Panniculitis

National Skin School 22/4/2020

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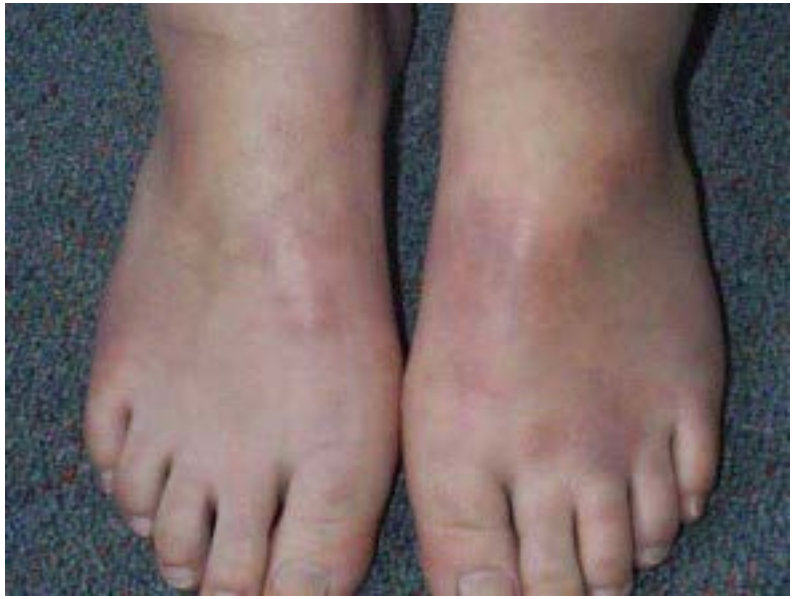
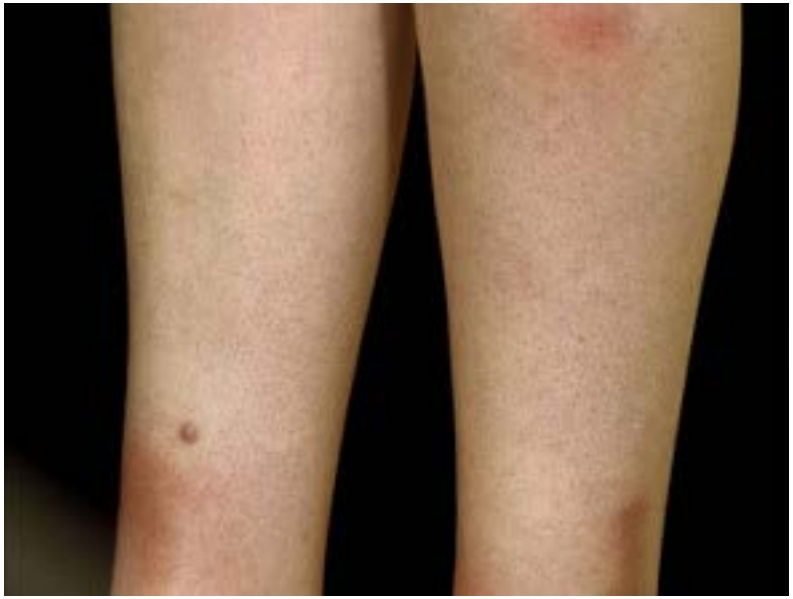
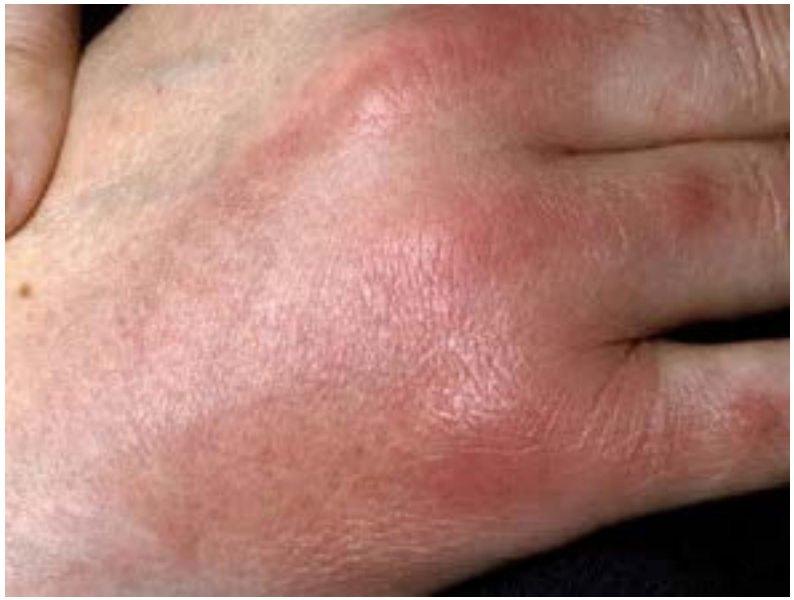
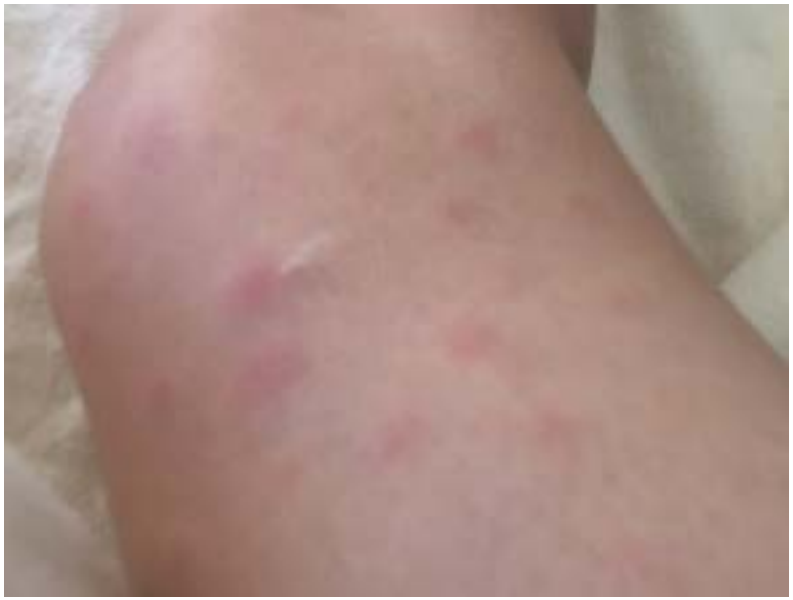
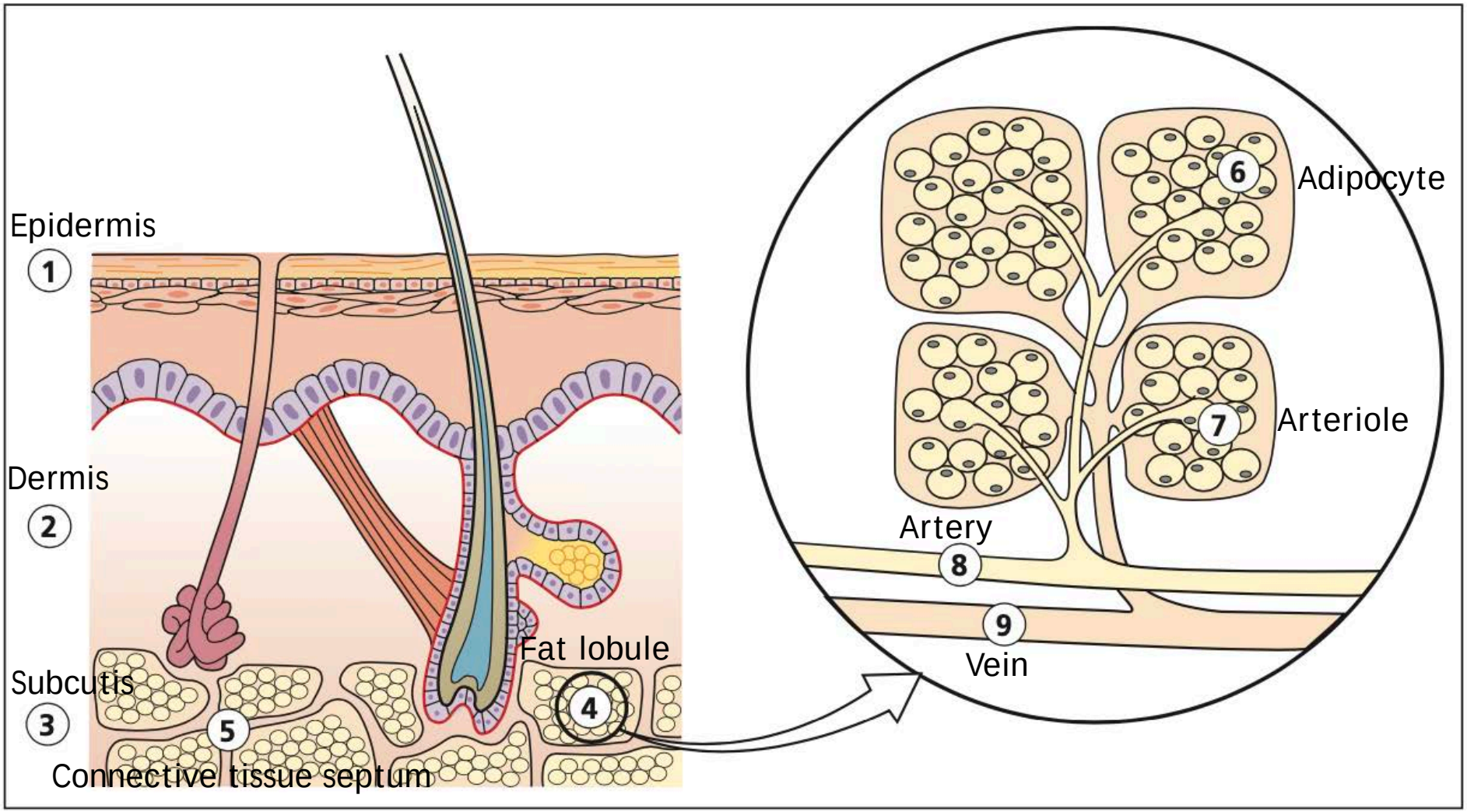






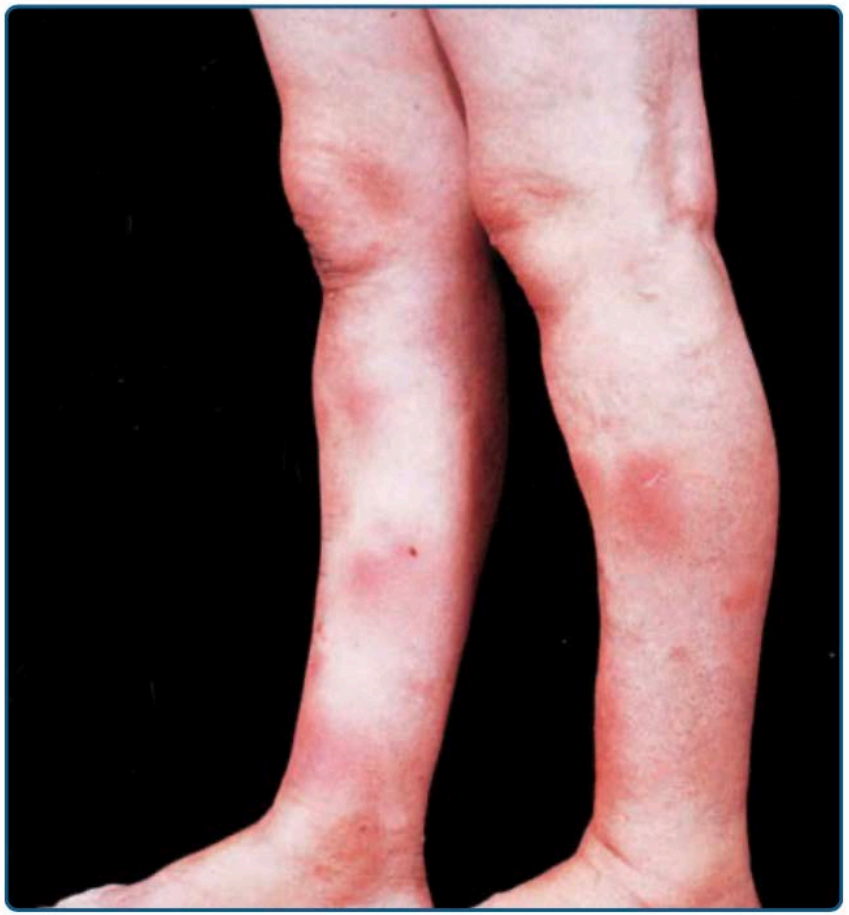


https://dermnetnz.org/topics/panniculitis/



Rook, Ninth Edition

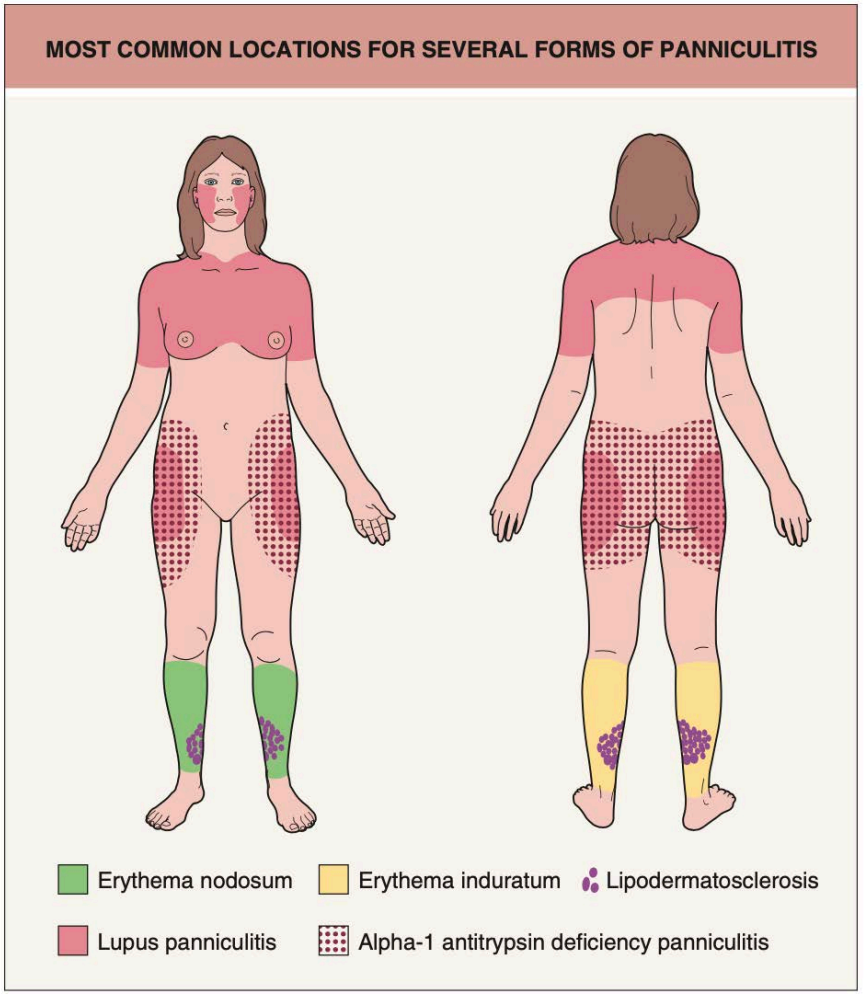
- 40 year old woman, presents with 1/52 history of tender nodules on the lower legs, associated with mild fever and fatigue
- History of “sore throat” 2-3 weeks ago
- Other questions? Investigations?
- DDx?



Fitzpatrick

Panniculitis: An approach

- History
- Examination: Distribution, morphology
- Investigations: Histology, other
- Management



Bolognia

Panniculitis

Lobular

Vasculitis

Erythema induratum
of:
- Bazin
- Whitfield (Nodular vasculitis)

Erythema nodosum leprosum

No vasculitis

Pancreatic

Alpha-1 antitrypsin

Newborn,
subcutaneous fat necrosis

Neonatal sclerema

Infiltrates (lymphoma, infectious, gout, factitious)

CTD (lupus, DM, eosinophilic fasciitis),
Cytophagic histiocytic panniculitis,
Cold, Crystals (gout, cholesterol, calcium)

Unknown (Weber Christian)

Lipodermatosclerosis, lipoatrophy, lipodystrophy, lymphoma

Insect bite reaction and other eosinophilic (Well's, parasite, hypereosinophilic)

Trauma

Injected or induced (factitial)

Sweets, post-steroid, sarcoid

Septal

Vasculitis

Polyarteritis nodosa

Leukocytoclastic vasculitis

Superficial thrombophlebitis

No vasculitis

Granuloma annulare (deep)

Rheumatoid nodules

Erythema nodosum

NLD

Sclereoderma / morphoea

Panniculitis: Mnemonics

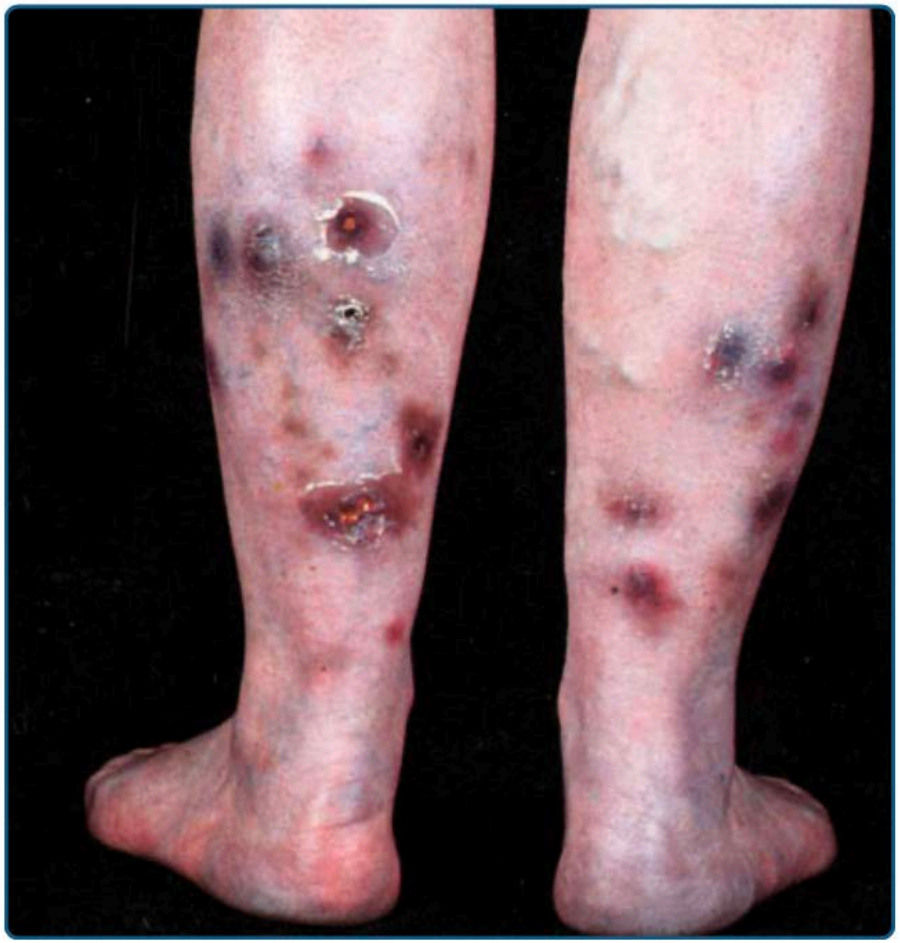
- Lobular with vasculitis: EE
- Lobular without vasculitis: PANNICULITIS
- Septal with vasculitis: PLS
- Septal without vasculitis: GRENS

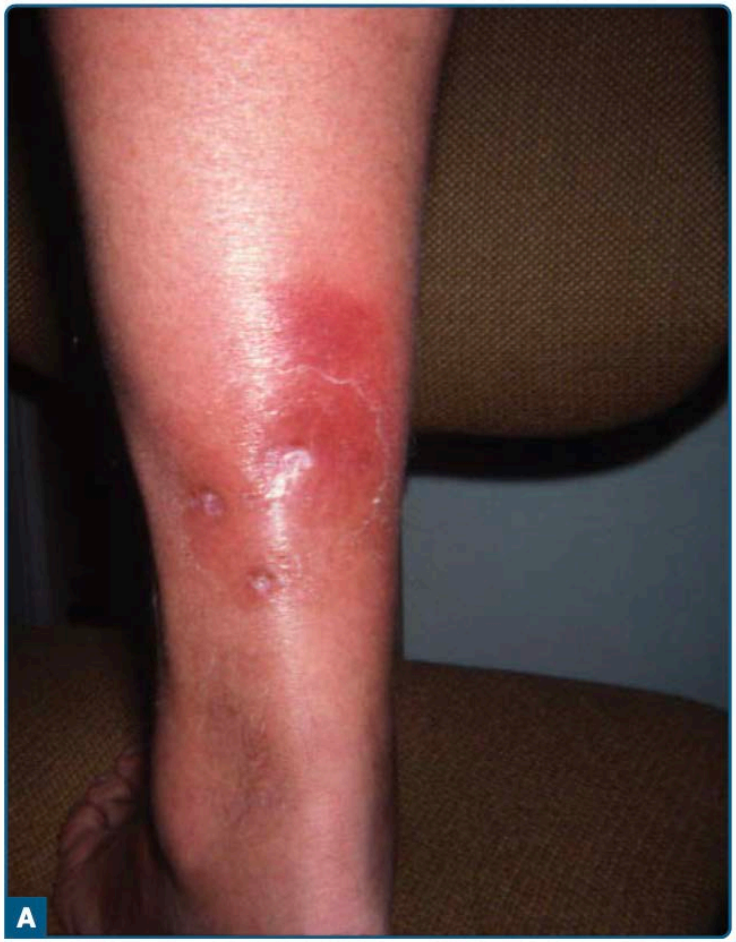
- Ulcerating panniculitis: NICE PLANT

Neutrophilic (assoc/w RA, subcutaneous Sweet syndrome)
Infective (Erythema Induratum)
Calciphylaxis, Cytophagic histiocytic panniculitis
Enzymatic (pancreatic, alpha-1-antitrypsin)

Polyarteritis nodosa
Lymphoma
Alpha-1-antitrypsin
NLD
Trauma, factitial

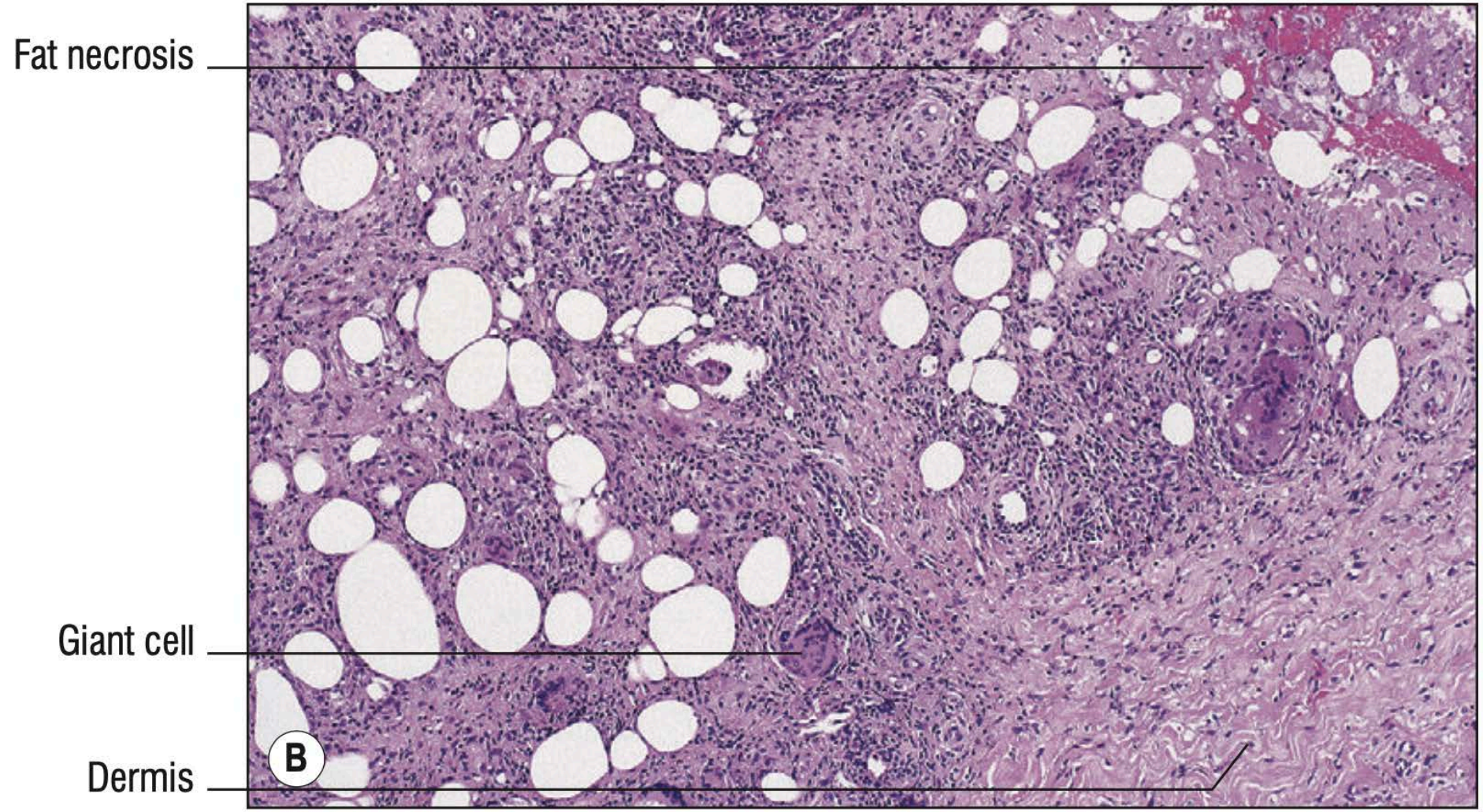
- 40 year old woman, presents with 12/12 history of tender nodules on the posterior lower legs, fluctuating course, occasional ulceration and scarring
- Other questions? Investigations?
- DDx?





Fitzpatrick

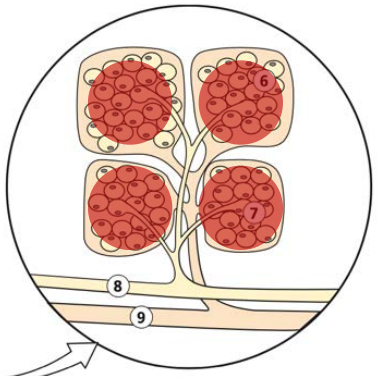
Histology from incisional biopsy:



Lobular with vasculitis

Erythema induratum of:
- Bazin
- Whitfield

Erythema nodosum leprosum



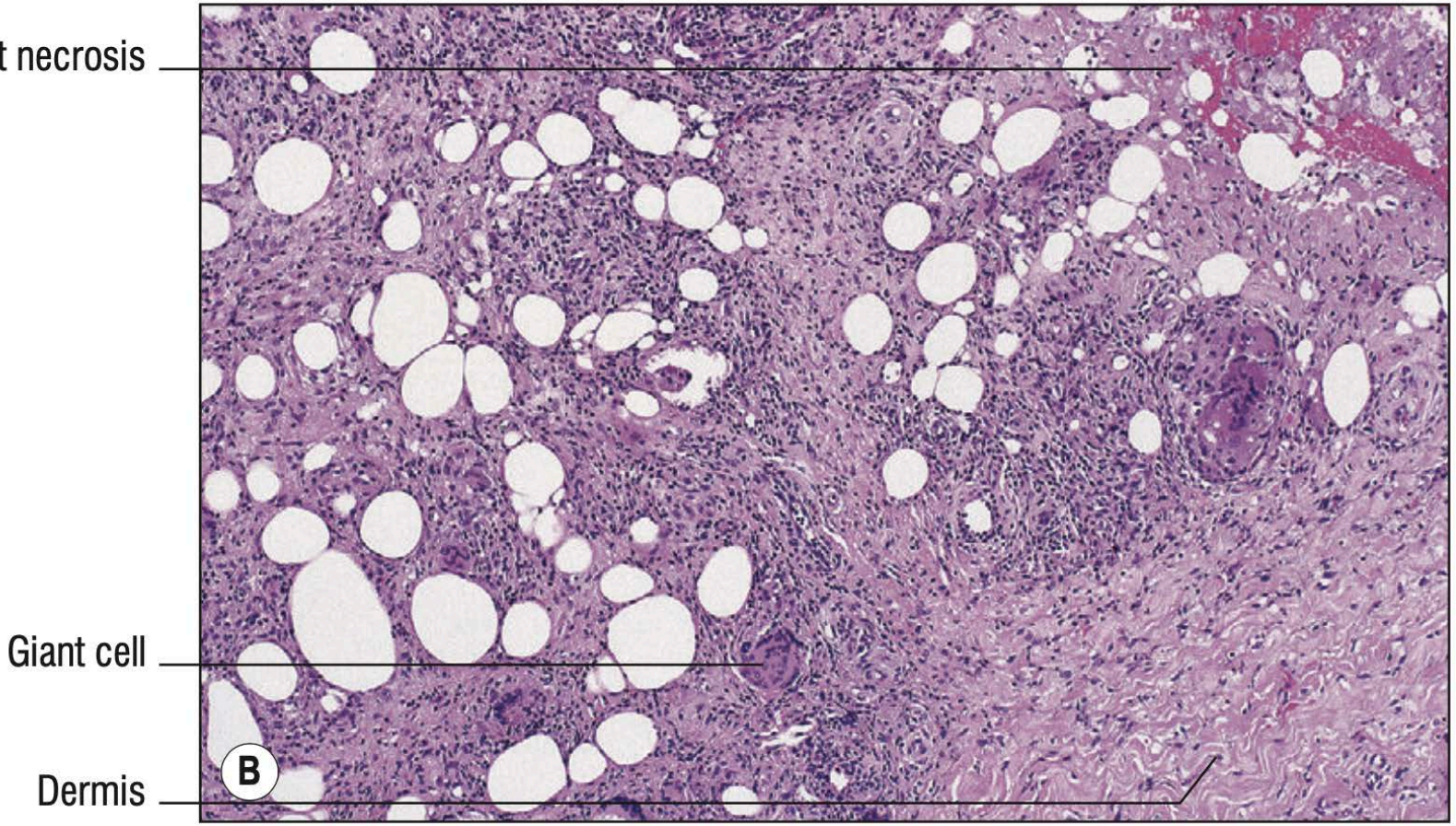
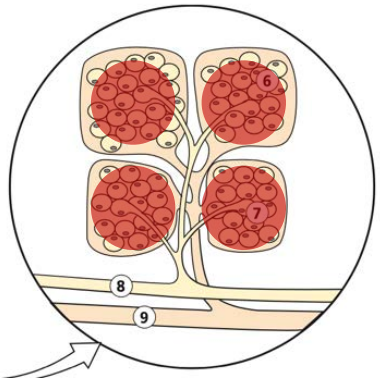


Fig. 16.6 B Erythema induratum (medium mag.).

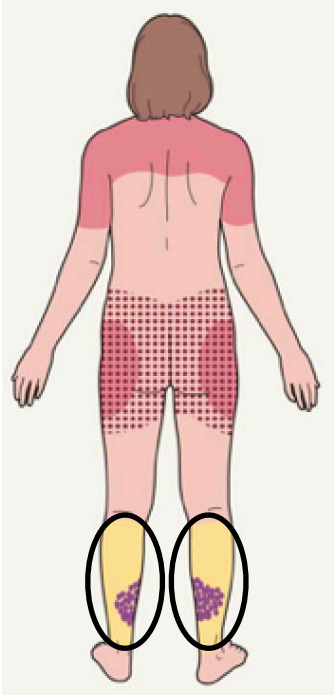
Erythema induratum of Bazin

Associated with TB, lobular with vasculitis



Pathogenesis:
Immune complex vasculitis vs. type IV cell-mediated response to an antigenic stimulus

Epidemiology / presentation
- Young to middle aged (mean 30-40 years), more common in women
- Prevalent in India, Hong Kong and some parts of South Africa
- Presents as tender, erythematous to violaceous painful nodules on the posterior calves. May also present on the feet, thighs, buttocks and arms. May be annular (especially TB-associated)
- Ulceration and drainage may occur, tend to heal with scarring
- Minimal clinical differences between TB and non-TB associated cases



Associations:
- Tuberculosis: past or present history of TB at extracutaneous site in 50% (pulmonary > cervical lymphadenitis > others)

Investigations:
Biopsy
- Lobular or mixed septal/lobular panniculitis with neutrophils, lymphocytes, macrophages, giant cells
- Vasculitis involving arteries or veins of connective tissue septa and small venules of fat lobules – can be neutrophilic, lymphocytic or granulomatous; not always present and not required for diagnosis
- Necrosis in 50% (can be caseation-like, especially TB-associated)
- PCR for M Tuberculosis: rapid and sensitive

FBE, ESR may be elevated , TB PCR on tissue , QF-gold, CXR for evidence of active or previous infection , Hepatitis C, Consider HIV

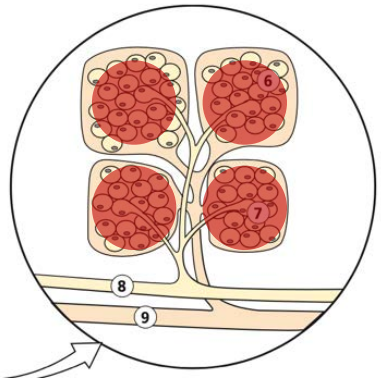
Management:
- General measures: bed rest, analgesia (including NSAIDs), dressings, support stockings, avoid smoking
- Bazin type
  - Antituberculous therapy (isoniazid 300mg/d, ethambutol 15mg/kg/day, rifampicin 600mg/d, pyrazinamide 25-40mg/kg/day for 2 months, then isoniazid 300mg/d and rifampicin 600mg/d for further 4 months)
  - After treatment for tuberculosis, treatment is the same as for erythema nodosum (naproxen, potassium iodide)
- Systemic prednisolone, Potassium iodide, Tetracyclines, gold, MMF

CAN ULCERATE

Bolognia, Fitzpatrick, Rook

Erythema induratum of Whitfield

a.k.a. nodular vasculitis, NOT assoc. with TB, lobular with vasculitis



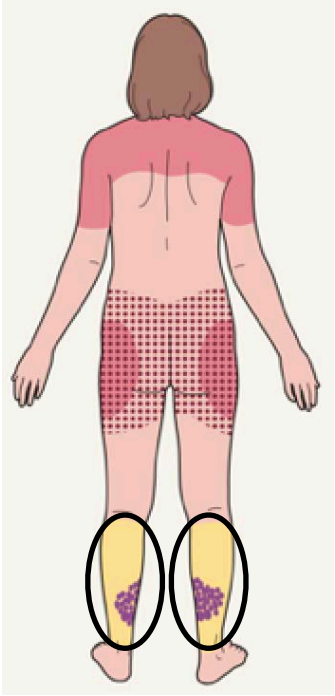
Pathogenesis:
Immune complex vasculitis vs. type IV cell-mediated response to an antigenic stimulus

Epidemiology / presentation:
- Not TB-associated, different trigger
- Clinically otherwise essentially similar to Erythema induratum of Bazin

Associations:
- Other infections eg. nocardia, hepatitis C, other fungal, viral and protozoal
- Drugs eg. propylthiouracil
- Idiopathic

Investigations:
- As for Erythema induratum of Bazin

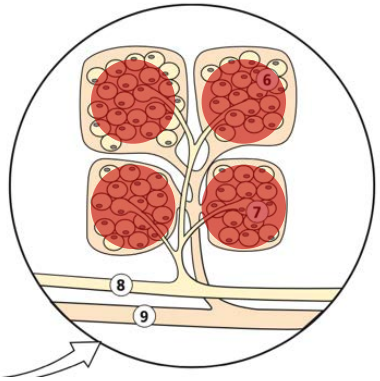
Management:
- General measures: bed rest, analgesia (including NSAIDs), dressings, support stockings, avoid smoking
- Treat infectious cause
- Hepatitis C associated: interferon and ribavirin
- Systemic prednisolone, Potassium iodide, Tetracyclines, gold, MMF



CAN ULCERATE

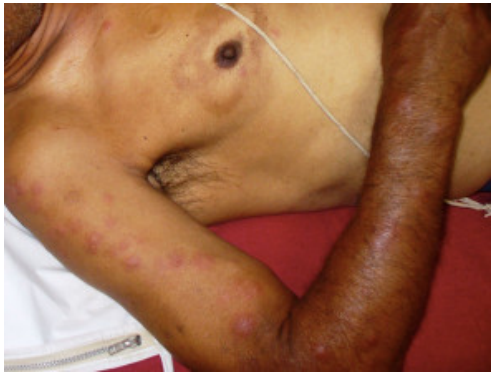
Bolognia, Fitzpatrick, Rook

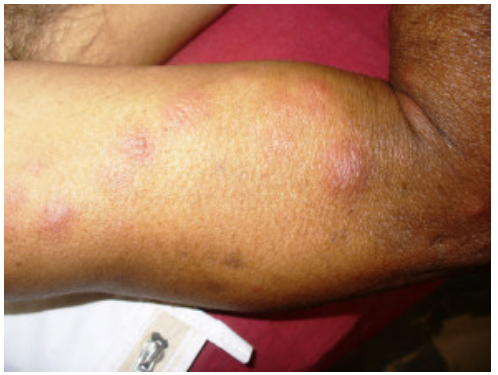
Erythema nodosum leprosum



Pathogenesis:
Type II lepra reaction characterised by necrotising vasculitis involving small to medium sized vessels of the deep dermis and subcutis (immune complex vasculitis)

Epidemiology / presentation:
- Occurs in patients with lepromatous or borderline lepromatous leprosy, usually during treatment
- Also associated with puberty, pregnancy and lactation
- Presents as multiple small painful nodules, sterile pustules and ulcers, superficial, deep dermal or subcutaneous
- Lesions usually on extensor aspects of limbs and on the face, but can be anywhere
- May have associated iridocyclitis, orchitis, renal impairment, cholestasis, lymphadenopathy, arthralgia, fever, fatigue





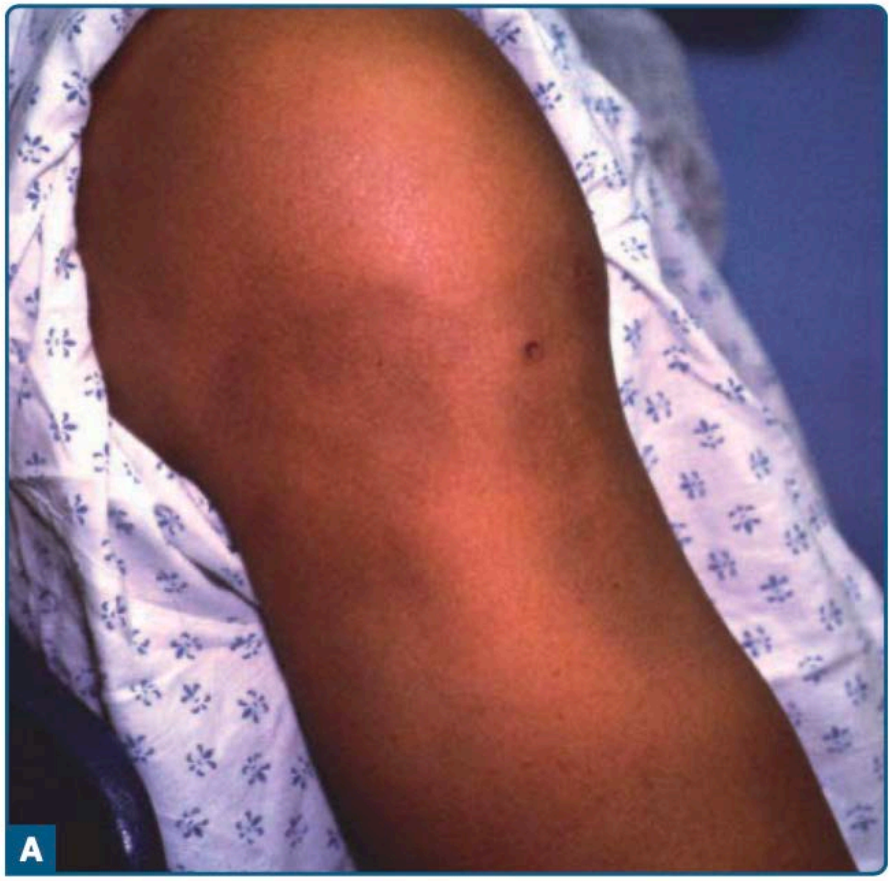
Investigations:
- Histology shows lobular panniculitis with heavy neutrophilic infiltrate, superimposed on chronic inflammation (lymphohistiocytic infiltrate). Associated vasculitis of small to medium sized vessels. Extensive AFBs (*M. leprae*) within lobule, shown with Wade-Fite or ZN stains.
- Biopsy should be taken from new tender nodule (ideally <24 hours old)
- May also have elevated WCC and protein C, elevated creatinine, and deranged LFTs

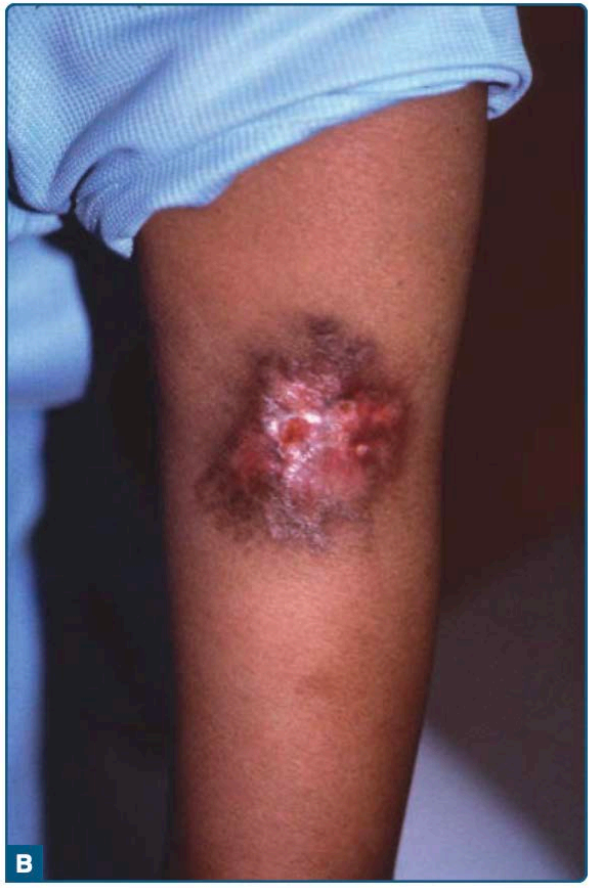
Management:
- Depends on severity of reaction
- Mild reactions: analgesia, anti-pyretics, monitoring
- Severe reactions: prednisolone 1mg/kg, rapid tapering, clofazimine, thalidomide
- Cyclosporin, azathioprinem, methotrexate, mycophenolate mofetil, pentoxifylline have also been described

CAN ULCERATE

Rook, https://dermnetnz.org/topics/lepra-reactions/

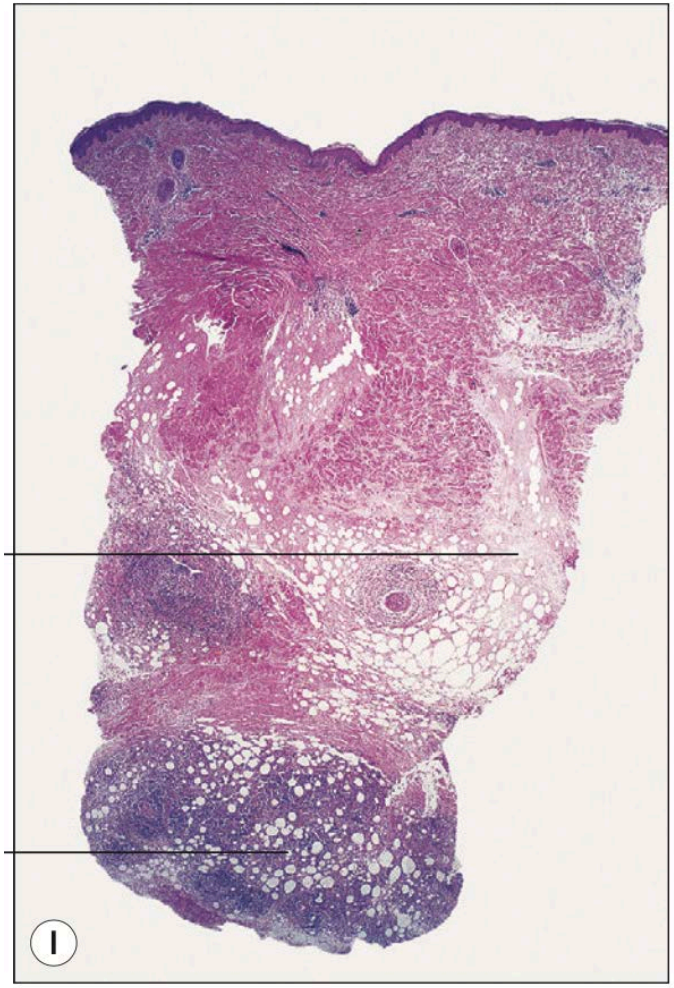
- 40 year old woman, presents with 12/12 history of tender lesions on upper arms, fluctuating course
- Other questions? Investigations?
- DDx?

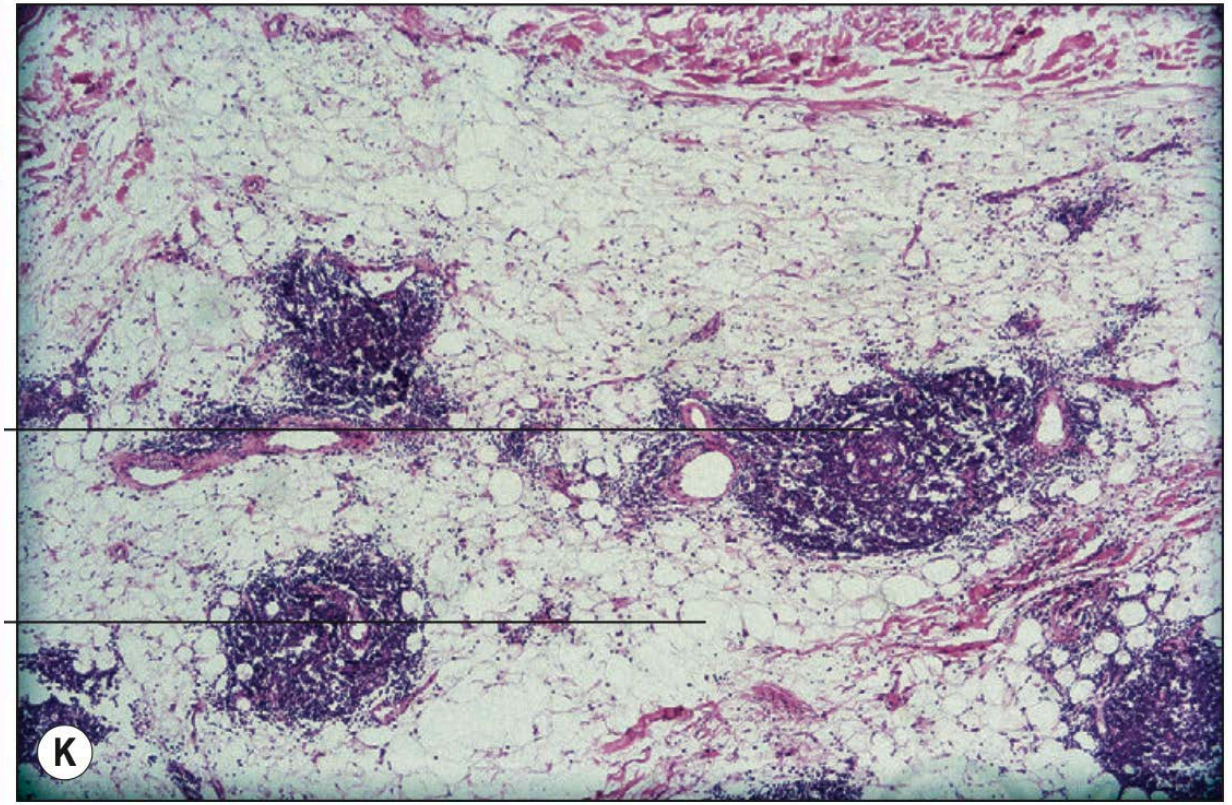




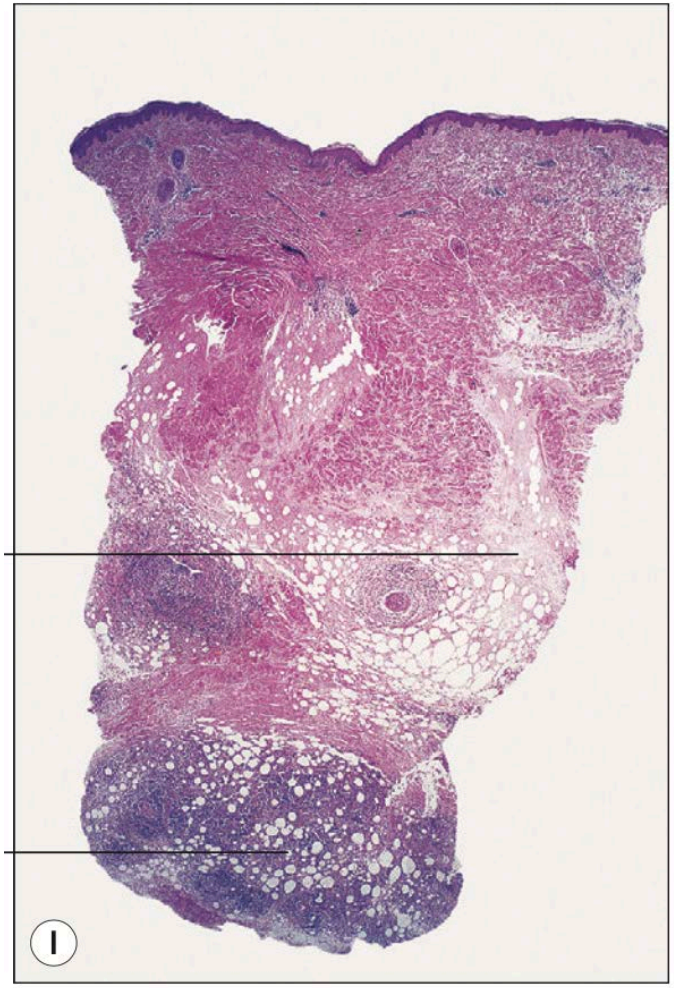
Fitzpatrick

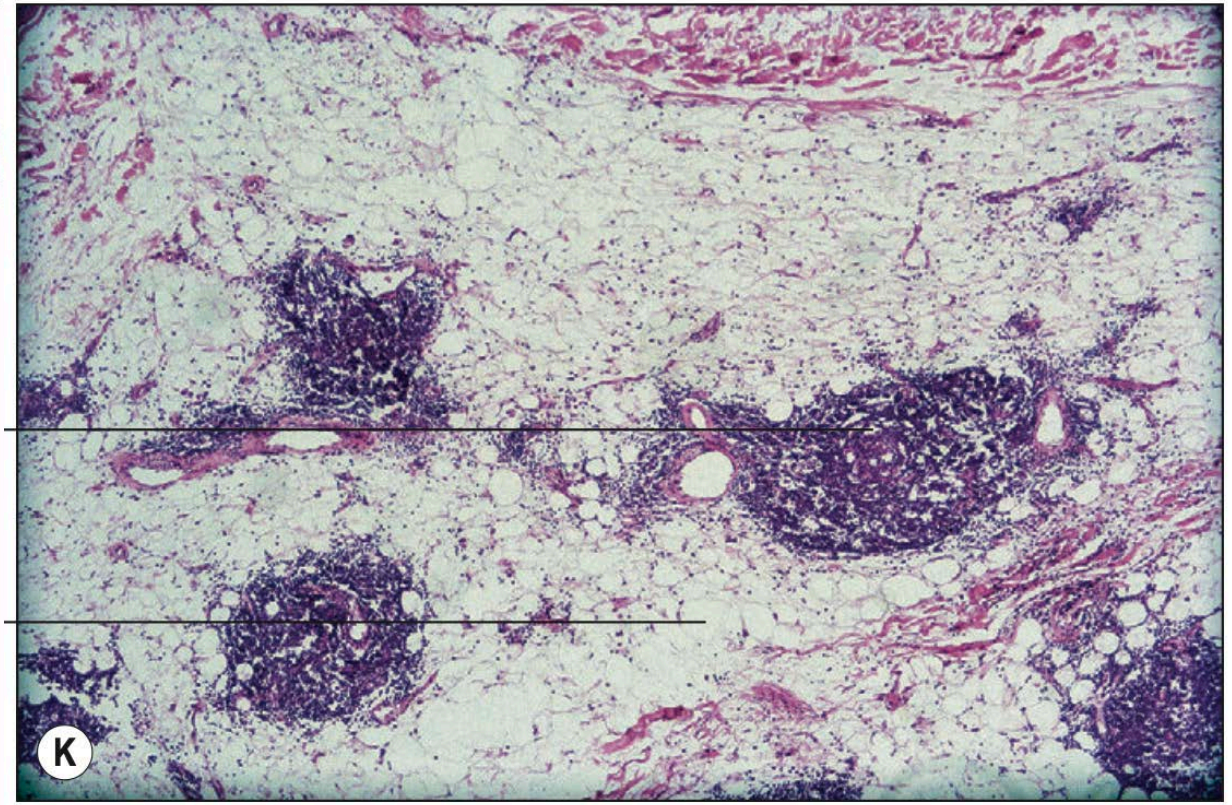
- Histology:



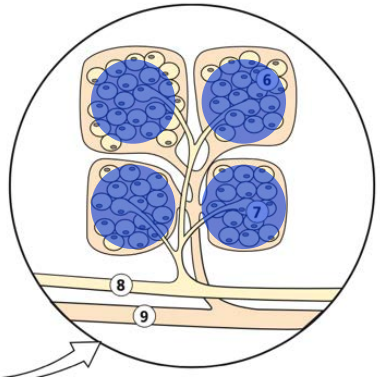


- Lupus panniculitis: lobular without vasculitis





Lobular without vasculitis



PANNICULITIS

Pancreatic

Alpha-1 antitrypsin

Newborn, subcutaneous fat necrosis

Neonatal sclerema

Infiltrates (lymphoma, infectious, gout, factitious)

CTD (lupus, DM, eosinophilic fasciitis), Cytophagic histiocytic panniculitis, Cold, Crystals (gout, cholesterol, calcium)

Unknown (Weber Christian)

Lipodermatosclerosis, lipoatrophy, lipodystrophy, lipodermatosclerosis, lymphoma

Insect bite reaction and other eosinophilic (Well's, parasite, hypereosinophilic)

Trauma

Injected or induced (factitial)

Sweet syndrome, post-steroid, sarcoid

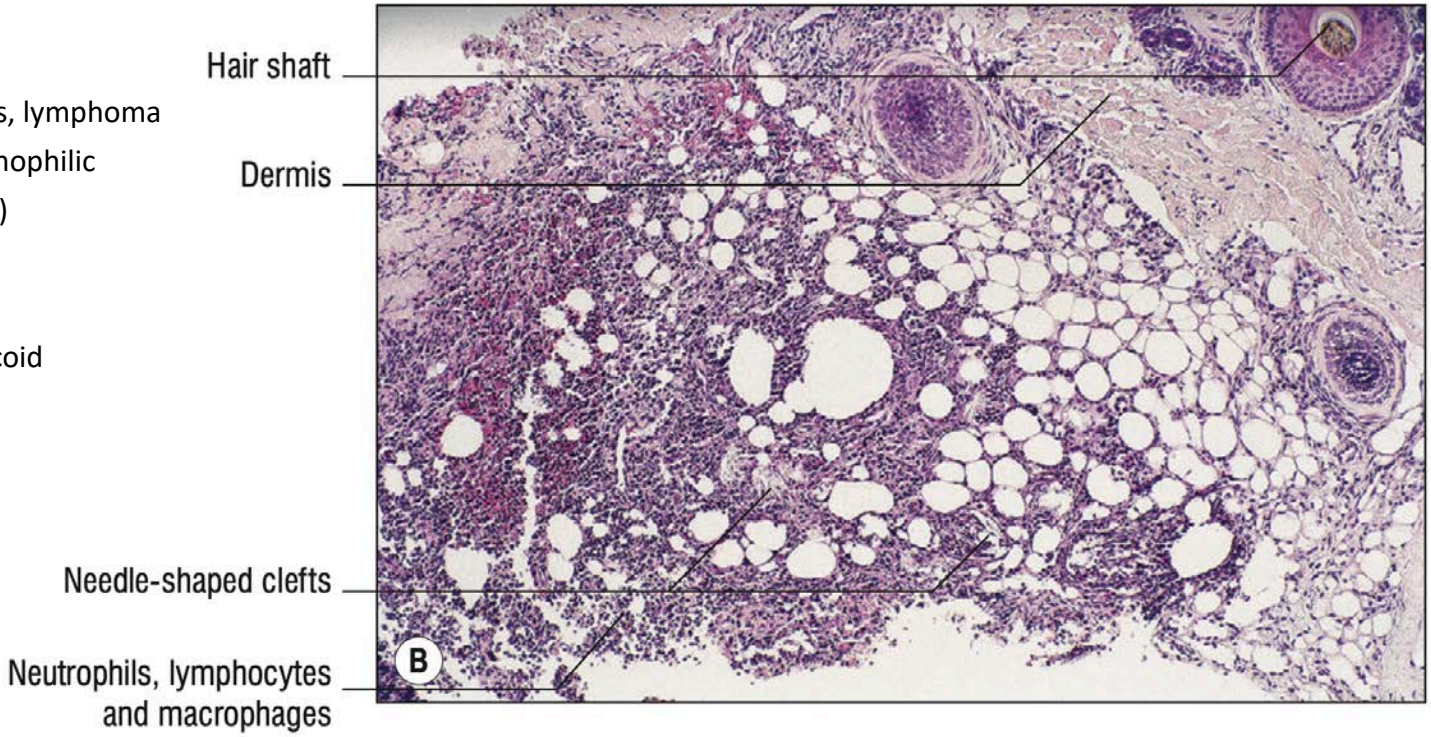
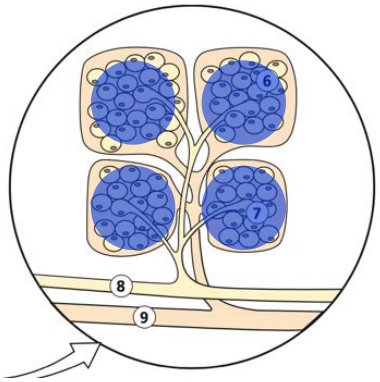


Fig. 16.5 B Subcutaneous fat necrosis of the newborn (medium mag.).

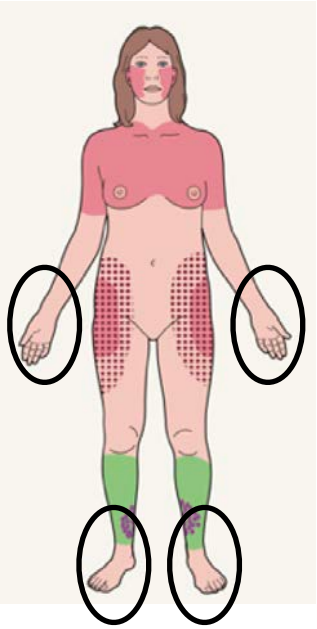
Rapini

Pancreatic panniculitis



Pathogenesis:
Affects 2-3% of all patients with diseases of the pancreas
Pancreatic enzymes (lipase, trypsin and amylase) digest lobular fat and induce fat necrosis

Epidemiology / presentation:
- Associated with pancreatic disease (pancreatic cancer, acute or chronic pancreatitis of any cause, trauma)
- Usually poor prognosis, especially when associated with pancreatic carcinoma
- Presents as painful, thickened, firm nodules and / or plaques on the lower limbs / distal extremeties. May have suppuration of brown, sterile, viscous fluid (liquefied fat) and ulceration
- May have associated fever, poly arthritis and abdominal pain, pleural effusions, ascites
- "Schmid triad" of panniculitis, arthritis and eosinophilia may be more common with pancreatic carcinoma



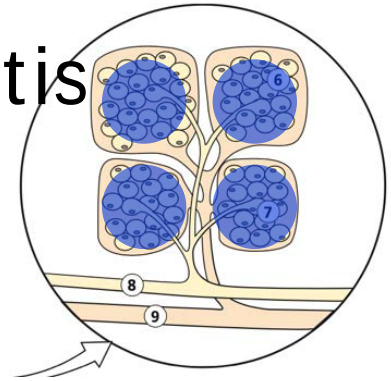
Investigations:
- Histology: Very early stages show mostly septal panniculitis with lymphoplasmacytic inflammation. As condition progresses, characterised by lobular panniculitis without vasculitis. May have "ghost cells" (necrotic adipocytes, amorphous or granular blue-grey substance) with varying degrees of calcification, with associated neutrophilic and granulomatous inflammation. shows lobular panniculitis with
- Markedly elevated serum amylase and lipase
- CT scan: delineate pancreatic lesion and areas of subcutaneous fat necrosis

Management:
Treatment of underlying pancreatic pathology
- ETOH: bowel rest, nutritional support
- Gallstones, pseudocysts, operable pancreatic cancer: surgery
- Inoperable pancreatic cancer: chemotherapy or radiotherapy to reduce serum lipase and therefore development of lesions

CAN ULCERATE

Fitzpatrick, Bolognia, Rook, https://www.dermnetnz.org/search.html?q=pancreatic%20panniculitis

Alpha-1-antitrypsin deficiency panniculitis

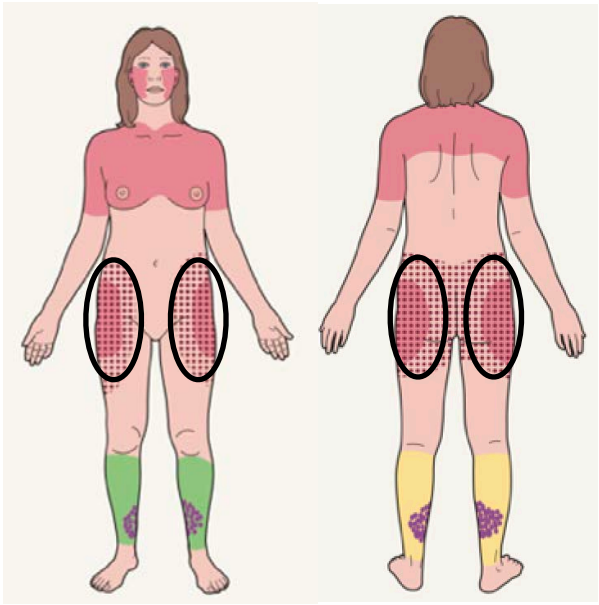


Pathogenesis:

- Autosomal co-dominant disorder (ie. different alleles expressed, activity determines phenotype)
- Deficiency of alpha-1 protease inhibitor (alpha-1 antitrypsin) – inhibits trypsin, neutrophil elastase, pancreatic elastase, serine proteases, collagenase and others. Deficiency thus leads to enzymatic tissue destruction
- Leads to activation of lymphocytes and phagocytes (producing severe inflammation) and tissue necrosis secondary to protease action
- Severe deficiencies can be associated with emphysema, hepatitis, cirrhosis, chronic pancreatitis, membranoproliferative glomerulonephritis, vasculitis, urticaria, angioedema and panniculitis

Epidemiology / presentation:

- Can occur from infancy to old age, most commonly presents as lung disease (emphysema) or liver cirrhosis
- Can involve skin lesions, precipitated by trauma and exacerbated by surgical debridement
- Early lesions may resemble cellulitis, may progress to ulcerative lesions which occur mainly on the trunk and proximal extremities
- May have associated fever



Investigations:

- Histology shows predominantly lobular panniculitis without vasculitis, may have some septal involvement. Infiltrate composed of neutrophils and macrophages. May show severely necrotic and suppurative panniculitis, localised vasculitis/haemorrhage can occur in areas of severe inflammation leading to extensive liquefactive necrosis of the dermis and subcutis, transepidermal elimination of necrotic material
- Alpha-1-antitrypsin genotyping and phenotyping (ZZ, MZ, MS and SS) (F=fast, normal phenotype)
- Serum Alpha-1 antitrypsin levels, LFTs, lipase
- Pulmonary function tests, CXR, HRCT

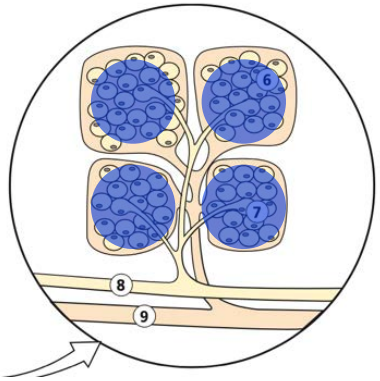
Management:

- Dapsone, doxycycline 200mg/day can be effective
- If severe manifestations (eg. emphysema, lung fibrosis, liver failure) replacement with weekly alpha-1-antitrypsin (expensive)
- Liver transplantation in severe ZZ disease
- Systemic corticosteroids, HCQ, immunosuppressives often given inconsistent response

CAN ULCERATE

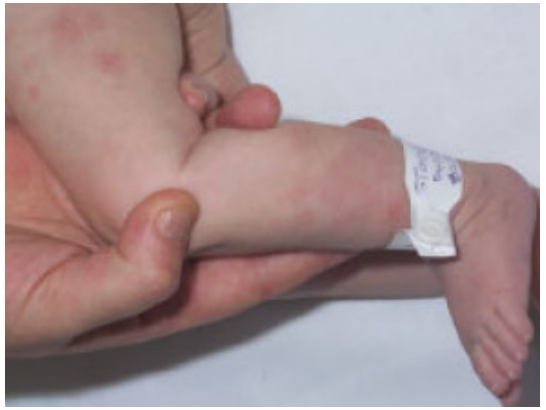
Fitzpatrick, Bolognia, Rook, https://dermnetnz.org/topics/alpha-1-antitrypsin-deficiency-panniculitis/

Subcutaneous fat necrosis of the newborn



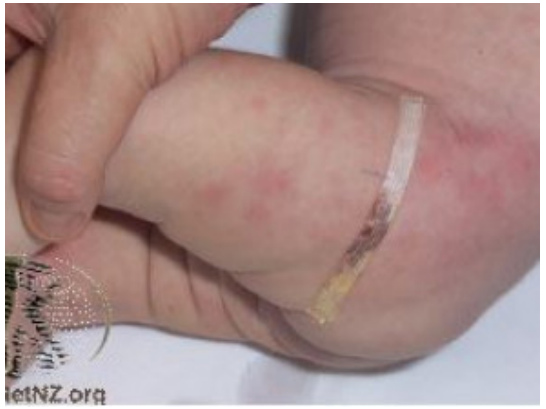
Pathogenesis:
- Unknown. Possible associations with perinatal complications (foetal stress during delivery, low oxygen levels, cold temp, caesarean section, large birth weight, infection, etc. etc.)
- Localised and transient hypoxia may be an etiological factor, mechanical pressure may contribute. Cold may also contribute (newborn fat has higher melting temp. and could thus crystallise when cold, causing necrosis. Newborn fat also has more brown fat, with higher metabolic activity)

Epidemiology / presentation:
- Newborns!
- Lesions usually on shoulders and buttocks, can also be on face, thighs, back and distal extremities. Lesions tend to spare anterior trunk.
- Nodules may rarely ulcerate, discharging oily contents and heal with atrophic scars



Associations:
- Most healthy, but **25% develop hypercalcaemia**, which can persist for weeks or months (need to rule out endocrine abnormalities)
- Transient thrombocytopenia in some patients (sequestration), hyperlipidaemia in some patients

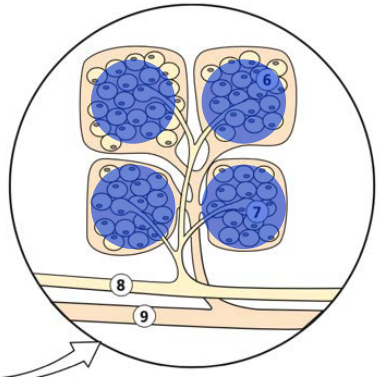
Investigations:
- Biopsy shows lobular panniculitis without vasculitis, inflammatory infiltrate with lymphocytes, histiocytes, lipophages, multinucleate giant cells and sometimes eosinophils. Doubly refractile narrow **needle-shaped clefts** radially arranged in some adipocytes, stain with oil red O. Septal fibrosis in late stage lesions, with areas of calcification and lipoatrophy in the fat lobule



Management:
- Treatment supportive, most resolve spontaneously
- Important to detect and treat hypercalcaemia, maintain adequate hydration with N-saline.
- Low calcium feeds
- Frusemide helpful in some patients
- Bisphosphonates may be useful in cases of refractory hypercalcaemia, but caution because of effect on bone production
- Avoid prednisolone, as it interferes with metabolism of vitamin D / calcium

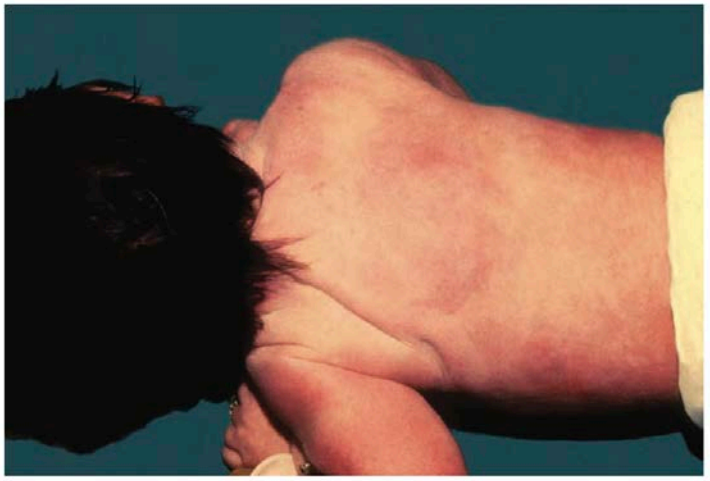
Fitzpatrick, Rook, https://dermnetnz.org/topics/subcutaneous-fat-necrosis-of-the-newborn/

Neonatal sclerema (sclerema neonatorum)



Pathogenesis:
- Cause unknown

Epidemiology / presentation:
- Very uncommon, affects very sick preterm low birth weight infants, usually in the first week of life
- Presents as diffuse hardening of skin / subcutaneous tissue - skin cannot be pitted or pinched
- High mortality (up to 75%)



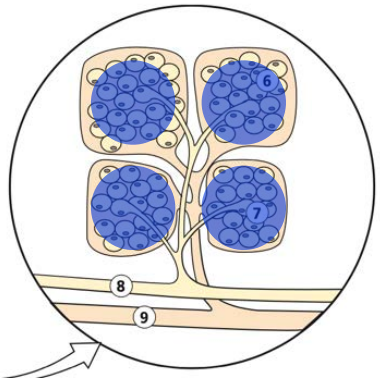
Associations:
- Affected infants are almost always severely ill from conditions such as septicaemia, disseminated infections, congenital heart disease, pneumonia, diarrhoea, dehydration, intestinal obstruction or other congenital developmental defects

Investigations:
- Biopsies shows lobular panniculitis. Minimal inflammation but extensive fat necrosis

Management:
- Often ICU admission for supportive care, treatment of underlying conditions

Rook

Infiltrates: lymphoma
e.g. SP-TCL or PCGD-TCL



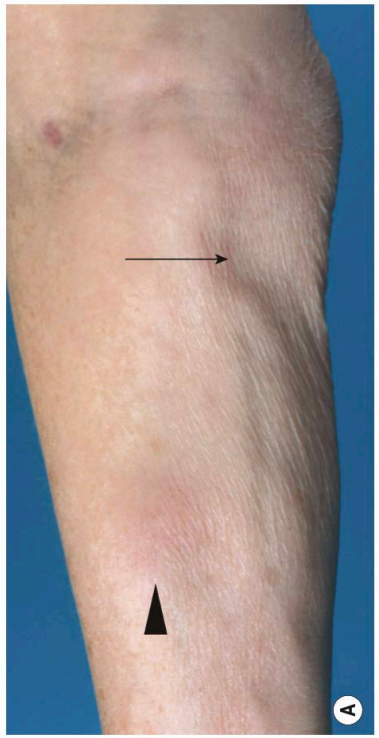
Pathogenesis:
- Malignant infiltrate of α/β T-cell phenotype (subcutaneous panniculitis-like T-cell lymphoma; SP-TCL) or γ/δ T-cell phenotype (primary cutaneous gamma delta T-cell lymphoma; PCGD-TCL)
- a.k.a. cytophagic histolytic panniculitis

Epidemiology / presentation:
- Rare condition (<1% of TCL), affects any age
- Presents as solitary or multiple nodules, or deep plaques of varying diameter
- Primarily affects extremities and trunk, less commonly the face
- Can resolve with lipoatrophy, SP-TCL rarely ulcerates, PCGD-TCL can ulcerate
- Over half of patients have systemic symptoms - fever, fatigue, weight loss
- May initially be mistaken for lupus panniculitis

Associations:
- May have associated haemophagocytic syndrome (~15%)

Investigations:
- Biopsy: Lobular panniculitis without vasculitis, atypical, pleomorphic lymphocytes in the subcutis, infiltration between collagen bundles of the dermis or around adnexal structures, with supporting immunohistochemical studies
- May also have associated cytopenias, deranged LFTs, and elevated LDH

Management:
- Multidisciplinary input with Haematology
- Systemic steroids, cyclosporin, methotrexate, etc. for SP-TCL
- Systemic chemotherapy for PCGD-TCL



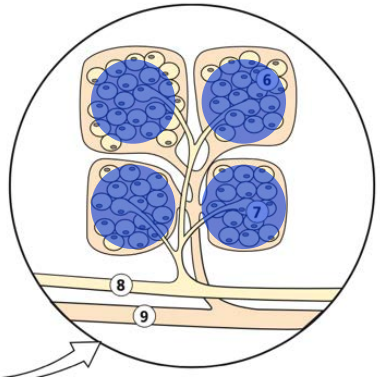
CAN ULCERATE (PCGD-TCL)

Bolognia, Fitzpatrick

COMPARISON OF SUBCUTANEOUS PANNICULITIS-LIKE T-CELL LYMPHOMA AND PRIMARY CUTANEOUS GAMMA/DELTA T-CELL LYMPHOMA WITH SUBCUTANEOUS INVOLVEMENT		
	SPTCL	**PCGD-TCL with subcutaneous involvement**
Phenotype	α/β T-cell phenotype	γ/δ T-cell phenotype
T-cell receptor	$\beta F1^+$, $TCR\gamma1^-$	$\beta F1^-$, $TCR\gamma1^+$
T-cell phenotype	$CD3^+$, $CD4^-$, $CD8^+$	$CD3^+$, $CD4^-$, $CD8^-$
Coexpression of CD56	Absent	Common
Architecture	Subcutaneous	Subcutaneous and epidermal/dermal
Clinical features	Nodules and plaques Rarely ulceration	Nodules and plaques Ulceration common
Hemophagocytic syndrome	Uncommon	Common
Survival (5-year)	>80%	<10%
Treatment	Systemic corticosteroids	Systemic chemotherapy
WHO-EORTC classification (2004)[3] WHO classification (2008)/2016[4]	Subcutaneous panniculitis-like T-cell lymphoma	Primary cutaneous gamma/delta T-cell lymphoma

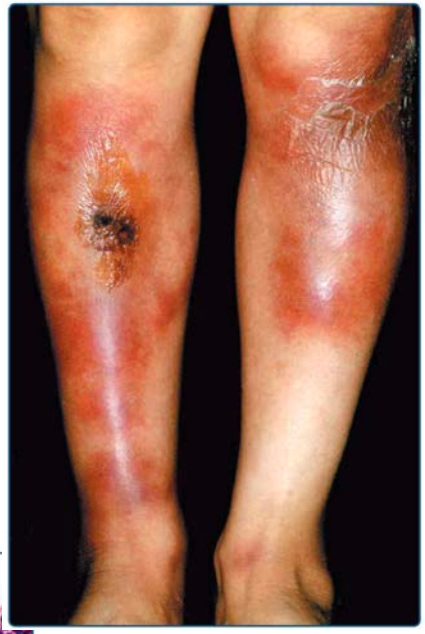
Table 120.7 Comparison of subcutaneous panniculitis-like T-cell lymphoma (SPTCL) and primary cutaneous gamma/delta T-cell lymphoma (PCGD-TCL) with subcutaneous involvement[1,2]. βF1, positivity reflects α/β T-cell origin; TCR, T-cell receptor.

Cytophagic histiocytic panniculitis



Pathogenesis:
- Often associated with malignancy (lymphoma)
- May have genetic basis predisposing (e.g. perforin mutations)

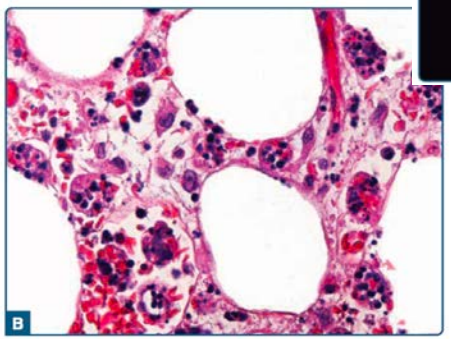
Epidemiology / presentation:
- Majority of patients have lymphoma (usually PCGD-TCL or EBV associated extra nodal NK/ TCL, nasal type, less commonly SP-TCL. Rarely no lymphoma
- Presents with painful nodules at multiple sites, with associated systemic symptoms. May have fever, cytopenias, hepatosplenomegaly, liver failure



Associations:
- Haemophagocytic syndrome (haemophagocytic lymphohistiocytosis; HLH) involving the liver, spleen and bone marrow (leading to pancytopenia)

Investigations:
- Biopsy shows lobular panniculitis without vasculitis, with infiltrates containing erythrocytes, lymphocytes and karyorrhectic debris. Phagocytic histiocytes contain intact or fragmented cells and nuclear debris - “beanbag cell”

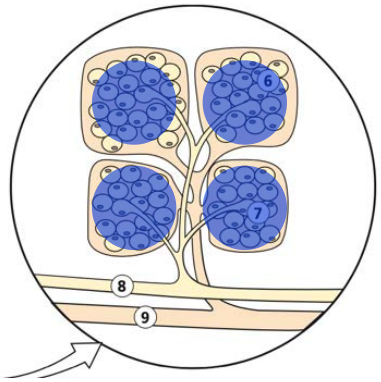
Management:
- Multidisciplinary input with Haematology
- Diagnosis and management of lymphoma
- Systemic corticosteroids, cyclosporin
- Also described: tacrolimus, azathioprine, anakinra, cyclophosphamide, IVIG
- When associated with HLH or macrophage activating syndrome, requires aggressive supportive care and chemotherapy



CAN ULCERATE

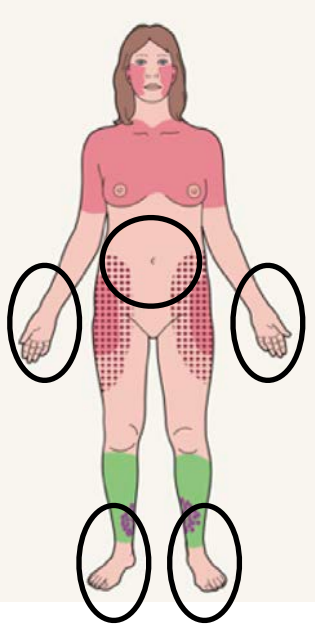
Bolognia, Fitzpatrick, https://dermnetnz.org/topics/cytophagic-histiocytic-panniculitis/

Infiltrates: Infectious panniculitis



Pathogenesis:
- Caused by a wide variety of infectious agents (bacteria, fungi, parasites, viruses)
- Primary inoculation or haematogenous spread

Epidemiology / presentation:
- Often immunosuppressed patients (organ transplantation, leukaemia, solid tumours, HIV, autoimmune connective tissue disease)
- More common with diabetes
- Presents as erythematous plaques, nodules, accesses and ulcers with local swelling and erythema, may have purulent discharge, fluctuant nodules that ulcerate and drain
- Lesions on the legs and feet are common, other sites include the gluteal region, abdomen, axillae, arm or hand



Investigations:
- Histopathologic findings vary, but often include mixed septal / lobular panniculitis, neutrophilic and suppurative granulomatous infiltration, haemorrhage and necrosis. Special stains for organisms (gram stain, PAS, Wade-Fite, ZN)
- culture of drainage and tissue

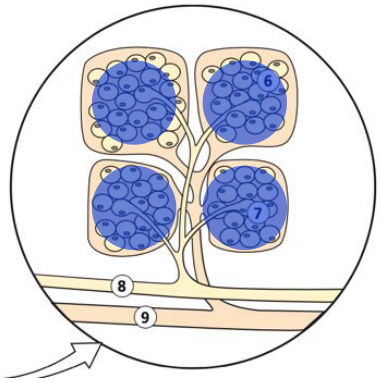
Management:
- Multidisciplinary input with Infectious Diseases
- Treatment of responsible infection

CAN ULCERATE

Bolognia, Fitzpatrick

INFECTION-INDUCED PANNICULITIS – REPORTED CAUSATIVE AGENTS
Bacteria
Staphylococcus aureus Group A *Streptococcus* *Pseudomonas aeruginosa* *Brucella melitensis* *Nocardia asteroides* *Tropheryma whipplei* (causative agent of Whipple disease)
Mycobacteria
M. tuberculosis *M. marinum, M. avium-intracellulare, M. chelonae, M. fortuitum, M. ulcerans*
Coxiella
C. burnetii
Borrelia
B. burgdorferi
Fungi
Blastomyces dermatitidis, Histoplasma capsulatum *Microsporum* spp. (including *M. canis*) *Candida* spp. (including *C. albicans*) *Cryptococcus neoformans* *Aspergillus* spp. (including *A. flavus*), *Mucor* or related zygomycetes, *Fusarium* spp., *Aureobasidium pullulans*
Helminths & protozoa
Nematodes (*Gnathostoma* spp.) Trematodes (*Fasciola hepatica*, *Schistosoma* spp.)

Infiltrates: Gout

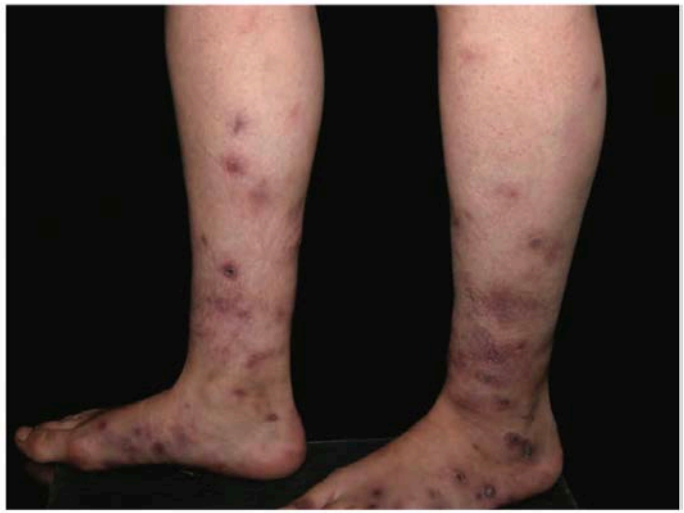


Pathogenesis:
- Uncommon complication of tophaceus gout, results from deposition of urate crystals in the fat lobules

Epidemiology / presentation:
- Rare manifestation of gout. May precede diagnosis, but often late manifestation
- Painful ulcerating nodules on the lower legs. Chalky substance may overly ulceration.

Investigations:
- Biopsy: Lobular panniculitis, with no vasculitis. Basophilic amorphous deposits in the lobules, which are fine radially orientated needle-shaped urate crystals, appear surrounded by granulomatous inflammation, occasionally with neutrophilic inflammation. Histiocytes and multinucleate giant cells form a palisade around the urate crystals.
- May have associated hyperuricaemia

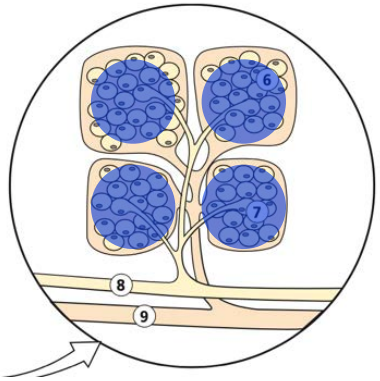
Management:
- Management of gout - low purine diet, colchicine, allopurinol, probenecid etc.
- Acute panniculitis may benefit from systemic corticosteroids
- Surgery for non-healing ulcerated lesions



CAN ULCERATE

Rook, Fitzpatrick

Factitious panniculitis (trauma)



Pathogenesis:
- Can be caused by mechanical trauma, chemical substances and thermal injury
- May be accidental, intentional or iatrogenic
- Can also be caused by injection of cosmetic fillers, or extravasation of systemic chemotherapy
- Has also been associated with cupping or acupuncture techniques

Epidemiology / presentation:
- Variable clinical presentation, depending on causative agent
- Self-induced panniculitis more common in young or middle aged patients, with a history of psychiatric or drug addiction comorbidities
- Self-induced panniculitis tends to occur in accessible areas of the body
- Often bizarre clinical appearance - RED FLAG = does not fit with other causes of panniculitis

Associations:
- May have associated psychiatric disorders leading to self-harm

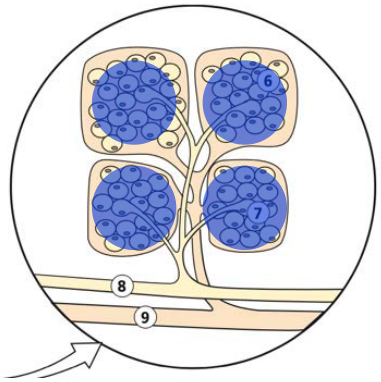
Investigations:
- Biopsy findings vary depending upon the causative agent
- In most cases, early lesions show features of a predominantly neutrophilic lobular panniculitis, with severe fat necrosis and an intense inflammatory infiltrate
- May have superimposed infection

Management:
- Antibiotics as appropriate
- Good wound care
- Zinc bandages
- Appropriate psychiatric and social supports

CAN ULCERATE

Rook, Fitzpatrick

CTD: Lupus panniculitis



Pathogenesis:
- Subcutaneous manifestation of lupus erythematosus. Inflammation leading to destruction of subcutaneous fat

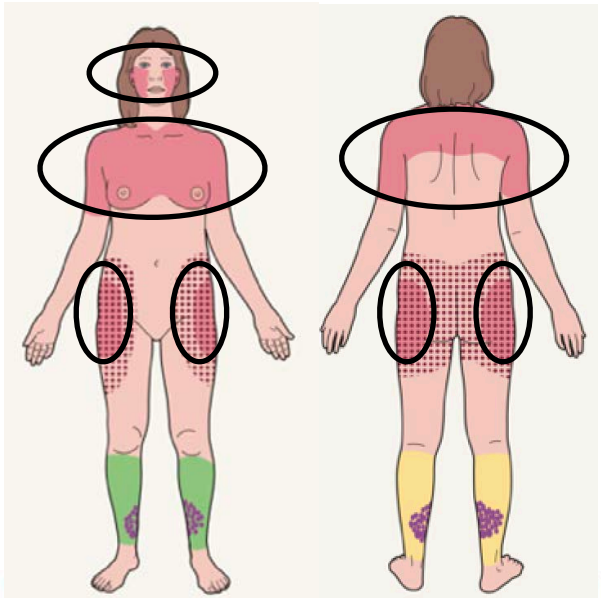
Epidemiology / presentation:
- Tender subcutaneous nodules and indurated plaques which resolve with lipoatrophy. Can present initially with lipoatrophy alone.
- Face, upper arms, upper trunk, breasts, buttocks and thighs most commonly affected
- Often precedes other manifestations of lupus erythematosus

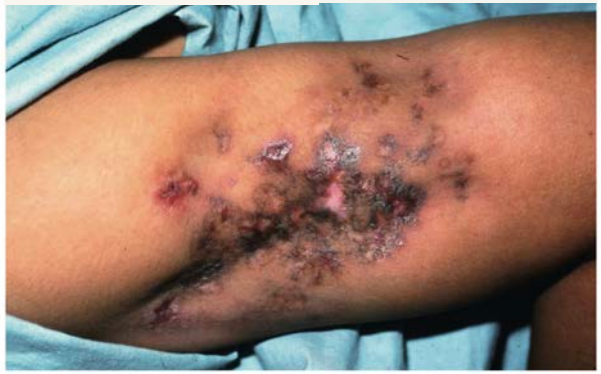
Differential diagnosis:
- Dermatomyositis associated panniculitis has identical histological findings - different distribution (although uncommon manifestation of DM)
- SP-TCL or PCG-DTCL in early stages may present similar to lupus panniculitis, overlap cases have also been described

Associations:
- DLE in >1/3 patients, SLE in 10-15% of patients

Investigations:
- Biopsy shows predominantly lobular panniculitis with hyaline necrosis, but may also have septal involvement, with or without lymphocytic vasculitis. May have thickening and sclerosis of collagen bundles at the septa, but infiltrate is mostly lobular. Lymphocytic infiltrate with numerous plasma cells, nodular aggregates of lymphocytes are common
- Overlying epidermal or dermal changes of lupus erythematosus frequently present
- TCR PCR polyclonal (useful for ruling out lymphoma)

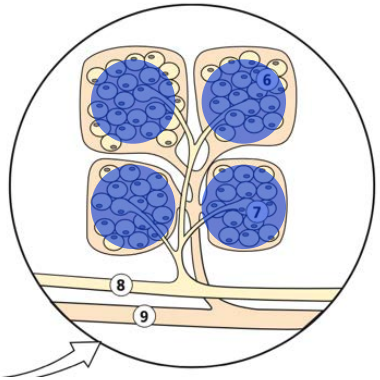
Management:
- Multidisciplinary input with Rheumatology if SLE
- Topical and intralesional steroids. Systemic steroids if active and severely inflamed
- HCQ, Dapsone, cyclosporine, methotrexate, intravenous immunoglobulin, rituximab, azathioprine, tacrolimus, thalidomide





Bolognia, Rook

Cold panniculitis

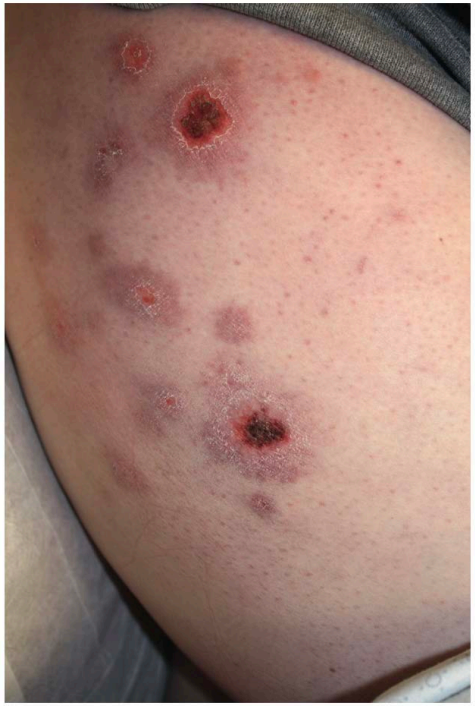


Pathogenesis:
- Damage to fat lobules due to cold
- Related to fluctuations in blood flow with low temperatures and tight fitting clothing / compression, also crystal formation

Epidemiology / presentation:
- Infants and small children are most at risk for cold panniculitis (more brown fat with higher metabolic activity). Popsicle panniculitis also described!
- In adults, more common in obesity. Most commonly affects upper thighs and gluteal region
- Variant also in thighs of young female equestrian riders- exposure to cold in combination with tight fitting clothing
- Absence of systemic symptoms

Investigations:
- Biopsy shows lobular panniculitis, may have variable septal involvement. Absence of needle-shaped clefts in lipocytes (compared to subcutaneous fat necrosis of the newborn), also most intense inflammation near dermal-subcutaneous interface and periadnexally. Mixed infiltrate consisting of lymphocytes, neutrophils, foamy macrophages, poorly developed granulomas, music, adipocyte necrosis and microcysts

Management:
- Identification (and avoidance) of triggers - usually resolves spontaneously
- Intralesional steroids to treat inflammation if severe
- Supportive care - treat any associated infection, wound care, analgesia

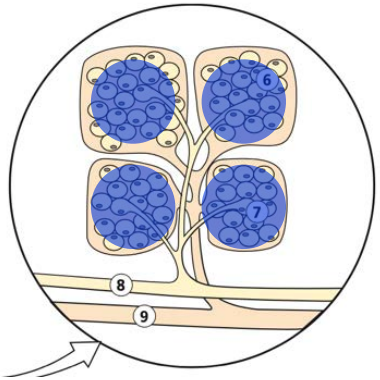


CAN ULCERATE (or crust)

Bolognia, Rook, Fitzpatrick

Calcific uraemic arteriolopathy

a.k.a. calciphylaxis (crystals)



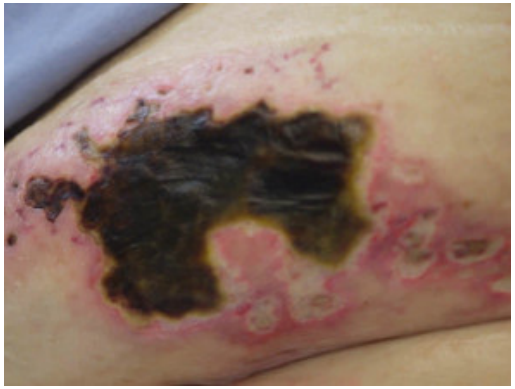
Pathogenesis:
- Vascular mural calcification, leading to end-vascular fibrosis, occlusion and necrosis
- Loss of inhibitors of vascular calcification (Matrix Gla, fetuin) - can be exacerbated by warfarin

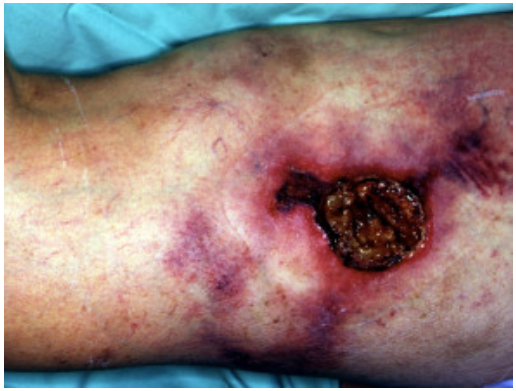
Epidemiology / presentation:
- Most common in patients with end-stage renal failure, elevated serum calcium and phosphate
- Presents with retiform purpura, bleeding, blood-filled bullae and stellate areas of necrosis and violaceous lesions, deep and extensive ulcers. Extremely painful, may also have itch or burning sensation
- Most commonly occurs on fatty areas of lower limb or abdomen
- Can lead to secondary infection, sepsis and death

Associations:
- Triggering factors can include low albumin, arterial hypertension, obesity, systemic corticosteroids, Vit D supplementation, high serum calcium and phosphate, etc.

Investigations:
- Histology shows small and medium sized vascular calcification (blue with H&E, black with Von Kossa stains), involving small arteries, arterioles and venules. Earliest sites are media and / or intima of cutaneous arterioles. Panniculitis may be lobular or septal, with associated ischaemic necrosis, and secondary infection

Management:
- Multidisciplinary care with renal team
- Treat infection
- Wound debridement if necrotic, good wound care
- Low calcium and phosphate dialysate, calcium and phosphate binders
- Surgical removal of parathyroids if indicated
- Sodium thiosulphate



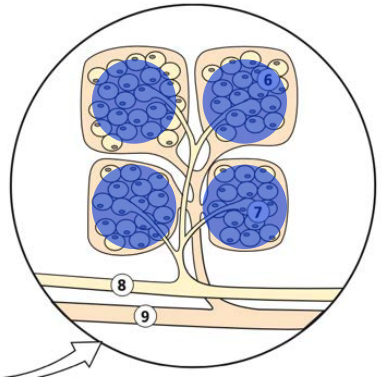


CAN ULCERATE

Bolognia, Rook, dermnetnz.org/topics/calciphylaxis

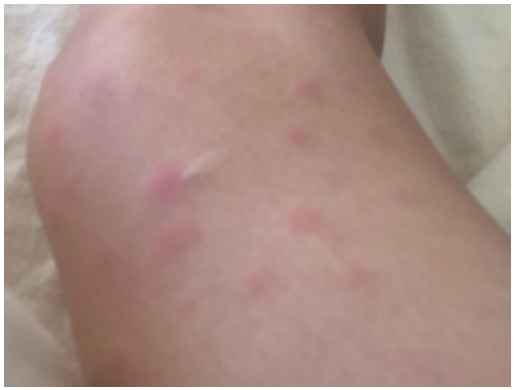
Nodular panniculitis

(previously known as Weber Christian Disease)



Pathogenesis:
- Cause unknown, possibly autoimmune or auto inflammatory granulomatous reaction
- White blood cells infiltrate and damage the subcutaneous fat, causing necrosis and fibrosis

Epidemiology / presentation:
- Rare entity. Occurs in all ages, but most commonly affects young adult women
- Presents as one or multiple recurrent subcutaneous nodules, thighs and lower legs bilaterally
- Associated with acute systemic symptoms such as fever, malaise and abdominal pain
- Diagnosis of exclusion, also referred to as relapsing, febrile, non-suppurative panniculitis
- May settle down over weeks or months, may be single episode or have relapsing / remitting course



Associations:
- Associated with autoimmune conditions such as Sjogren syndrome, IBD, SLE, diabetes mellitus
- Can involve visceral organs; polyarthralgia, polymyalgia, bowel perforation, pleural effusion, anaemia, vasculitis (risk of mortality depending on visceral organ involvement)

Investigations:
- Biopsy: lobular panniculitis with or without vasculitis

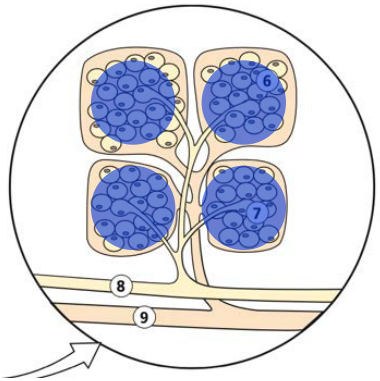
Management:
- Multidisciplinary management if visceral organ involvement
- If no visceral organ involvement, treat symptomatically
- Analgesia, NSAIDs
- Systemic corticosteroids if severe
- Other drugs described: MMF, thalidomide, clofazimine, hydroxychloroquine, tetracyclines, dapsone, azathioprine, cyclosporin
- Wound care for ulcers

CAN ULCERATE

https://dermnetnz.org/topics/nodular-panniculitis/

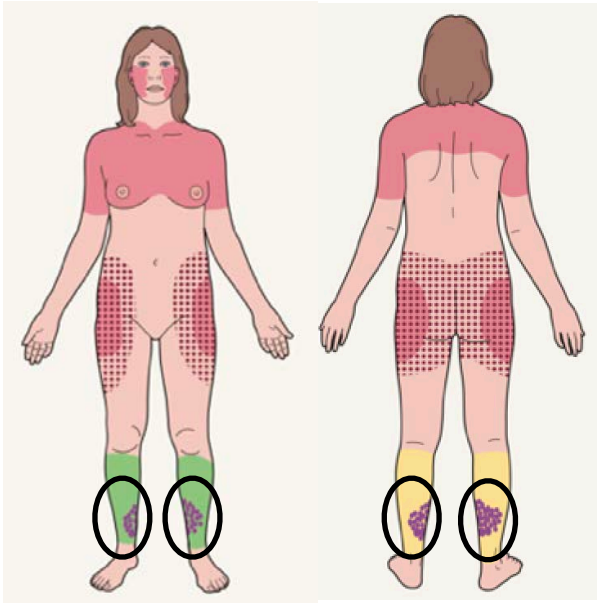
Lipodermatosclerosis

a.k.a. sclerosing panniculitis



Pathogenesis:
- Usually develops in the setting of chronic venous insufficiency

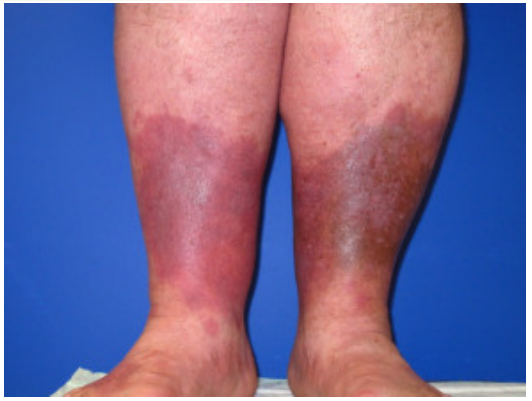
Epidemiology / presentation:
- Most common in women over the age of 40
- Presents with pain, warmth and erythema of the lower legs, with associated induration, wood-like consistency
- Acute phase may be misdiagnosed as infectious cellulitis
- Favours the medial aspect of the lower legs above the malleolus
- Chronic phase progresses to induration with red-brown to violet-brown discolouration
- "inverted wine bottle" appearance, may also have hyperpigmentation and haemosiderin deposition



Associations:
- Obesity, protein C and S deficiency

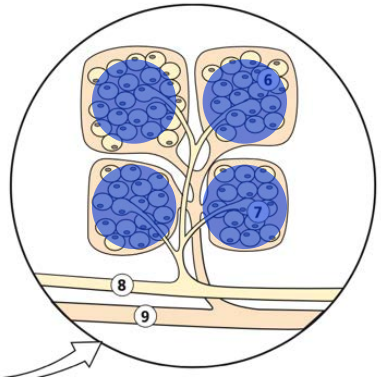
Investigations:
- Biopsy can show both septal and lobular panniculitis. Early lesions show mid-lobular ischaemic necrosis with lymphocytic infiltrate in the septa rimming the fat lobules, capillary congestion and thrombosis, and haemorrhage with haemosiderin deposition. Advanced lesions show **thickened, fibrotic septae** and **membranocystic changes**

Management:
- Leg elevation and compression
- Physical therapy (exercise), weight reduction
- Emollient, soap free wash, topical steroids if venous stasis dermatitis
- Pentoxifylline has been reported as beneficial if associated venous ulcers
- Intralesional corticosteroids in some patients
- Tetracyclines, hydroxychloroquine have been reported
- Anabolic steroids have been reported (danazol, oxandrolone)
- Vascular surgery referral for management of venous insufficiency (ligation and stripping, sclerotherapy)

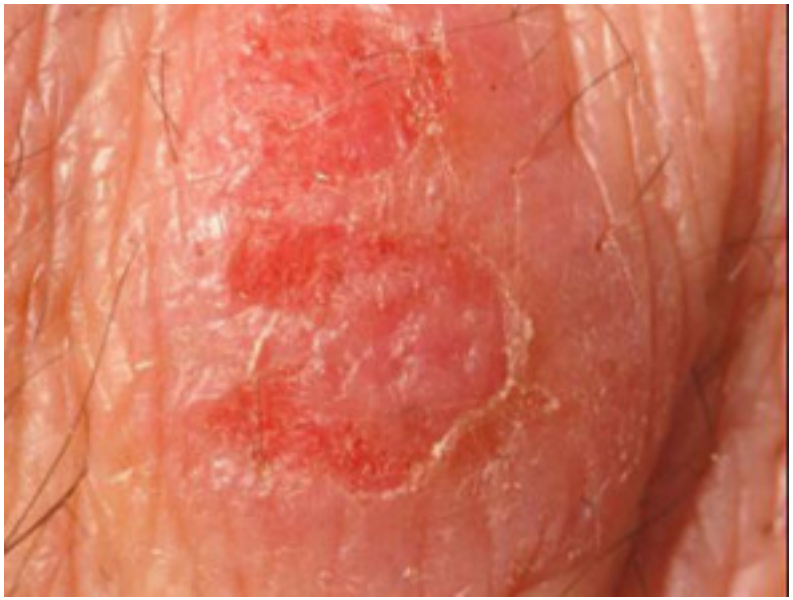


Fitzpatrick, Bolognia, https://dermnetnz.org/topics/lipodermatosclerosis/

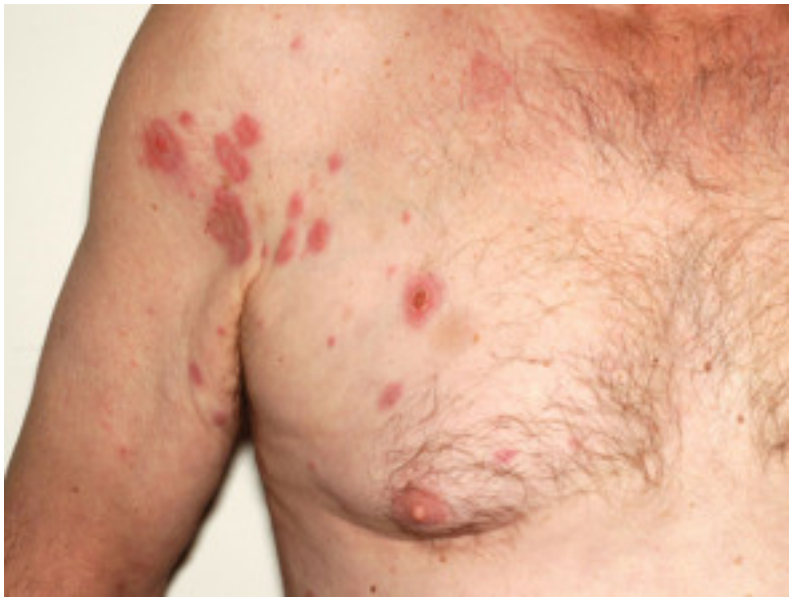
Wells syndrome (eosinophilic cellulitis)
also Hypereosinophilic syndrome



Histology includes many eosinophils and “flame figures”
Eosinophilic panniculitis has been reported as a rare association
Underlying causes of eosinophilia such as parasitic infection should be ruled out

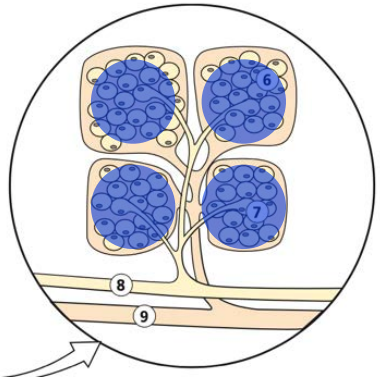


https://dermnetnz.org/topics/wells-syndrome/



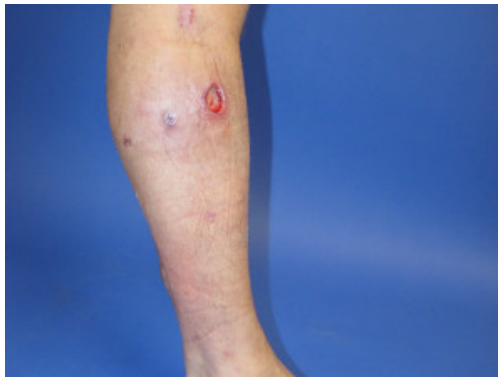
https://dermnetnz.org/topics/hypereosinophilic-syndrome/

Sweet syndrome
(subcutaneous Sweet syndrome)

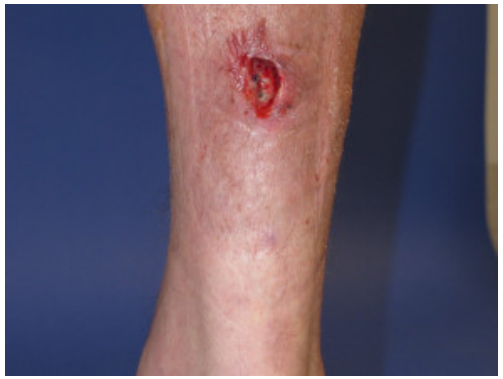


Pathogenesis:
- Acute febrile neutrophilic dermatosis- autoinflammatory condition often associated with systemic disease

Epidemiology / presentation:
- Most often occurs in middle aged women. May affect health individuals, but often arises in the context of acute or chronic infection, as a drug reaction, or associated with haematology malignancy
- Subcutaneous Sweet syndrome presents with deep, painful nodules or plaques, skin lesions may ulcerate and discharge oily material
- May also have more common skin manifestations (papules, plaques, nodules, vesicles or pseudovesicles)
- Associated systemic symptoms of fever, malaise or joint pains



Associations:
- More common if HLAB54 positive
- May follow sun exposure, URTI (esp. streptococcal throat infection), IBD, RA, LE, haematology malignancy, solid organ tumours (bowel, GU or breast), pregnancy, GI infection, vaccination, or drug exposure (azathioprine, G-CSF, NSAIDs, trimethoprim + sulphamethoxazole, TNF-alpha inhibitors, carbamazepine, etc.)



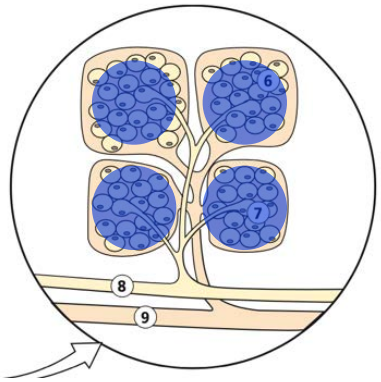
Investigations:
- Biopsy shows lobular neutrophilic panniculitis in the subcutaneous fat, without vasculitis

Management:
- Identification of cause, avoidance of trigger as appropriate
- Multidisciplinary input as required
- Systemic corticosteroids
- Topical or intralesional corticosteroids
- Dapsone, colchicine, minocycline, potassium iodide, NSAIDs (indomethacin), Cyclosporin, mycophenolate, Clofazimine, thalidomide

CAN ULCERATE

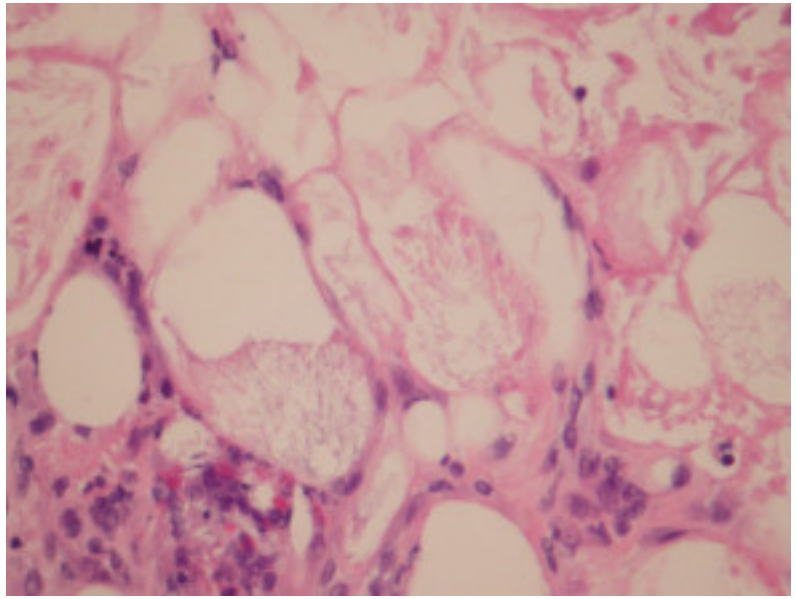
https://dermnetnz.org/topics/acute-febrile-neutrophilic-dermatosis/

Poststeroid panniculitis



Pathogenesis:
- Precise mechanism unknown, but occurs on rapid decrease or withdrawal of prednisolone, usually after cumulative doses of 2000mg to 6000mg

Epidemiology / presentation:
- Rare, but typically a disorder of children - older age group than sclerema neonatorum or subcutaneous fat necrosis of the newborn, usually between 20 months ago 14 years old, rarely in adults
- Presents as subcutaneous nodules on the cheeks, arms and trunk (areas where fat accumulates from steroid use). Lesions 0.5 to 4cm, and with overlying erythema



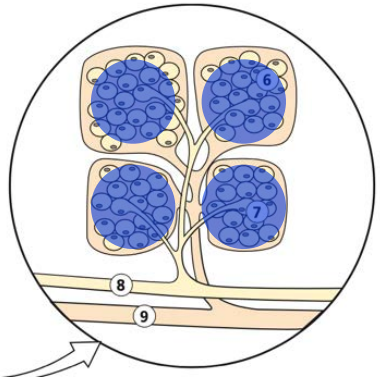
Investigations:
- Biopsy shows granulomatous lobular panniculitis with needle shaped clefts within both lipocytes and giant cells (similar histology to subcutaneous fat necrosis of the newborn)

Management:
- Treatment is usually unnecessary (may resolve spontaneously), but can wean steroids more gradually for improvement

Fitzpatrick, Bolognia, Rook, https://dermnetnz.org/topics/poststeroid-panniculitis-pathology/

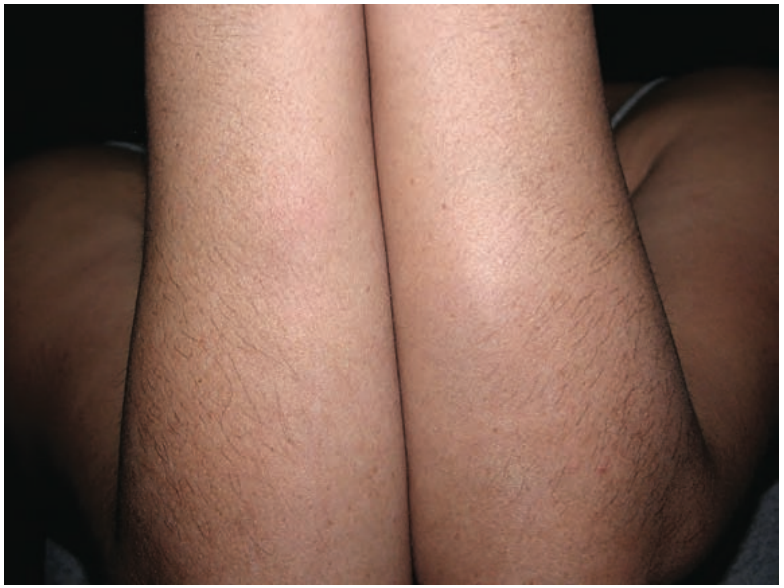
Sarcoid

(subcutaneous sarcoidosis, a.k.a. Darier-Roussy sarcoid)



Pathogenesis:
- Cause unkown, thought o be chronic cell-mediated immune response to unknown antigen
- Activated macrophages and CD4 T-lymphocytes release cytokines that trigger granuloma formation
- Specific clinicopathological variant of sarcoidosis involving exclusively subcutaneous fat (i.e. not just nodular dermal nodules with subcutaneous extension)
- Rarely may be associated with unusual host reaction to M. paratuberculosis, histoplasmosis or fungi

Epidemiology / presentation:
- Rare, between 1.4% and 6% of patients with systemic sarcoidosis
- Incidence peaks age 20-29, and also women over 50
- Presents with deep-seated, firm subcutaneous nodules on the trunk and extremities
- May be asymptomatic or mildly tender



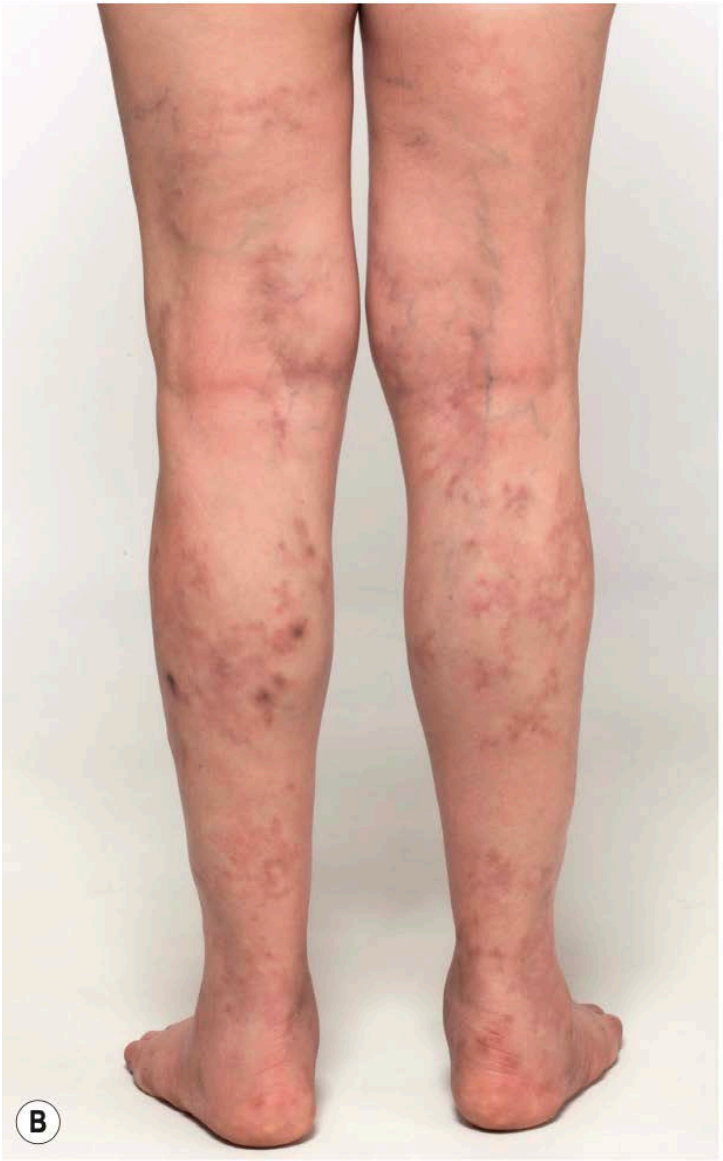
Associations:
- Usually associated with indolent and non-aggressive form of systemic sarcoidosis
- May have fever, malaise, weight loss, cough, SOB, arthritis, uveitis, hepatosplenomegaly
- May have cardiac arrhythmias, heart failure
- May be associated with other autoimmune disorders
- Note that **sarcoid can also be a cause for Erythema Nodosum**

Investigations:
- Biopsy shows non-caveating granulomas involving fat lobules, without vasculitis
- Minimal to no septal involvement. Sarcoidal granulomas are usually small and uniform
- Occasionally may have small foci of eosinophilic necrosis (need to rule out TB), may have some multinucleate giant cells
- Bloods for lymphopenia, haemolytic anaemia, thrombocytopenia, hypercalcaemia, elevated ALP, renal impairment

Management:
- Multidisciplinary input if required
- Treatment not always required
- Treatment as for sarcoid - oral corticosteroids, NSAIDs, HCQ, minocycline, dapsone, allopurinol, Mtx, clofazimine, PI, ILK

Rook, https://dermnetnz.org/topics/darier-roussy-subcutaneous-sarcoidosis/

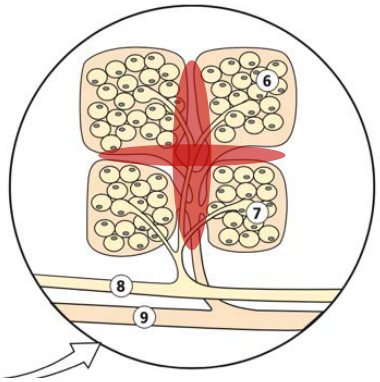
- 40 year old woman, presents with 4/52 history of tender nodules on the lower legs, associated livedo racemosa, occasional ulceration and scarring
- Other questions? Investigations?
- DDx?



Rook

Septal with vasculitis

- Polyarteritis nodosa
- Leukocytoclastic vasculitis (severe)
- Superficial thrombophlebitis



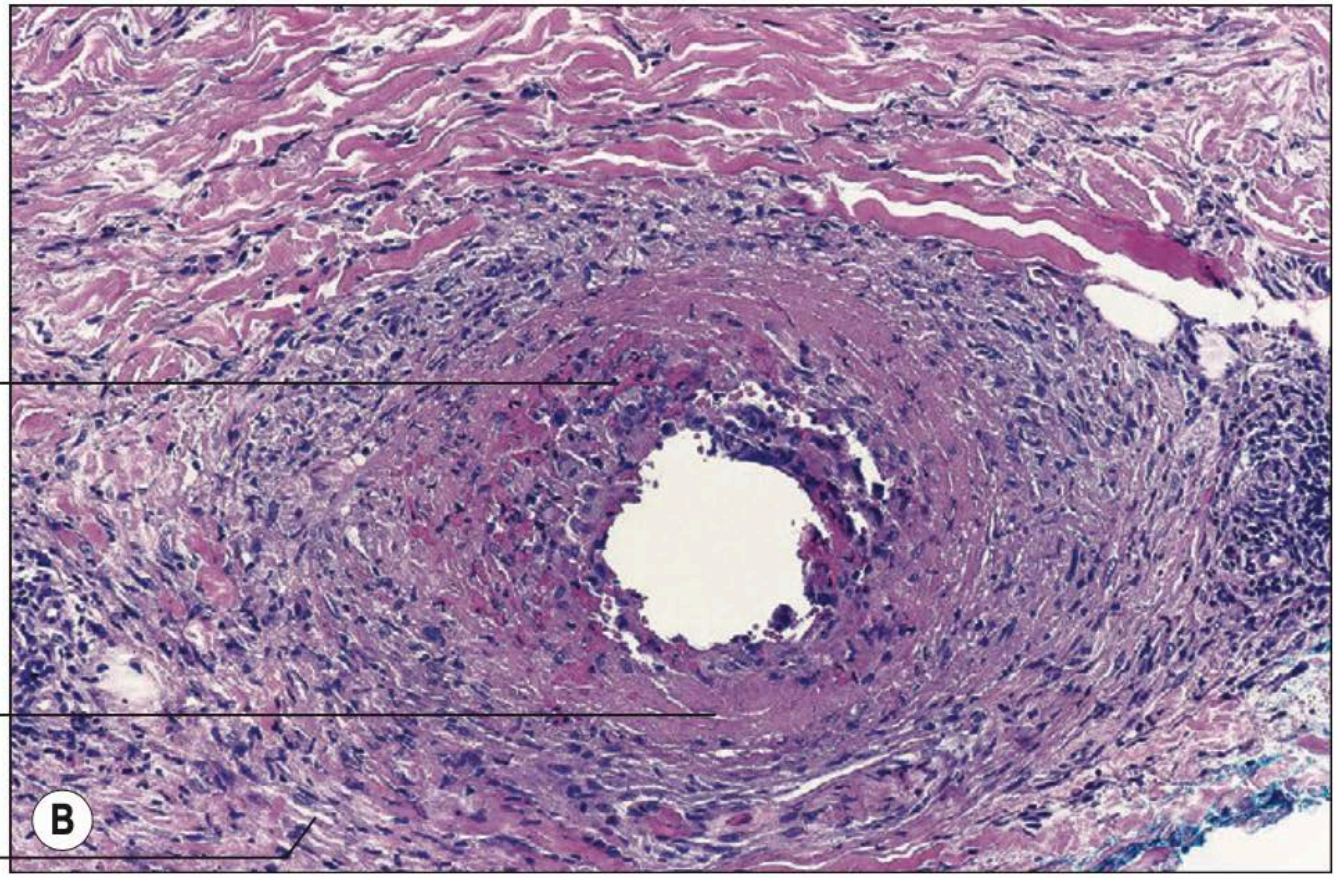
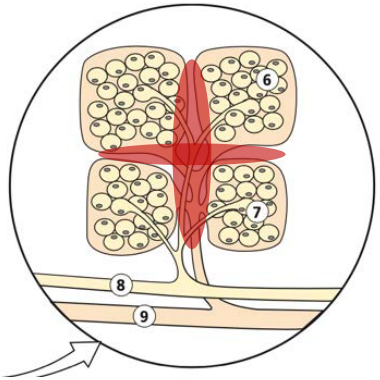


Fig. 16.7 B Superficial thrombophlebitis (high mag.). Rapini

Polyarteritis nodosa



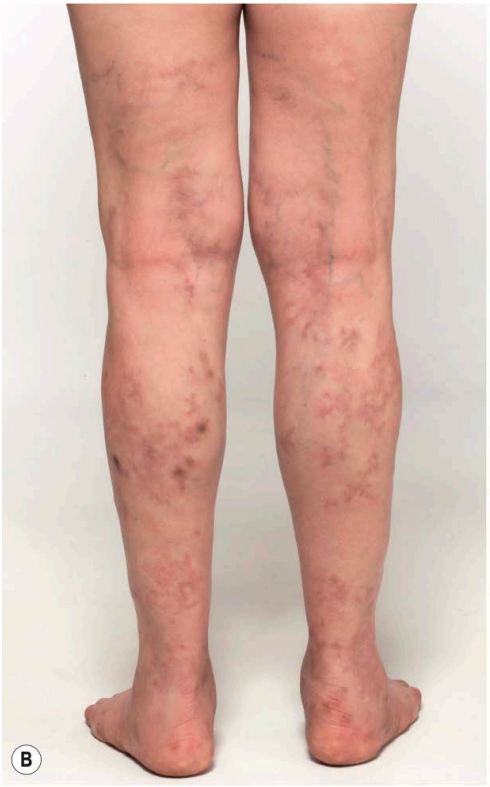
Pathogenesis:
- Cutaneous polyarteritis nodosa (cPAN)- vasculitis of small to medium sized arteries of the dermis and subcutaneous tissue (compared with systemic polyarteritis nodosa; sPAN, see below)
- cPAN ANCA ELISA usually negative (although associated with p-ANCA with IIF)
- Most cases triggered by infection - Group A strep, Hep B, Hep C, HIV, parvovirus B19 (causes fifth disease)
- Autosomal recessive mutations in CERC1 gene have been implicated

Epidemiology / presentation:
- Rare, often starts in childhood or adolescence
- Presents with tender nodules under the skin, usually on the thighs and lower legs. May also have larger inflammatory plaques, purpura, blistering and ulceration, livedo reticularis (vasculitic lesions)
- May have associated fever, malaise, myalgia, sorethroat, arthralgia, numbness, tingling, sensory disturbances, weakness, absent reflexes
- Relapsing / remitting course
- Cutaneous PAN is chronic but relatively benign, systemic PAN can be life-threatening

Associations:
- Systemic polyarteritis nodosa can involve the liver, kidney, heart, lung, GI tract, musculoskeletal and nervous systems

Investigations:
- Biopsy will show pan-arteritis, septal panniculitis. Usually minimal inflammation in lobule
- Bloods including ANCA
- Need to rule out microaneurysms of systemic PAN with renal / mesenteric angiogram

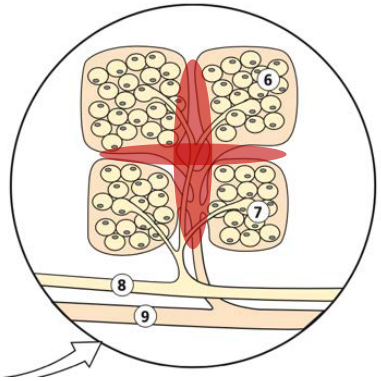
Management:
- Treat any infective trigger or secondary infection
- Multidisciplinary input if visceral organ involvement
- Wound care if required
- Oral corticosteroids, colchicine, IVIG, cyclophosphamide
- TNF-alpha or IL6 blockers have been described



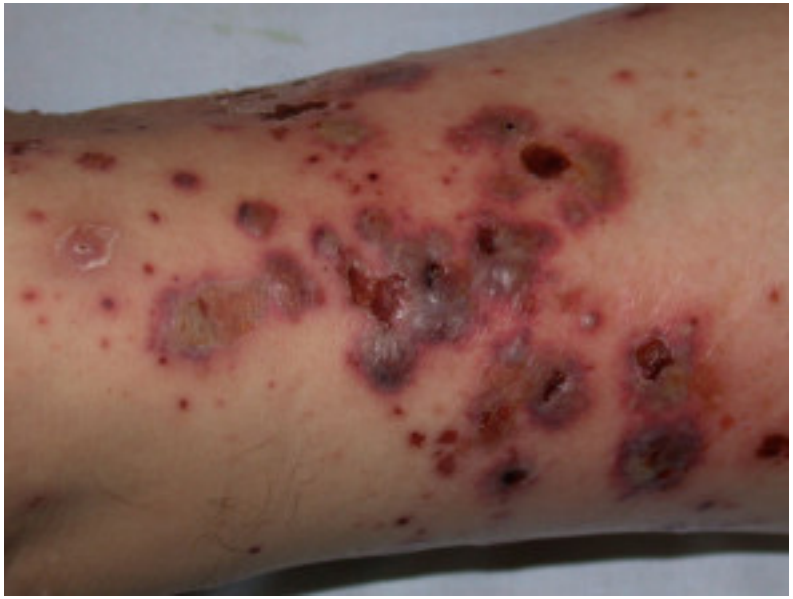
CAN ULCERATE

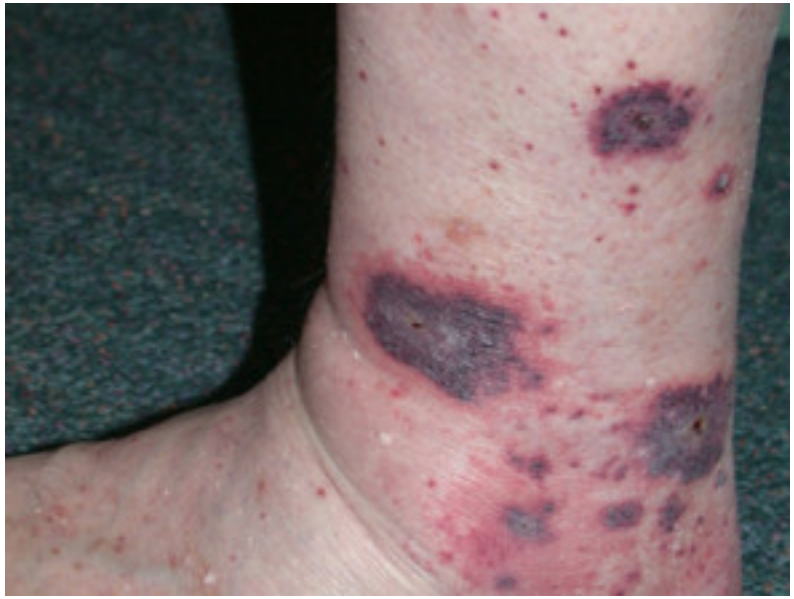
Bolognia, Rook, https://dermnetnz.org/topics/cutaneous-polyarteritis-nodosa/

Leukocytoclastic vasculitis



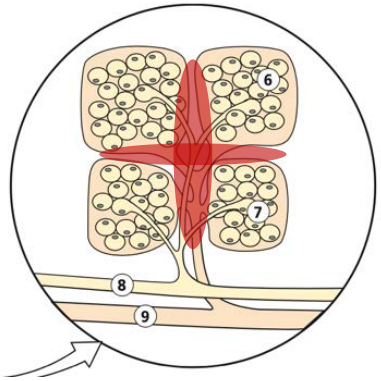
Cutaneous small vessel vasculitis (many causes, covered elsewhere)
Can lead to septal panniculitis, usually has associated overlying cutaneous vasculitic lesions





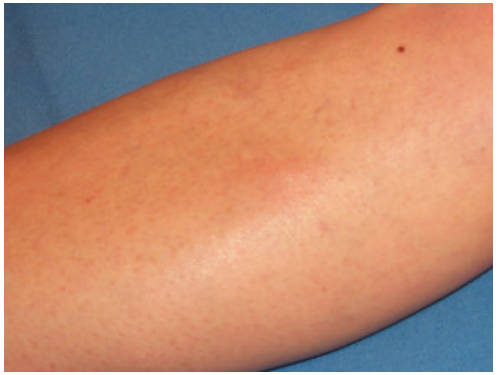
https://dermnetnz.org/topics/cutaneous-vasculitis/

Superficial thrombophlebitis



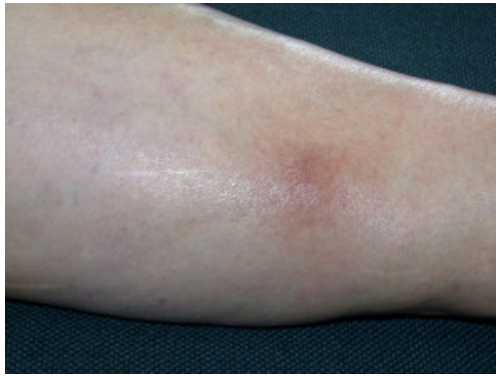
Pathogenesis:
- Inflammation of a superficial vein due to thrombus, can lead to septal panniculitis
- May occur as a result of damage to vessel wall (e.g. after cannulation), abnormal blood flow, primary and secondary hypercoagulable states

Epidemiology / presentation:
- Can occur spontaneously, but risk factors = varicose veins / venous insufficiency of the lower limbs, trauma or infusion sites, clotting abnormalities (see below), and pregnancy, OCP, smoking, complications of sclerotherapy, etc.
- Mild swelling, erythema and tenderness along part of the affected vein
- Vein may feel like hard, rope-like cord. May have associated PIH if chronic



Associations:
- Primary hypercoagulable states: Deficiency of Protein C, Protein S, Heparin co-factor II, Antithrombin III, Factor XII, Tissue plasminogen activator, Factor V Leiden
- Secondary hypercoagulable states: paraneoplastic (assoc. malignancy), Behcet syndrome, Buerger disease, HIV-associated immune reconstitution syndrome (IRIS), secondary syphilis, sepsis

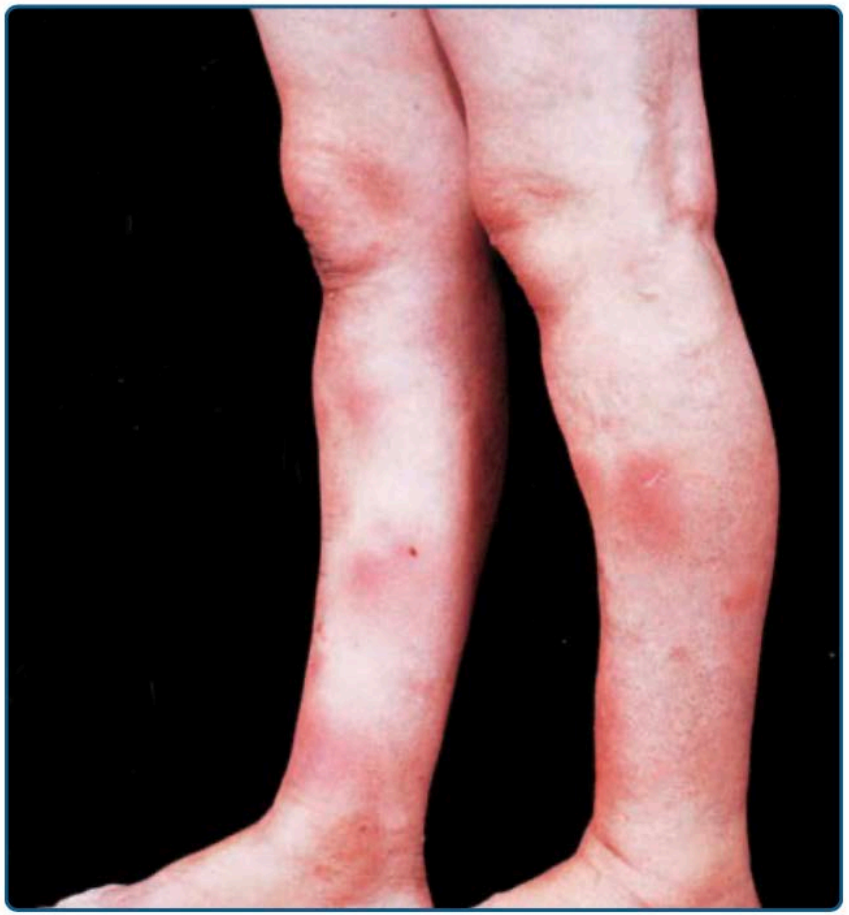
Investigations:
- Histology shows thrombosis and associated inflammation around large veins of the septa in upper subcutaneous tissue, with little to no involvement of adjacent fat lobule
- Coag. screen if clinically indicated, malignancy screen etc. if clinically indicated



Management:
- Mild cases may not need treatment, may resolve within 3-4 weeks
- Elevation, compression
- Analgesia if required
- Treat any associations
- Surgical excision and ligation if septic thrombophlebitis

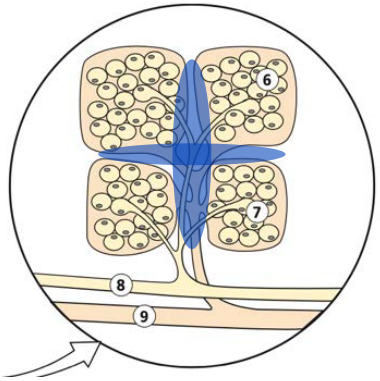
Rook, https://dermnetnz.org/topics/superficial-thrombophlebitis/

- 40 year old woman, presents with 1/52 history of tender nodules on the lower legs, associated with mild fever and fatigue
- History of “sore throat” 2-3 weeks ago
- Other questions? Investigations?
- DDx?



Fitzpatrick

Septal without vasculitis



- Granuloma annulare (deep)
- Rheumatoid nodules
- Erythema nodosum
- NLD
- Scleroderma/Morphoea

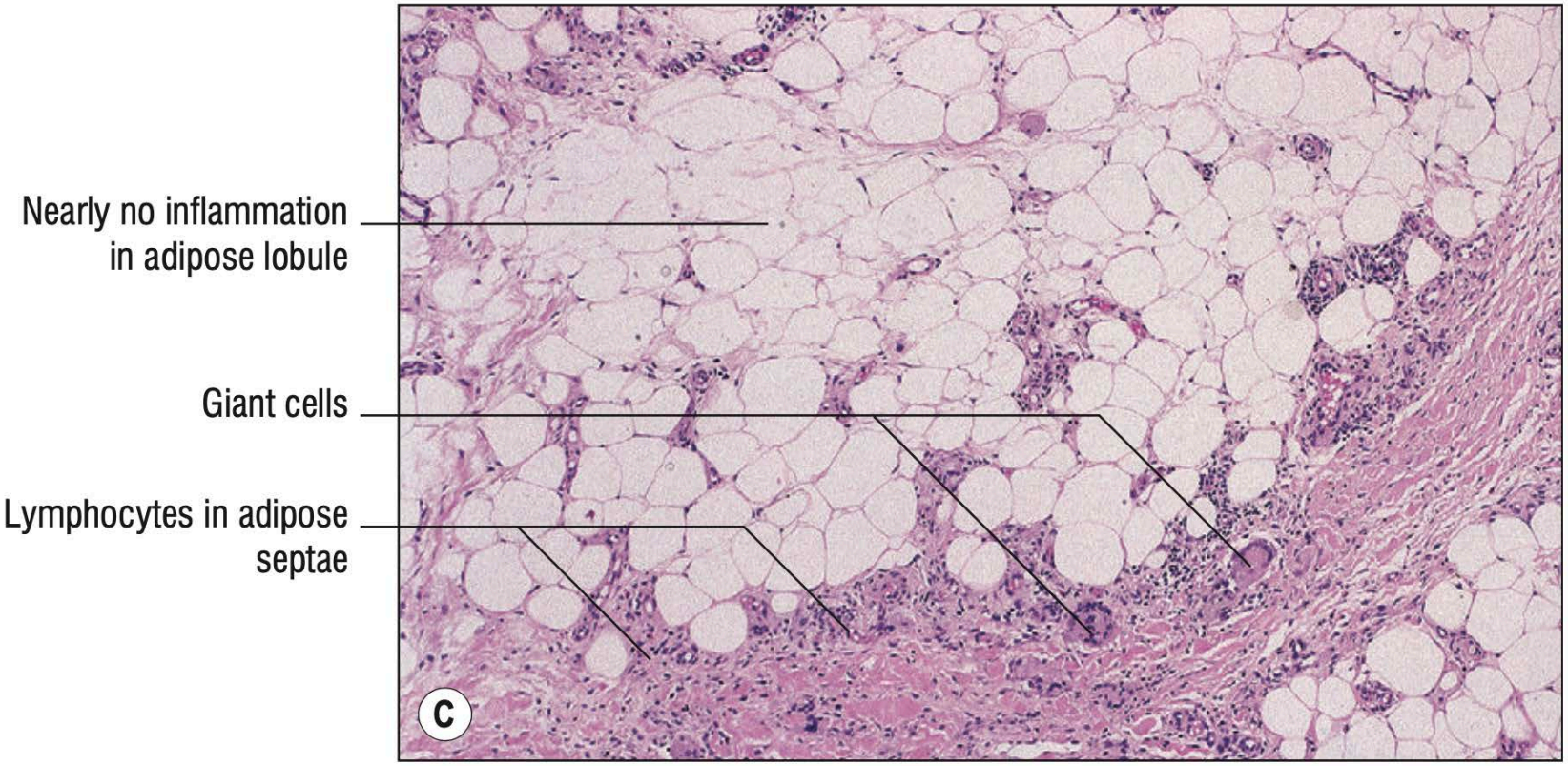
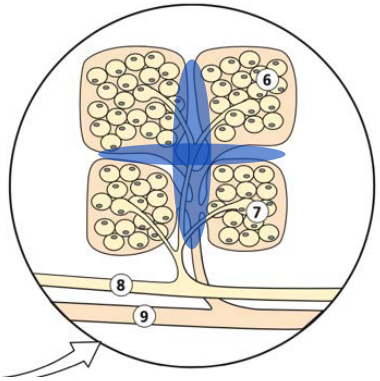


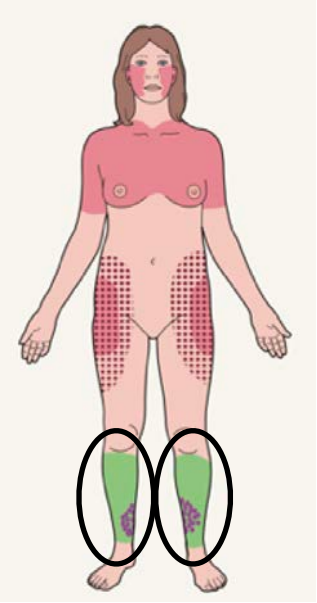
Fig. 16.1 C Erythema nodosum (high mag.).

Erythema nodosum



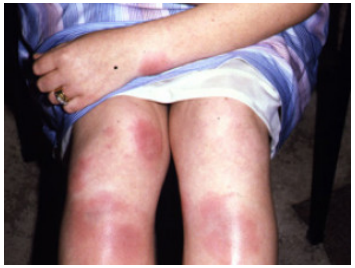
Pathogenesis:
- Hypersensitivity reaction causing septal panniculitis
- Mechanism not well understood

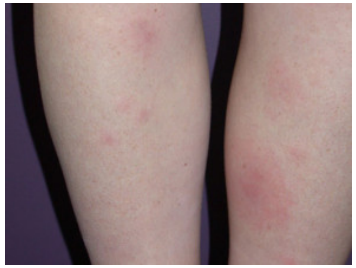
Epidemiology / presentation:
- Most common in women between 25 and 40, 3-6x more common in women (but equal male/female in adolescents and younger)
- Presents as tender red nodules on the anterior shins bilaterally. Less commonly may affect the thighs and forearms. No ulceration
- May be accompanied by fever and joint pain
- Resolve to appear more like bruises (erythema contusiformis)
- Most cases resolve in days to weeks, but may occasionally be persistent for months



Associations:
- Multiple know triggers / associations, such as infections, drug, inflammatory condition, or malignancy (see next slides)

Investigations:
- Histology shows septal panniculitis without vasculitis (but may have secondary vasculitis if neutrophils + ++), early lesions may have Miescher microgranulomas (small, well formed clusters of histiocytes around a central banana-shaped cleft). As lesions progress, septa become widened and have mixed infiltrate, including granulomas
- Other investigations to consider:
    - FBE, CRP (infectious and inflammatory causes)
    - CXR (sarcoid and tuberculosis)
    - Throat swab and ASOT
    - Viral serology
    - Stool OCP
    - QF gold





Fitzpatrick, Rook, Bolognia, https://dermnetnz.org/topics/erythema-nodosum/

CAUSES OF ERYTHEMA NODOSUM		
Incidence	**Cause**	**Comments**
Most common	Idiopathic	Still the largest single category, accounting for a third to a half of cases
	Streptococcal infections, especially of the upper respiratory tract	The largest single infectious cause
	Other infections: Viral upper respiratory tract infections Bacterial gastroenteritis – *Yersinia* > *Salmonella, Campylobacter*	Overall, infection may account for a third or more of cases
	Coccidioidomycosis	Erythema nodosum is associated with a lower incidence of disseminated disease
	Drugs*	Especially estrogens and oral contraceptive pills; also sulfonamides, penicillin, bromides, iodides; occasionally, TNF inhibitors, BRAF inhibitors^
	Sarcoidosis**	10–20% of cases in some series
	Inflammatory bowel disease	Crohn disease has a stronger association with erythema nodosum than does ulcerative colitis
Uncommon	Infections: *Brucella melitensis* *Chlamydophila*† *pneumonia* *Chlamydia trachomatis* *Mycoplasma pneumoniae* *Mycobacterium tuberculosis* *Histoplasma capsulatum* Hepatitis B virus‡	
	Neutrophilic dermatoses: Behçet disease Sweet syndrome	"Erythema nodosum" in Behçet disease more closely resembles erythema induratum (nodular vasculitis)
	Acne fulminans, including isotretinoin-associated	
	Pregnancy	
Rare	Pernicious anemia	
	Diverticulitis	
	Infections: *Neisseria gonorrhoeae*, *N. meningitidis* *Escherichia coli*, *Bartonella henselae*, *Bordetella pertussis* *Treponema pallidum* Dermatophytes (kerion), *Blastomyces dermatitidis* HIV Giardiasis, amoebiasis (abscesses)	*Erythema nodosum leprosum* is a different disease that is characterized by a cutaneous small vessel vasculitis
	MonoMAC syndrome (*GATA2* mutations)	
	Malignancy, most often acute myelogenous leukemia, Hodgkin disease	May overlap with Sweet syndrome
	Lupus erythematosus	One of several forms of panniculitis reported in LE, in addition to lupus panniculitis

*To be distinguished from panniculitis that can develop at sites of injection of medications, e.g. glatiramer acetate, interferon-β, phytonadione (vitamin K), interleukin-2, heparin (eosinophilic panniculitis), pentazocine, vaccines (e.g. tetanus).

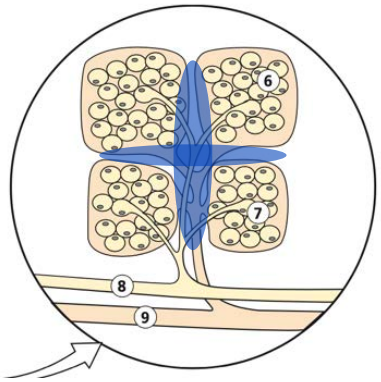
**Löfgren syndrome is an acute, spontaneously resolving form of sarcoidosis characterized by erythema nodosum, hilar lymphadenopathy, fever, polyarthritis and uveitis.

^Also lobular neutrophilic panniculitis.

†Previously referred to as *Chlamydia*.

‡Erythema nodosum secondary to the hepatitis B vaccine has also been reported.

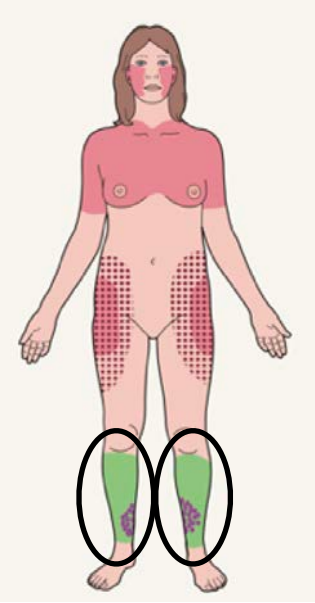
Causes of erythema nodosum



Behcet syndrome
Estrogens
Drugs (e.g. OCP, sulphonamides, penicillin, bromides, TNFi, BRAFi)

Recent infection (strep, yersinia)
Enteropathy (Crohns, UC)
Sarcoid (e.g. Lofgren syndrome)
Tuberculosis

also haematologic malignancy



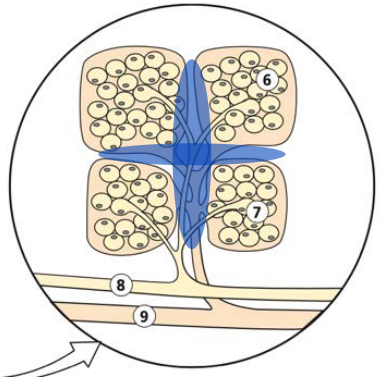
TREATMENT RECOMMENDATIONS FOR ERYTHEMA NODOSUM	Rx
In all patients	Discontinue possible causative medications Diagnose and treat underlying cause Bed rest and leg elevation Compression
First-line	Nonsteroidal anti-inflammatory medications (3)* Salicylates Potassium iodide (2) (see Table 100.6)
Second-line**	Colchicine (3)# Infliximab (3)## Hydroxychloroquine (3)^ Adalimumab (3)^ Etanercept Mycophenolate mofetil (3)
Third-line**	Systemic corticosteroids (3) Thalidomide (3)^^ Cyclosporine (3) Dapsone (3)

*May trigger a flare of inflammatory bowel disease.
**Immunosuppressives to be used only if underlying infection has been excluded and/or treated.
#Helpful for erythema nodosum associated with Behçet disease.
##Helpful for erythema nodosum associated with inflammatory bowel disease.
^Helpful for chronic erythema nodosum.
^^May transiently exacerbate erythema nodosum associated with Behçet disease.

Table 100.5 Treatment recommendations for erythema nodosum. Key to evidence-based support: (1) prospective controlled trial; (2) retrospective study or large case series; (3) small case series or individual case reports.

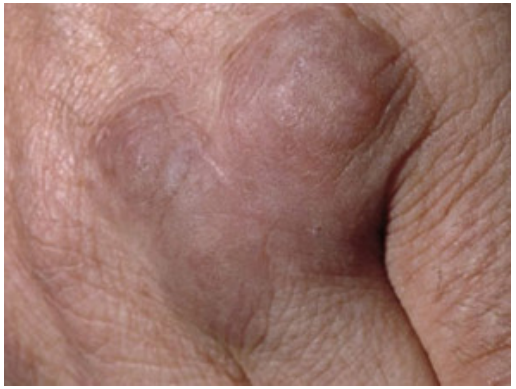
Granuloma annulare (deep)

a.k.a. subcutaneous granuloma annulare

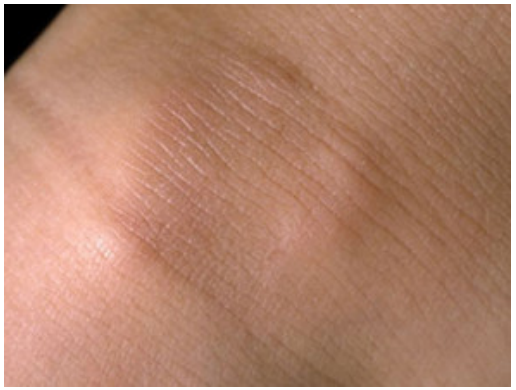


Pathogenesis:
- Specific clinical pattern of GA, possible hypersensitivity reaction to subcutaneous antigen

Epidemiology / presentation:
- Rare condition
- Most commonly occurs in children, presents as rubbery nodules on scalp margins, fingertips and shins
- May look similar to rheumatoid nodules (but no RA)
- May appear in isolation (~75% panniculitis only) or associated with classical dermal papular lesions (~25%)



Associations:
- GA has reported associations with autoimmune thyroiditis, diabetes, hyperlipidaemia, lymphoma, HIV infection, solid tumours
Very rarely can extend to deeper tissues and cause destructive arthritis and limb deformity

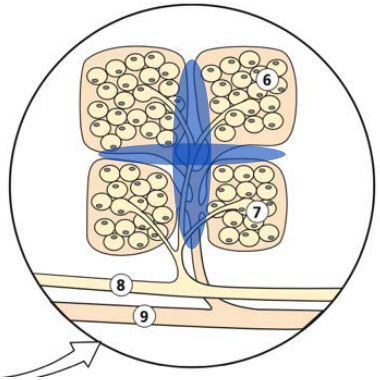


Investigations:
- Histology shows septal panniculitis with basophilic degeneration of collagen bundles with peripheral palisading granulomas, may also include multinucleate giant cells. Central necrobiotic areas contain increase mucin and nuclear dust from neutrophils

Management:
- May resolve spontaneously
- Intralesional steroids
- Systemic steroids
- Isotretinoin, HCQ, Mtx, PI, Dapsone, Pentoxifylline, Allopurinol, monthly antibiotics (rifampicin, ofloxacin, minocycline), cyclosporin, TNF-alpha inhibitors, tofacitinib

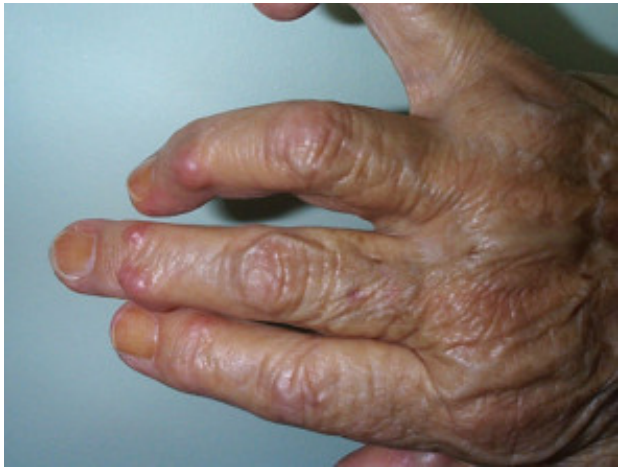
Rook, https://dermnetnz.org/topics/granuloma-annulare/

Rheumatoid nodules



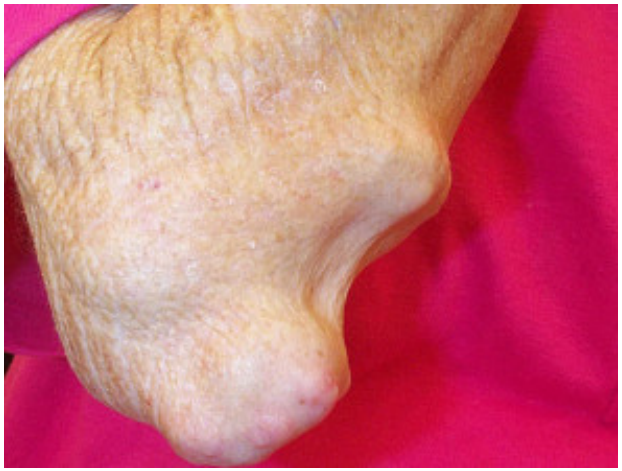
Pathogenesis:
- Extra-articular manifestation of rheumatoid arthritis, pathophysiology unknown

Epidemiology / presentation:
- Usually found in proximity to joints or extensor surfaces, or areas subjected to mechanical pressure, but can also develop in pleura or meninges
- Variable size and consistency, usually asymptomatic but may be tender



Associations:
- Rheumatoid arthritis
- Accelerated rheumatoid nodulosis (ARN) is a clinical variant, often in Mtx treated patients

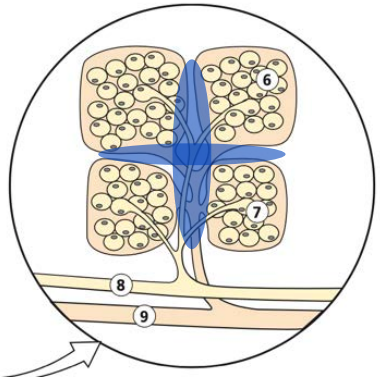
Investigations:
- Histology: early lesions show granulation tissue surrounded by mononuclear cells and fibroblasts in the septae. Later lesions show central areas of degenerate collagen. May have mixed infiltrate of multinucleate giant cells, lymphocytes, plasma cells, mast cells and eosinophils at the periphery. In late stages there may be extensive fibrosis and cystic degeneration



Management:
- Multidisciplinary input with Rheumatology
- Management of RA
- If ARN, can try HCQ, colchicine, sulfasalazine

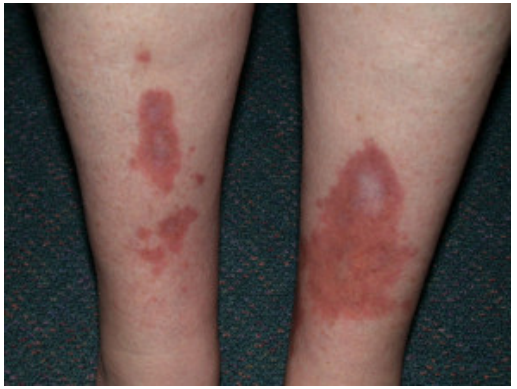
Rook, https://dermnetnz.org/topics/rheumatoid-arthritis/

Necrobiosis lipoidica



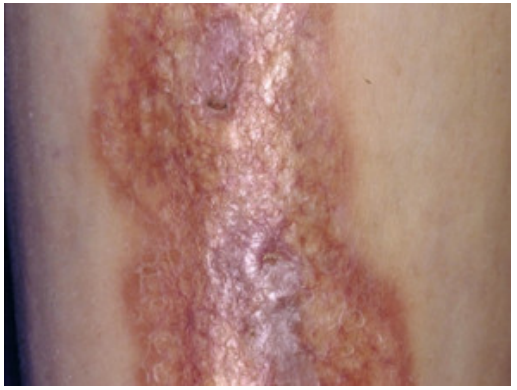
Pathogenesis:
- Cause unknown. Usually affects insulin-dependent diabetics, but can more rarely occur in the absence of diabetes

Epidemiology / presentation:
- 3-5x more common in females than males
- 0.3% of diabetics (type 1 or 2) have necrobiosis lipoidica, and 11-65% of NL patients have diabetes or pre-diabetes. Diabetes can be well controlled or poorly controlled
- Presents as one or more yellowish brown patches or plaques over the shins bilaterally that develop slowly over several months. Centre of the patch becomes shiny, pale, thinned, with associated telangiectasia
- Minor injuries can cause ulceration (painful or painless), which may lead to secondary infection



Associations:
- Diabetes, obesity, hypertension, dyslipidaemia, thyroid disease

Investigations:
- Histopathology shows septal panniculitis with characteristic granulomatous inflammatory reaction around destroyed collagen. Not a true panniculitis as it's an extension of the dermal process. May look histologically similar to GA or rheumatoid nodules
- Fasting glucose, HbA1c

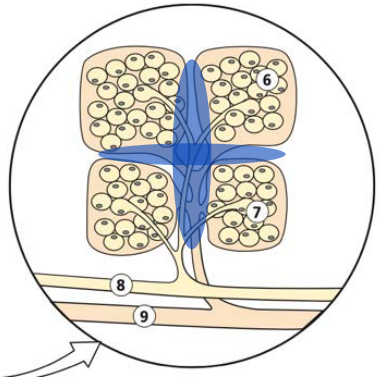


Management:
- Treat any secondary infection
- Topical steroids, can use under occlusion
- ILKA, systemic prednisolone
- Aspirin / dipyridamole, pentoxifylline, niacinamide
- PUVA, PDT

CAN ULCERATE

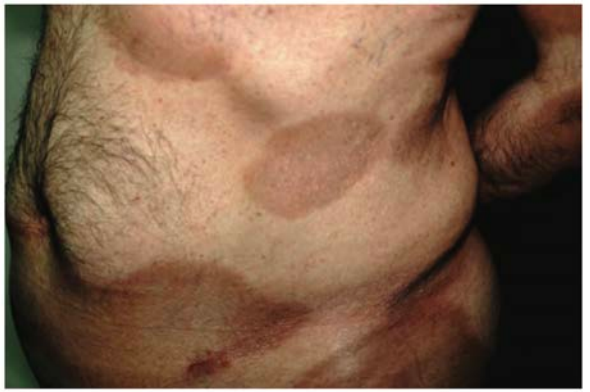
Rook, Bolognia, https://dermnetnz.org/topics/necrobiosis-lipoidica/

Scleroderma / Morphoea
(Deep morphoea)

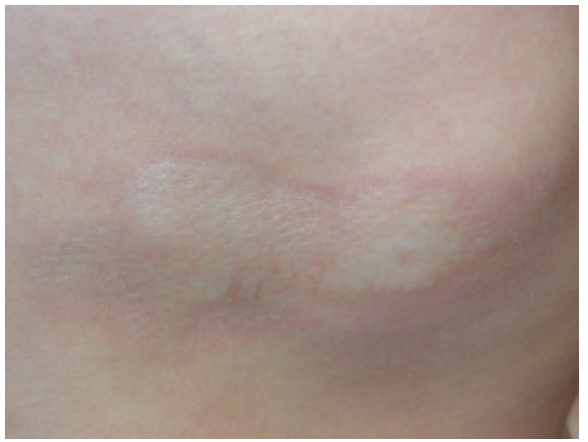


Pathogenesis:
- As for morphoea, but involving subcutaneous connective tissue and fat (may also involve overlying dermis)
- HLA-DRB1*04:04 and HLA-B*37 are associated with an increased risk of morphoea

Epidemiology / presentation:
- Rare, estimated to have an incidence of 1–3 per 100,000 children
- Three times more common in females compared to males, often begins in childhood
- May develop from external trigger (insect bite, injection, vaccination, friction, surgery, radiotherapy, trauma)
- Presents as indurated plaques (dermal sclerosis), which may have puckered, cobblestone or orange peel appearance (peau d'orange)
- May be guttering along blood vessels (groove sign). (Eosinophilic fasciitis can be considered a form of pan sclerotic morphoea with deep fascial involvement
- Involvement over joints may cause joint pain and limit range of motion (contractures). May also constrict breathing over chest wall
- Patients with severe or generalised morphoea may have systemic symptoms (fatigue, lethargy, arthralgia, myalgia, Raynaud phenomenon)



Investigations:
- Biopsy may showed sharply squared off "cookie cutter" sign, atrophic epidermis, thickened hyalinised collagen in dermis with loss of appendages, thickened septae with hyalinised collagen and lymphoplasmacytic infiltrate (septal panniculitis, without vasculitis)
- Eosinophil count may be raised, ESR, CRP
- ANA positive but Scl-70 negative (to rule out systemic sclerosis)
- MRI to assess deeper tissue involvement



Management:
- ILKA if limited extent
- PUVA or UVA may be helpful, ECP also described
- Methotrexate, systemic corticosteroids, mycophenolate mofetil
- Hydroxychloroquine, cyclosporin, Abatacept, Tocilizumab also described

Rook, Bolognia, https://dermnetnz.org/topics/morphoea/

Summary: diagnostic approach to panniculitis

Clinical (history, examination):

Some forms of panniculitis will have classic clinical features (e.g. lupus, DM, morphoea), or distribution/morphology (e.g. calciphylaxis, alpha-1-antitrypsin panniculitis)
vs. ill-defined, lower legs, etc.

Histology:

Ensure deep enough biopsy (usually need incisional biopsy)
Septal vs lobular vs mixed, with or without vasculitis
Other classic features (see next slide)

Other investigations

A few histology pearls from Bolognia

Medium sized vessel with lobular or mixed - **erythema induratum (nodular vasculitis)**

Fat necrosis with saponification and “calcium soap” formation - **pancreatic**

Needle shaped clefts within lipocytes - **sclera neonatorum, subcutaneous fat necrosis of the newborn, or post-steroid panniculitis**

Lymphoplasmacytic appearance of infiltrate - **connective tissue disease (but can also be T-cell lymphomas)**

Central nidus of inflammation or evidence of needlestick injury - **traumatic or factitial panniculitis**

Lobular panniculitis with predominance of neutrophils - **infection induced, assoc. with IBD or RA, Sweet syndrome, traumatic (less so in pancreatic or alpha-1-antitrypsin)**

Membranocystic changes in subcutis - **lipodermatosclerosis**

Widespread necrosis, haemorrhage, neutrophilic aggregates - **infection**

Monotonous or atypical cells - **T-cell lymphomas or other malignancies**

Large cells with cytophagic activity - **consider γ/δ T-cell lymphoma**

UNUSUAL OR RECENTLY DESCRIBED FORMS OF PANNICULITIS			
Type of panniculitis	**Clinical features**	**Microscopic findings**	**Comments**
Crystal deposition panniculitis	Red nodules, sometimes with necrosis; may have drainage; legs and elsewhere	Necrotizing and/or granulomatous panniculitis; calcium oxalate crystals in subcutaneous vessels; subcutaneous deposits of sodium urate crystals	Oxalosis: primary (inherited) or secondary (chronic renal failure) Urate deposition: may be an isolated cutaneous finding in gout
Idiopathic palmoplantar hidradenitis (see Ch. 39)	Sudden onset of painful erythematous nodules; soles > palms Self-limited	Neutrophilic eccrine hidradenitis	Precipitated by trauma (mechanical, thermal) Mimicked by erythema nodosum, pseudomonas hot-foot syndrome, cold panniculitis
Sweet panniculitis (subcutaneous Sweet syndrome)*	Erythematous nodules that may be painful; extremities; associated with leukemias (e.g. AML, hairy cell leukemia), treatment of acute promyelocytic leukemia with all-*trans*-retinoic acid, and, rarely, solid tumors	Predominantly neutrophilic lobular panniculitis, without vasculitis; immature myeloid forms have been described	Must exclude other neutrophil-rich forms of panniculitis, such as infection-induced, traumatic, alpha-1 antitrypsin deficiency and pancreatic panniculitides
Panniculitic bacterid	Sudden onset of tender subcutaneous nodules; lower extremities; polyclonal hypergammaglobulinemia, cold agglutinins, cryofibrinogens	Lobular panniculitis, predominantly neutrophils with microabscesses; angiopathy; extravascular granulomas	Triggered by non-tuberculous infections; underlying disorders include atopy, antiphospholipid antibody syndrome
Plasma cell panniculitis	Hyperpigmentation and induration; trunk and extremities	Sclerosis of subcutaneous septa; plasma cells prominent component of infiltrate	Not a single entity; manifestation of morphea profunda, other autoimmune connective tissue disorders, and postirradiation pseudosclerodermatous panniculitis
Panniculitis of Lyme disease	Tender nodules or diffuse fasciitis; fever, chills, photophobia, polyarthritis	Acute septal panniculitis; may contain eosinophils, plasma cells; lymphocytic vasculopathy	Detection of *Borrelia* spp. in tissues; positive serologies confirm the diagnosis
Fasciitis–panniculitis syndrome	Subcutaneous induration, sometimes with regional pain	Chronic inflammation, accompanied by replacement of fat lobules by fibrous tissue; thickening of fascia	Term used primarily in the rheumatologic literature; encompasses several autoimmune connective tissue diseases; also described as a paraneoplastic syndrome with hematologic, pancreatic and gastrointestinal malignancies
Atypical lymphocytic lobular panniculitis	Recurrent, infiltrative plaques; lower extremities, abdomen	Interstitial subcutaneous infiltrate with well-differentiated lymphocytes; no significant fat necrosis	Molecular studies show clonal or oligoclonal profile; no progression to lymphoma; considered T-cell dyscrasia
Infantile-onset panniculitis with uveitis and systemic granulomatosis	High fever, anemia, hepatosplenomegaly, uveitis, arthritis	Histiocytic lobular panniculitis, with lymphocytes and neutrophils initially; granulomas in later stage	Resemblance to Blau syndrome, but lacks *NOD2/CARD15* mutations; may respond to TNF inhibitors

*Neutrophilic panniculitis also may precede the lipodystrophy of proteasome-associated autoinflammatory syndrome/CANDLE (chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature) syndrome (see Table 45.7).

Table 100.12 Unusual or recently described forms of panniculitis. AML, acute myelogenous leukemia; TNF, tumor necrosis factor.

Thanks!

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