, erythematous, subcutaneous nodules ranging from 1 to 5 cm and located predominantly on the trunk and the proximal extremities. Nodules break down and discharge a clear serous or oily fluid. Diagnosis is substantiated by a decrease of serum α_1-antitrypsin, and treatment consists of oral dapsone in doses up to 200 mg/d. The intravenous infusion of human α_1-proteinase inhibitor concentrate has been shown to be very effective.

[1]The reader is also referred to Aronson IK et al., in Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, Orringer JS (eds.): *Fitzpatrick's Dermatology in General Medicine* 9th edition. New York, NY: McGraw-Hill: 2019.

TABLE 7-2 Summary of Different Types of Panniculitis

Panniculitis	Age Groups	Associated Factors	Clinical Course and Manifestations	Histopathology	Treatment
Erythema nodosum	Young women, 2nd to 4th decades	Infections (commonly streptococcal), medications, malignancies (leukemias, lymphomas)	Acute onset; symmetric, tender, nodules and plaques Affecting anterior lower extremities Fever, fatigue, arthralgias, arthritis, headache, no ulceration, no atrophy, no scarring	Septal Panniculitis No vasculitis Neutrophils (early), Meischer granulomas (late)	Bed rest, aspirin, NSAIDs SSKI, 2–10 drops thrice daily Colchicine Corticosteroids (rarely indicated)
Erythema induratum	Young/middle-aged women	Venous insufficiency, obesity Infectious etiology: MTB, hepatitides B, C	Erythematous SQ nodules on lower extremities May affect calves, anterolateral leg Tenderness, ulceration, scarring Protracted course, with recurrent episodes 3–6 weeks duration	Lobular, often with vasculitis (90%). Early central necrosis of adipocytes; neutrophilic infiltrate In older lesions, epithelioid histiocytes, multinucleated giant cells	If MTB testing is positive, full course of multidrug therapy Treat underlying cause SSKI, NSAIDs, colchicine, antimalarials, corticosteroids, gold Bed rest Pentoxifylline, compression
Lipodermatosclerosis (sclerosing panniculitis, hypodermitis sclerodermiformis, chronic panniculitis with lipomembranous changes, sclerotic atrophic cellulitis, venous stasis panniculitis)	Overweight women older than 40 years	Venous insufficiency Obesity Systemic sclerosis Pulmonary Infarction Hypertension	Indurated, woody plaques on lower extremities, with acute and chronic changes (most commonly, anteromedial calf area) Intense pain is the most frequent symptom Stage: acute inflammatory Chronic fibrosis Inverted champagne bottle	Stasis changes Lobular panniculitis No vasculitis Ischemic necrosis at center Thickened, fibrotic septa, atrophy of subcutaneous fat Membranocystic changes	Compression therapy is the major recommended treatment (30–40 mm Hg) Stanozolol: to decrease pain, erythema, induration Pentoxifylline, horse chestnut seed extract, oxerutins, flavonoid fraction Weight loss

Infectious panniculitis	—	Wide variety of bacteria, fungi, parasites, viruses Either primarily inoculated, or hematogenous *Staphylococcus aureus* panniculitis with juvenile diabetes Panniculitis of mycetoma, chromoblastomycosis, sporotrichosis	Erythematous plaques, nodules, abscess with purulent discharge (fluctuant/abscess-type lesions) Most commonly on legs and feet Upper extremities, trunk, face may be involved	Mostly lobular panniculitis, but with a mixed pattern Pattern dependent on whether infection was inoculation related or hematogenous Neutrophilic infiltrate	Depends on the known organisms
α_1-Antitrypsin panniculitis	Most common in 30–60 years of age groups MM: most common phenotype (normal AAT) ZZ: 10%–15% of N levels; associated with >60% of cases	Pulmonary and hepatic disease (emphysema in COPD, cirrhosis, hepatocellular CA), highest risk ZZ phenotype Panniculitis uncommon in AAT deficiency	Painful erythematous nodules and plaques Cellulitis, fluctuant abscess type Most common site: lower trunk, also buttocks, proximal extremities May be life-threatening	Early necrosis of SQ fat Splaying of neutrophils between collagen bundles is characteristic Liquefactive necrosis	MILD–MODERATE: dapsone, doxycycline SEVERE: protein replacement therapy
Pancreatic panniculitis	Occurs in 2%–3% of patients with pancreatic disorders	Pancreatitis, pancreatic CA	Erythematous nodules with spontaneous ulceration Lower extremities, especially periarticular areas (knee, ankle) Crops of lesions; red–brown Atrophic, hyperpigmented scarring Oily abscesses	Lobular panniculitis No vasculitis Intense necrosis at center of lobule Ghost adipocytes Saponification and calcification	Octreotide Plasmapheresis

(Continued)

TABLE 7-2 Summary of Different Types of Panniculitis *(Continued)*

Panniculitis	Age Groups	Associated Factors	Clinical Course and Manifestations	Histopathology	Treatment
Lupus panniculitis	Females more frequently affected than males (4:1) 30–60 years old, also in childhood May occur before or after diagnosis of lupus erythematosus or discoid lupus erythematosus	Systemic lupus erythematosus Sjögren syndrome Rheumatoid arthritis	UPPER ARMS (lateral), shoulders, face, scalp, hips, buttocks, breasts Rare on lower extremities Deep, tender SQ nodules; no surface changes Resolves with depressed lipoatrophic areas Chronic, with yearly/periodic flares Duration: average of 6 years	Vacuolar alteration of basal cell layer, thickened basement membrane, mucin deposition, superficial and deep perivascular infiltrate Mostly lobular panniculitis, with lymphoid follicles, variable hyaline fat necrosis, sclerotic collagen bundles, lymphocytic and plasma cell infiltrate	Hydroxychloroquine is first-line treatment Quinacrine
Panniculitis with dermatomyositis	Very rare	Dermatomyositis	Erythematous nodules and plaques, affecting arms, buttocks, thighs, abdomen	Mixed septal and lobular panniculitis, lymphocytic and plasma cell infiltrate, hyaline sclerosis of septal collagen; calcification, membranocystic changes in late stages	Corticosteroids alone, or corticosteroids with methotrexate
Cytophagic histiocytic panniculitis	Rare; seen in adults, adolescents, and children	HLH MAS	SQ erythematous to violaceous plaques on extremities, trunk Fulminant cases may have: ulceration, fever, hepatosplenomegaly, hemocytophagocytosis in BM, LN, liver, CNS May be acute and intermittent, or have a rapidly fatal course	Lobular panniculitis No vasculitis Bean bag cells: macrophages with intact or fragmented erythrocytes, leukocytes, or platelets Necrosis	Corticosteroids Cyclosporine Multidisciplinary care in a hospital setting

Subcutaneous fat necrosis of the newborn	Rare, first few weeks of life	History of perinatal complications (meconium aspiration, hypothermia, hypoxemia, gestational diabetes)	Erythematous to violaceous, firm nodules or plaques affecting buttocks, back, shoulders, cheeks, thighs Anterior trunk spared Oily/chalky white material Late hypercalcemia (monitor for 6 months)	Lobular panniculitis No vasculitis Needle-shaped clefts in radial array Nodules and plaques, resolving spontaneously	Spontaneous resolution Monitor serum calcium for hypercalcemia Systemic glucocorticoids may be considered; nephrocalcinosis
Cold panniculitis (Haxthausen disease)	Scrotal cold panniculitis in 9–14-year-old males	Exposure to cold weather, popsicles, ice packs, swimming	Indurate, erythematous plaques or nodules at sites of cold exposure; affects face, thighs, scrotal fat of prepubertal boys Resolution within 3 months	Lobular panniculitis No vasculitis Perivascular lymphohistiocytic infiltrate	Spontaneous resolution
Factitial panniculitis	—	Associated with personality aberrations	SQ implantation (medications, cosmetic fillers, oils, human waste)	Lobular panniculitis No vasculitis Suppurative granuloma involving fat lobule Refractile foreign material	Psychiatric treatment; Intralesional steroids, surgical excision

AAT, α_1-antitrypsin; BM, bone marrow; CA, cancer; COPD, chronic obstructive pulmonary disease; HLH, hemophagocytic lymphohistiocytosis; LN, lymph node; MAS, macrophage activation syndrome; MTB, *Mycobacterium tuberculosis*; NSAID, nonsteroidal anti-inflammatory drug; SQ, subcutaneous; SSKI, saturated solution of potassium iodide.

Source: Reproduced with permission from Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, Orringer JS, eds. *Fitzpatrick's Dermatology*. 9th ed. McGraw Hill; 2019, Table 73-1.

FIGURE 7-10 • Pancreatic panniculitis There is a painful, erythematous nodule that fluctuates on the ventral malleolar region but similar lesions were also found on the trunk and on the buttocks.

PERNIOSIS (CHILBLAINS) ICD-10: T69.1

- Localized inflammatory lesions in sites of cold exposure (**Fig. 7-11**).
- More common in young to middle-aged women.
- Single or multiple burning erythematous or purplish swellings on proximal fingers, toes, heels, nose, and ears; also on calves and thighs (e.g., often seen in bicycle or horseback riders).
- Resolves in 2 to 3 weeks.
- Management and prophylaxis: warm, loosely fitting clothes.

FIGURE 7-11 • Perniosis (Chilblains) Erythematous to slightly violaceous swellings on the distal digits and palm There is burning and pain.