Neutrophilic Vascular Reactions and Selected Autoinflammatory Syndromes

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Conflict of Interest

Advisory Boards/Honoraria
Amgen
Neutrophilic Vascular Reactions

- Cutaneous small vessel vasculitis
- Sweet’s syndrome
- Behcet’s Disease
- Bowel-associated dermatosis-arthritis syndrome
- Rheumatoid neutrophilic dermatosis
- Pyoderma gangrenosum

Fig. 27.1 Non-infectious neutrophilic dermatoses. Entities in the darker box are discussed in this chapter.

From Bologna, Jorizzo & Rapini: Dermatology 2e. © 2008 Elsevier, Ltd.
Possibilities for a patient who presents with a complex medical dermatosis and systemic signs and symptoms:

1. Clinicopathologic diagnosis of dermatosis integrates all findings eg. Sarcoidosis – skin, eye, lungs, etc
2. Clinicopathologic diagnosis reveals a reactive dermatosis – communication with internist or pediatrician will outline underlying medical conditions eg. Vasculitis
3. No direct relationship – eg. Scabies/Fibromyalgia
Step 1. – Clinicopathologic diagnosis - Caution influence of therapy on biopsy and clinical appearance

Step 2. – Assess the extent (internal manifestations of disease)

Step 3. – Assess for etiology

Step 4. - Therapeutic ladder
Sweet’s Syndrome

Key features

- Constitutional signs and symptoms such as fever and malaise
- Clinically, erythematous plaques are seen; occasionally they are bullous
- Histologically, dense perivascular neutrophilic infiltrate, edema and, infrequently, bullae; leukocytoclasia with minimal to no evidence of vasculitis
- Associated conditions include infections, malignancies (especially acute myelogenous leukemia), inflammatory bowel disease, autoimmune disorders, drugs and pregnancy
# Systemic Manifestations of Sweet’s Syndrome

<table>
<thead>
<tr>
<th>Category</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>COMMON (≥50%)</strong></td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td></td>
</tr>
<tr>
<td>Leukocytosis</td>
<td></td>
</tr>
<tr>
<td><strong>LESS COMMON (20–50%)</strong></td>
<td></td>
</tr>
<tr>
<td>Arthralgias</td>
<td></td>
</tr>
<tr>
<td>Arthritis: asymmetric, non-erosive, favors knees and wrists</td>
<td></td>
</tr>
<tr>
<td>Myalgias</td>
<td></td>
</tr>
<tr>
<td>Ocular involvement: conjunctivitis, episcleritis, limbal nodules, iridocyclitis</td>
<td></td>
</tr>
<tr>
<td><strong>UNCOMMON</strong></td>
<td></td>
</tr>
<tr>
<td>Neutrophilic alveolitis: cough, dyspnea and pleurisy; radiographic findings include interstitial infiltrates, nodules, pleural effusions</td>
<td></td>
</tr>
<tr>
<td>Multifocal sterile osteomyelitis (SAPHO syndrome)</td>
<td></td>
</tr>
<tr>
<td>Renal involvement (e.g. mesangial glomerulonephritis): hematuria, proteinuria, renal insufficiency, acute renal failure</td>
<td></td>
</tr>
<tr>
<td><strong>UNUSUAL/RARE</strong></td>
<td></td>
</tr>
<tr>
<td>Hepatitis</td>
<td></td>
</tr>
<tr>
<td>Acute myositis</td>
<td></td>
</tr>
<tr>
<td>Aseptic meningitis, encephalitis</td>
<td></td>
</tr>
<tr>
<td>Pancreatitis</td>
<td></td>
</tr>
<tr>
<td>Gastrointestinal involvement</td>
<td></td>
</tr>
</tbody>
</table>

Table 26.2 Systemic manifestations of Sweet’s syndrome. SAPHO, synovitis, acne, pustulosis, hyperostosis and osteitis.
Sweet’s Syndrome Related Articles 2018 alone

1. Clinicopathologic Expansion: SQ variant (not new); Hands (not new) Histiocytoid
   Full blown histopathologic LCCV (not new) Insect bite overlap on histopathology
2. Internal Involvement (Sterile neutrophilic lesions)
   Neuro Sweet’s, Upper respiratory tract, Lung
   Eye – optic nerve, keratitis
3. Etiology
   Many more drugs
   More cancers
   More infections (Sporotrichosis, leprosy, schistosomiasis
   More autoimmune diseases – SLE, thyroiditis
Behcet’s Disease
Behcet’s Disease

Key Features

- A multisystem, polysymptomatic disease
- Diagnosis is based on International Study Group criteria of recurrent oral ulceration, recurrent genital ulceration, ocular abnormalities (e.g., uveitis, retinal vasculitis) and cutaneous lesions
- Cutaneous findings range from sterile papulopustules and palpable purpura to erythema nodosum-like lesions
- Histologically, a neutrophilic angiocentric infiltrate with leukocytoclastic (early) or lymphocytic (late) vasculitis is the characteristic finding
### Systemic Manifestations of Behçet’s Disease

<table>
<thead>
<tr>
<th><strong>Ocular</strong> (Leading Cause of Morbidity) $^{30,32,33}$</th>
<th><strong>Neurologic</strong></th>
</tr>
</thead>
</table>
| - Occurs in 90% of patients; favors men, in whom it is more severe  
  - Can be painful and may lead to blindness  
  - Retinal vasculitis (more frequently associated with blindness)  
  - Posterior uveitis (most characteristic ocular finding)  
  - Anterior uveitis (Fig. 26.18), hypopyon  
  - Secondary glaucoma, cataracts  
  - Conjunctivitis, scleritis, keratitis, vitreous hemorrhage, optic neuritis | - Usually appears later during the evolution of the disease  
  - Associated with a poor prognosis  
  - Acute meningo-encephalitis which may resolve spontaneously  
  - Cranial nerve palsies  
  - Brainstem lesions that can induce swallowing difficulties, laughter and crying  
  - Pyramidal or extrapyramidal signs |

<table>
<thead>
<tr>
<th><strong>Joints</strong></th>
<th><strong>Vascular</strong></th>
</tr>
</thead>
</table>
| - Approximately 50% of patients develop arthritis  
  - In majority (~80% of patients), duration of attacks is <2 months  
  - Mono- or poly-arthritis and non-erosive  
  - Most commonly knees, wrists and ankles | Aneurysmal or occlusive arterial disease  
  - Superficial or deep venous thrombosis |

<table>
<thead>
<tr>
<th><strong>Gastrointestinal</strong></th>
<th><strong>Cardiopulmonary</strong></th>
</tr>
</thead>
</table>
| Abdominal pain and/or hemorrhage may be difficult to distinguish from IBD (see Table 26.12)  
  - Ulcerations* develop within the small bowel (in particular the ileocecal region) as well as the transverse and ascending colon and esophagus; perforation can occur | - Coronary arteritis, valvular disease, myocarditis  
  - Recurrent ventricular arrhythmias  
  - Pulmonary artery aneurysms |

<table>
<thead>
<tr>
<th><strong>Renal</strong></th>
<th><strong>Neurologic</strong></th>
</tr>
</thead>
</table>
| - Glomerulonephritis | - Usually appears later during the evolution of the disease  
  - Associated with a poor prognosis  
  - Acute meningo-encephalitis which may resolve spontaneously  
  - Cranial nerve palsies  
  - Brainstem lesions that can induce swallowing difficulties, laughter and crying  
  - Pyramidal or extrapyramidal signs |

*Resemble anogenital aphthae.

Table 26.11: Systemic manifestations of Behçet’s disease. IBD, Inflammatory bowel disease.
# INTERNATIONAL STUDY GROUP CRITERIA FOR THE DIAGNOSIS OF BEHÇET’S DISEASE

<table>
<thead>
<tr>
<th>Major criterion</th>
<th>Required features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent oral ulceration</td>
<td>Aphthous (idiopathic) oral ulceration observed by physician or patient, recurring at least three times in a 12-month period</td>
</tr>
</tbody>
</table>

**PLUS ANY TWO OF THE FOLLOWING MINOR CRITERIA:**

<table>
<thead>
<tr>
<th>Minor criterion</th>
<th>Required features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Recurrent genital ulceration</td>
<td>Aphthous genital ulceration or scarring, observed by physician or patient</td>
</tr>
<tr>
<td>Eye lesions</td>
<td>Anterior or posterior uveitis; cells in the vitreous by slit lamp examination; or retinal vasculitis observed by ophthalmologist</td>
</tr>
<tr>
<td>Cutaneous lesions</td>
<td>Erythema nodosum-like lesions observed by physician or patient; papulopustular lesions or pseudofolliculitis; or characteristic acneiform nodules observed by physician in postadolescent patient not on corticosteroids</td>
</tr>
<tr>
<td>Pathergy test*</td>
<td>Interpreted at 24–48h by physician</td>
</tr>
</tbody>
</table>

*Pathergy test is performed on the flexor forearm by obliquely inserting a 20–22-gauge sterile hypodermic needle to a depth of 5 mm ± an intradermal injection of 0.1 ml of normal saline. A positive reaction is defined as the development of a papule or pustule.

Table 26.13 International Study Group criteria for the diagnosis of Behçet’s disease.
Important Issues Regarding Behcet’s Disease

1. Do not overdiagnose complex aphthosis

2. Exclude HLA-B27 – associated sacroileitis spectrum disease and/or inflammatory bowel disease

3. Use a therapeutic ladder mucosal/ocular and other major systemic are at polar ends.
Key Features

- Constitution signs and symptoms are serum sickness-like.
- Cutaneous lesions include erythematous and purpuric papules and vesicles as well as nodular panniculitis.
- Associated polyarthritis and tenosynovitis.
- Histopathology includes dermal nodular perivascular neutrophilic infiltrate with edema and lobular neutrophilic and septal panniculitis.
- Bowel bypass syndrome was the preceding condition.

Clinical points regarding Bowel-Associated Dermatosis-Arthritis Syndrome

- Bowel surgery suggests blind loops – evaluate carefully with gastroenterologist.
- Inflammatory bowel diseases are important causes of this syndrome.
- While dermatologic therapeutic ladder is useful – management of underlying disease is the focus.
Pyoderma Gangrenosum

Key Features

- Four major clinical forms: ulcerative, bullous, pustular, and superficial granulomatous
- Initial lesion is often a pustule on an erythematous base or an erythematous nodule
- Characteristic lesion is an ulcer with a necrotic undermined border; the base may be purulent or vegetative
Key Features (Continued)

- Histologically, early lesions are difficult to distinguish from Behcet’s lesions.
- Associated with inflammatory bowel disease, arthritis, monoclonal gammopathy and other hematologic disorders.
### Proposed Diagnostic Criteria for Classic Ulcerative Pyoderma Gangrenosum

#### Major Criteria

1. Rapid\(^a\) progression of a painful\(^b\), necrolytic cutaneous ulcer\(^c\) with an irregular, violaceous and undermined border
2. Other causes of cutaneous ulceration have been excluded\(^d\)

#### Minor Criteria

1. History suggestive of pathergy\(^e\) or clinical finding of cribriform scarring
2. Systemic diseases associated with pyoderma gangrenosum\(^f\)
3. Histopathologic findings (sterile dermal neutrophilia, ± mixed inflammation, ± lymphocytic vasculitis)
4. Treatment response (rapid response to systemic corticosteroids)\(^g\)

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\(^a\)Characteristic margin expansion of 1 to 2 cm per day, or a 50% increase in ulcer size within 1 month.

\(^b\)Pain is usually out of proportion to the size of the ulceration.

\(^c\)Typically preceded by a papule, pustule or bulla.

\(^d\)Usually necessitates skin biopsy and additional evaluation (see Table 26.8) to exclude other causes (see Table 26.9).

\(^e\)Ulcer development at sites of minor cutaneous trauma.

\(^f\)Inflammatory bowel disease, arthritis, IgA gammopathy, or underlying malignancy.

\(^g\)Generally responds to prednisone (1–2 mg/kg/day) or another corticosteroid at an equivalent dosage, with a 50% decrease in size within 1 month.

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Table 26.7 Proposed diagnostic criteria for classic ulcerative pyoderma gangrenosum. Diagnosis requires both of the major criteria and at least two minor criteria\(^{26}\).
THE DIFFERENTIAL DIAGNOSIS OF PYODERMA GANGRENOSUM

EARLY INFLAMMATORY NON-ULCERATIVE STAGE
(PAPULES, PUSTULES, PLAQUES OR NODULES)

- Follicular infections (folliculitis, furuncle, carbuncle of bacterial, fungal or viral origin)
- Cellulitis or cellulitis-like lesion (bacterial, mycobacterial or fungal origin)
- Insect bite reaction
- Cutaneous T- and B-cell lymphomas
- Halogenoderma (iododerma or bromoderma)
- Ranniculitides (inflammatory, infectious, metabolic, neoplastic)
- Cutaneous polyarteritis nodosa
- Sweet’s syndrome (see Table 26.4 for additional entities)
- Behçet’s disease
- Bowel-associated dermatosis—arthritis syndrome

LATER ULCERATIVE OR VEGETATIVE STAGE

- Infections – streptococcal synergistic gangrene, botryomycosis, echyma gangrenosum, gummata treponemal ulcers, cutaneous lesions of the deep mycoses (e.g. blastomycosis, coccidioidomycosis, paracoccidioidomycosis, chromomycosis) and atypical and typical mycobacterial infections
- Parasitic infections – leishmaniasis, amebiasis, schistosomiasis
- Vascular diseases – ulcerations due to venous hypertension, arterial insufficiency, non-septic emboli, hemoglobinopathies, and thrombosis (secondary to hypercoagulability; see Ch. 105)
- Vasculitis – cutaneous polyarteritis nodosa, microscopic polyangiitis, granulomatous vasculitides (Wegener’s granulomatosis, Churg–Strauss syndrome, temporal arteritis), autoimmune connective tissue disease (systemic lupus erythematosus, rheumatoid arthritis) and Behçet’s disease
- Malignancy – squamous cell carcinoma, basal cell carcinoma, cutaneous T- and B-cell lymphoma
- Miscellaneous – brown recluse spider bite, ulcerative necrobiosis lipoidica, pemphigus vegetans of the Hallopeau or Neumann type, blastomycosis-like pyoderma, non-healing surgical wound, factitious ulcers, ulcers in patients with Chédiak–Higashi syndrome and leukocyte adhesion deficiency

Table 26.9 The differential diagnosis of pyoderma gangrenosum (PG)\textsuperscript{17,20}. In a series of 95 patients misdiagnosed with PG, the most common etiologies were vascular (venous or arterial; 28), vasculitis (21), malignancy (16), infection (14) and drug-induced or exogenous tissue injury (13).\textsuperscript{25}
Clinical Points regarding Pyoderma Gangrenosum

- Most referred patients have large ulcers; but no inflammation – “Gulliver’s sign” (a pterygium)
- Literature is similar to Sweet’s regarding expansion of systemic manifestations and etiology
- Re-exclude mimics (diagnosis of exclusion but also contaminants on culture)
- Especially: Wegener’s, histoplasmosis, atypical AFB, Sporotrichosis, factitial disease
Neutrophilic Vascular Reactions: Update 2019

Patient Evaluation: Overview

- Confirm clinical diagnosis histopathologically
- Assess extent of disease (less critical than vasculitis)
- Attempt to establish etiology
- Therapeutic ladder
Neutrophilic Vascular Reactions: Update 2019

Etiology
Work with a colleague, generally in internal medicine, to perform sequential evaluations that include history and physical examination not just laboratory tests.

Categories include:

- **Drugs:** (be careful: association does not prove causation!)
- **Infections:** Viral, bacterial, Deep fungal, AFB, other
- **Disease with immune complexes:** Autoimmune connective tissue diseases, other autoimmune, inflammatory bowel disease, autoimmune liver disease, Behcet’s disease, malignancy especially myelodysplastic diseases. (Curth’s postulates)
Neutrophilic Vascular Reactions: Update 2019
Therapeutic Ladder:
Non-ulcerative Cutaneous Lesions

- No Therapy
- Topical therapies
  - (access to site of pathology)
- Gradient Support Hose
- Antibiotics
- Pentoxifylline
- Colchicine
- Dapsone/Sulfapyridine
- Combination Colchicine/Dapsone
Neutrophilic Vascular Reactions: Update 2019

Therapeutic Ladder: Ulcerative Cutaneous Lesions or Minimal Systemic Disease

- Various topical (from corticosteroids to dapsone to metronidazole to imiquimod)
- Weekly Pulse Methotrexate
- Prednisone with slow taper
- Thalidomide
Neutrophilic Vascular Reactions Update: 2019
Therapeutic Ladder - More Severe Diseases

- Prednisone alone or in combination (1 or 2 depending on subset)
- Pulse Prednisone
- Azathioprine
- Cyclophosphamide; pulse or daily (1-for larger vessel vasculitis)
- Mycophenolate mofetil
- Chlorambucil
- Cyclosporine
- TNF alpha inhibitors
- IL-12/23 antagonists
- IL-1 antagonists
- Leflunomide
- Rituximab (2-Mostly SLE patients with vasculitis)
- Gevokizumab (anti IL-1beta)
- Countless treatments aimed at underlying diseases
<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>INFLAMMATORY DISEASE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild disease and/or adjunctive</td>
<td></td>
<td></td>
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<tr>
<td>therapy</td>
<td></td>
<td></td>
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<tr>
<td>Superpotent topical corticosteroids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intrallesional corticosteroids</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Topical tacrolimus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oral antibiotics (e.g. sulfonamides, minocycline)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Colchicine</td>
<td>0.6 mg po thrice daily</td>
<td>3</td>
</tr>
<tr>
<td>Dapsone</td>
<td>50–150 mg po daily</td>
<td>3</td>
</tr>
<tr>
<td>Combination colchicine/dapsone</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Clofazimine</td>
<td>100–400 mg po daily</td>
<td>2</td>
</tr>
<tr>
<td>Other (e.g. oral potassium iodide, intrallesional cyclosporine, topical cromolyn sodium, nicotine patch or cream)</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>More severe disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td>60–120 mg po daily usual starting dose (including split-dose), with taper to alternate days</td>
<td>2</td>
</tr>
<tr>
<td>Methylprednisolone</td>
<td>1 g daily for 3–5 days (IV pulse)*</td>
<td>3</td>
</tr>
<tr>
<td>Thalidomide</td>
<td>50–150 mg po nightly</td>
<td>2</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>2.5–5 mg/kg po daily</td>
<td>2</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>0.1–0.2 mg/kg po daily</td>
<td>3</td>
</tr>
<tr>
<td>TNF-α inhibitors</td>
<td>Infliximab 5 mg/kg IV at weeks 0, 2 and 6; adalimumab 80 mg sc as initial dose then 40 mg sc weekly or every other week; etanercept 50–100 mg sc weekly (in 1 or 2 doses)</td>
<td>1 (infliximab); 3 (adalimumab); 3 (etanercept)</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>2.5–25 mg po or IM weekly</td>
<td>3</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>50–100 mg po twice daily</td>
<td>3</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>1–1.5 g po twice daily</td>
<td>3</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Variable oral (50–200 g daily) or IV pulse (500–1000 mg monthly) dosing</td>
<td>3</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>4–6 mg po daily</td>
<td>3</td>
</tr>
<tr>
<td>IMg</td>
<td>2–3 g/kg IV monthly (given over 2–5 consecutive days)</td>
<td>3</td>
</tr>
<tr>
<td>Granulocyte apheresis, plasmapheresis</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Total colectomy (severe chronic ulcerative colitis)</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td><strong>NON-INFLAMMATORY DISEASE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Bio-occlusive dressings</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Compression, limb elevation</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Followed by daily oral prednisone.

1Especially in patients with Behçet’s disease.

2Especially in patients with inflammatory bowel disease.

350–70% response rate.

4Often used in combination with other agents or as maintenance therapy.

Table 26.10 Therapeutic ladder for the treatment of pyoderma gangrenosum.28,29 Key to evidence-based support: (1) prospective controlled trial; (2) retrospective study or large case series; (3) small case series or individual case reports.
### Treatment of Behçet’s Disease

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Dose</th>
<th>Level of evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MUCOCUTANEOUS DISEASE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Viscous lidocaine, topical sulfacetate and other symptomatic treatments</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Topical and inhalant corticosteroids</td>
<td></td>
<td>2</td>
</tr>
<tr>
<td>Intrallesional corticosteroids</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Colchicine</td>
<td>0.6 mg po thrice daily</td>
<td>1</td>
</tr>
<tr>
<td>Dapsone</td>
<td>50–150 mg po daily (or sulfapyridine equivalent)</td>
<td>1</td>
</tr>
<tr>
<td>Combination oral colchicine and dapsone</td>
<td></td>
<td>3</td>
</tr>
<tr>
<td><strong>SEVERE MUCOCUTANEOUS DISEASE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thalidomide</td>
<td>50–150mg po nightly</td>
<td>1</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>2.5–25 mg po or IM weekly</td>
<td>3</td>
</tr>
<tr>
<td>Prednisone, intermittent with taper</td>
<td>40–80 mg po daily usual starting dose</td>
<td>2</td>
</tr>
<tr>
<td>Interferon-α-2a</td>
<td>Variable dose (3–9 \times 10^6 IU sc 3x weekly)</td>
<td>1</td>
</tr>
<tr>
<td>TNF-α inhibitors (e.g. etanercept, infliximab)</td>
<td>See Table 26.10</td>
<td>1 (etanercept)</td>
</tr>
<tr>
<td><strong>SYSTEMIC DISEASE</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prednisone</td>
<td>60–120 mg po daily usual starting dose (including split-dose), with taper to alternate days</td>
<td>2</td>
</tr>
<tr>
<td>Methylprednisolone acetate</td>
<td>40 mg IM 3x weekly</td>
<td>2</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>50–100mg po twice daily</td>
<td>1</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td>Variable oral dose (50–200 mg daily) or IV pulse (500–1000mg monthly then 500–1000mg every 3 months)</td>
<td>3</td>
</tr>
<tr>
<td>Chlorambucil</td>
<td>4–6mg po daily</td>
<td>1</td>
</tr>
<tr>
<td>Mycophenolate mofetil</td>
<td>1–1.5 g po twice daily</td>
<td>3</td>
</tr>
<tr>
<td>Cyclosporine</td>
<td>Variable doses (2–10 mg/kg po daily)</td>
<td>1</td>
</tr>
<tr>
<td>Tacrolimus</td>
<td>0.1–0.2mg/kg po daily</td>
<td>2</td>
</tr>
<tr>
<td>IVlg</td>
<td>2–3 g/kg IV monthly (given over 2–5 consecutive days)</td>
<td>3</td>
</tr>
<tr>
<td>TNF-α inhibitors (e.g. etanercept, infliximab)</td>
<td>See Table 26.10</td>
<td>2</td>
</tr>
</tbody>
</table>

*Key to evidence-based support: (1) controlled trial; (2) retrospective series; (3) small case series or in...*
Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis (SAPHO) Syndrome
Key Features

- Presence of aseptic pustular dermatosis and osteoarticular lesions
- Usually a gradual onset of painful, multifocal osteoarticular lesions, especially of the anterior chest and axial skeleton
- The course of osteoarticular lesions oscillates and is protracted, with gradual improvement that can be hastened by anti-inflammatory drugs
- Difficulty in establishing a come genetic association
Selected Auto Inflammatory Syndromes
Selected Auto Inflammatory Syndromes

- PAPA – Pyogenic arthritis, pyoderma gangrenosum, acne (E250k mutation in PSTPIP1 gene on chromosome 15q)
  (The proline–serine–threonine phosphatase–interacting protein 1 gene)
- PAPAS – Pyogenic arthritis, pyoderma gangrenosum, acne, and hidradenitis suppurativa
- PASH – Pyoderma gangrenosum, acne, and hidradenitis suppurativa – PTSTPIP1 gene
The usual approach to managing the neutrophilic disorders and the elements of the follicular occlusion triad (hidradenitis suppurativa, acne conglobata, and dissecting cellulitis of the scalp) are used.

However a dramatic role for agents which block Ih-1 receptor and reduce the activity of IL-1a and 1b is being reported with anakinra and other agents are being developed.