PANNICULITIS: WHAT SHOULD A RHEUMATOLOGIST KNOW?

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DISCLOSURES

There are no commercial relationships relevant to this talk.

REFERENCES / EBM


WHEN TO CONSIDER THE DIAGNOSTIC CATEGORY OF PANNICULITIS

• When palpation of lesions is consistent with a depth of involvement that is in the subcutaneous tissue.
• In general, palpation is more important than visual inspection in suspecting the diagnostic category of panniculitis.

WHY IS PANNICULITIS CHALLENGING?

• “Panniculitis is diagnostically challenging for dermatologists and pathologists.” JW Patterson
• “The histologic diagnosis of panniculitis remains one of the most difficult areas in dermatopathology.” JE Fitzpatrick

• Insufficiently specific clinical appearance – While there are numerous clinical conditions that can cause panniculitis, most present as deep erythematous nodules and plaques.
• Limited ways in which the subQ fat can respond to inflammation – The fat contains only fat lobules, fibrous septa, nerves, and blood vessels.
WHY IS PANNICULITIS CHALLENGING?

• Panniculitis is relatively uncommon, and many entities that cause panniculitis are rare. With the possible exception of erythema nodosum, there are few large studies of specific entities.
• Some terminology is confusing and/or outmoded. In some cases, there has been too much splitting (e.g., different names for stasis panniculitis) and in others, too much lumping (e.g., the term “Weber-Christian disease” for a variety of conditions such as alpha-1-antitrypsin deficiency, factitial panniculitis, lymphoma).

GENERAL ETIOLOGIC CATEGORIES AND EXAMPLES

• Infection (bacteria, mycobacteria, fungi)
• Trauma (cold injury, injections)
• Enzymatic destruction (pancreatic panniculitis)
• Malignancy (T cell lymphoma)
• Deposition (gout, calciphylaxis)
• Inflammation (erythema nodosum)

CLUES FROM CLINICAL EXAM: LOCATION

• Erythema nodosum – anterior lower legs
• Erythema induratum – posterior lower legs
• Stasis panniculitis – medial lower legs
• Alpha-1-antitrypsin deficiency – buttocks, flanks, and thighs
• Lupus panniculitis – face, scalp, upper arms, breasts, upper trunk, buttocks, thighs

CLUES FROM CLINICAL CONTEXT: EXAMPLES

• Pancreatitis – pancreatic fat necrosis
• Alpha-1-antitrypsin deficiency panniculitis
• Silicone injection – foreign body panniculitis
• Behçet’s – erythema nodosum
• Rheumatoid arthritis – rheumatoid nodule

CLUES FROM CLINICAL CONTEXT: AGE

• Subcutaneous fat necrosis of the newborn – uncommon; occasionally associated with hypercalcemia; usually resolves spontaneously
• Sclerema neonatorum – rare; severely ill premature neonates; poor prognosis
• Cold panniculitis – “popsicle panniculitis”; brown fat more susceptible; expect spontaneous resolution
DIAGNOSIS

• Diagnosis in some cases may reasonably be made by clinical evaluation.
• In many cases of acute panniculitis, and in most cases of chronic panniculitis, histology with clinical correlation is required.
• If biopsy is taken, it should include a generous sample of the subcutaneous tissue. That usually means excisional biopsy.

HISTOLOGIC EXAM

• Is the pathology primarily in the fat?
• Is the panniculitis predominantly septal, lobular, or mixed?
• What is the inflammatory infiltrate (e.g., neutrophils, lymphocytes, eos)?
• Is there vasculitis?
• Other (necrosis, organisms, crystals, calcium, foreign material)

HISTOLOGIC DX’S OF PANNICULITIS IN A DERMATOPATHOLOGY REFERRAL PRACTICE

• 40% erythema nodosum
• 31% panniculitis not otherwise specified
• 11% lupus panniculitis
• 7% stasis panniculitis
• 3% factitial
• 8% miscellaneous dx’s

**courtesy of James E Fitzpatrick, MD

OVERVIEW OF THIS PRESENTATION

• Common and less common (but not rare) panniculitides: erythema nodosum, stasis panniculitis, factitial panniculitis, erythema induratum, and lupus panniculitis
• Panniculitis related to rheumatic diseases: lupus, dermatomyositis, PSS / morphea, polyarteritis nodosa, sarcoidosis
• Focus on clinical and histologic findings

ERYTHEMA NODOSUM

• The most common form of panniculitis
• More common in women, more common in 2nd through 4th decades
• Crops of painful nodules on the shins and sometimes thighs and forearms
• Can have arthralgias, fever, and malaise
• Usually lasts a few weeks and resolves spontaneously, but recurs in some cases

ERYTHEMA NODOSUM – CAUSES

- Idiopathic – approximately 50%
- Streptococcal infection – probably the most common cause found
- Other infections: coccidiomycosis, bacterial gastroenteritis, viral URI, TB – prevalence of a particular infection depends on prevalence in the general population – e.g., TB more common in countries where TB is prevalent

ERYTHEMA NODOSUM – CAUSES

- Sarciodosis
- Inflammatory bowel disease, esp. Crohn’s
- Medications, esp. oral contraceptives
- Pregnancy (less common)
- Behcet’s (common in highly endemic areas – less common in the US)
- Sweet’s syndrome (less common)
- Many rare associations reported

ERYTHEMA NODOSUM HISTOLOGY

- Prototype of septal panniculitis
- Miescher microgranulomas (small septal granulomas with clear centers) not always present but near-pathognomonic of EN
- When inflammation is severe and extends into the lobules, definitive dx can be difficult
- Caveat: “On more than one occasion, I have seen an apparent EN with a septal pattern turn out to be PAN when the block was leveled.” JE Fitzpatrick

ERYTHEMA NODOSUM WORK-UP

- Biopsy not always indicated. E.g., young, healthy person with strep infection and self-resolving EN – Bx leaves significant scar and may be slow to heal.
- Search for underlying cause should be directed by clinical context.
- More comprehensive evaluation may be appropriate for more prolonged and symptomatic EN.

ERYTHEMA NODOSUM RX

- Leg elevation, support stockings, NSAIDs for idiopathic cases
- Treat underlying cause if one is found.
- Many other treatments have been used for EN, but no clearly superior treatment.

STASIS PANNICULITIS

- Synonyms: lipodermatosclerosis, sclerosing panniculitis, hypodermitis sclerodermiformis, chronic panniculitis with lipomembranous changes
- Relatively common - likely underappreciated
- One or both lower legs, often medial
- Usually occurs in the setting of venous insufficiency
- Can occur in other areas of stasis, e.g., abdominal pannus or breasts
STASIS PANNICULITIS
• Acute phase may be confused with cellulitis or erythema nodosum
• Chronic phase has sclerosis
• On the legs, the sclerosis may give the appearance reminiscent of an inverted wine bottle or piano leg
• Biopsy not always necessary, but biopsy findings often sufficiently diagnostic when combined with clinical correlation.

FACTITIAL PANNICULITIS
• Induced by deliberate human action – usually self-induced
• Atypical locations, unusual shapes of lesions
• Patient typically denies self-injection
• Many substances reported – oils, urine, feces, drugs, food, etc.
• Lesions may be infected, suppurative, and/or ulcerative

FACTITIAL PANNICULITIS
• Unless the histologic diagnosis is straightforward, panniculitis specimens should be polarized to check for foreign material.
• In cases where oils have been injected, there may be holes where the material washed out during processing.

ERYTHEMA INDURATUM
• Nodules on lower legs
• Typically in young to middle-aged women
• Clinically similar to e nodosum, but more often on posterior lower legs – much clinical overlap
• There is a well-established association with TB, but EI can be idiopathic or associated with other infections or drugs.

ERYTHEMA INDURATUM
• Mixed lobular and septal panniculitis – sometimes entirely lobular – with vasculitis
• E induratum and nodular vasculitis used synonymously by some. Others reserve the term “nodular vasculitis” for cases unassociated with TB.
LUPUS PANNICULITIS

• Distinctive locations on face, scalp, upper trunk, breasts, upper arms, buttocks, thighs
• May have concurrent discoid lesions
• A small percentage, perhaps 10%, have SLE.
• Overlying skin often feels bound down.
• Atrophy is common and often disfiguring.
• Treatment is usually with antimalarials.

LUPUS PANNICULITIS

• Histologic findings are sometimes diagnostic, particularly if there is an overlying discoid lesion. In the fat, there is a lobular or mixed pattern of inflammation with hyaline necrosis, mucin, lymphocytes, and lymphoid follicles.
• Direct IF is often positive, but usually not necessary. The distinct distribution of lesions together with histologic findings consistent with, even if not diagnostic, for LEP usually suffice to make the diagnosis.

LE PANNICULITIS HISTOLOGIC DIFFERENTIAL DX

• Some cases of subcutaneous panniculitis-like T-cell lymphoma show vacuolar interface dermatitis and abundant dermal mucin in addition to a lobular lymphocytic infiltrate.

DERMATOMYOSITIS AND PANNICULITIS

• Panniculitis rare in DM
• Cases reported have a distribution and histology somewhat similar to lupus panniculitis
• Lipoatrophy without preceding lesions of panniculitis has been reported, mainly in juvenile DM, in association with hyperlipidemia and insulin resistance.
MORPHEA / PSS
- Inflammation in the fat may occur in both morphea and PSS, although it is typically more pronounced in morphea.
- Inflammation in morphea can be in the dermis (typical morphea), fat (subcutaneous morphea / deep morphea), or fat and fascia (deep morphea / morphea profunda).
- Eosinophilic fasciitis may coexist with morphea.

MORPHEA HISTOLOGY
- Septal panniculitis with lymphocytic infiltrate and dermal and subcutaneous sclerosis
- Histology often diagnostic, although distinguishing between different subtypes of morphea requires clinical correlation

POLYARTERITIS NODOSA
- Classic PAN: medium-sized vessels – ulceration, necrosis, livedo reticularis, SC nodules that may follow the course of arterioles
- Primarily cutaneous PAN: arterioles in SC and lower dermis – SC nodules and livedo reticularis
- EN in clinical differential of cutaneous PAN, but not expected to have livedo reticularis

CUTANEOUS PAN
- Associations reported include hepatitis B, hepatitis C, and Crohn’s disease
- Not associated with significant internal disease, but course may be chronic and relapsing
- Treated relatively conservatively

SARCOIDOSIS
- Erythema nodosum often occurs as part of Löfgren’s syndrome, with bilateral hilar lymphadenopathy and acute iridocyclitis – identifies a good prognostic subset
- Subcutaneous nodules may occur in sarcoidosis.

TAKE-HOME POINTS
- While biopsy is often important for diagnosis, the pathology report should rarely be used as the final or only determinant of diagnosis.
- Clinical and histologic correlation is often required.
- In patients who have rheumatic diseases, consider in the differential the more common forms of panniculitis, even if they are not related to the patient’s rheumatic disease.