Neutrophilic Dermatoses

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Sweet’s Syndrome
(Acute Febrile
Clinical

- Acute onset of erythematous plaques, nodules, and occasionally pustules
- Assymetrically distributed over the face, neck, and extremities
- Fever and neutrophilic leukocytosis
- May last from 1 week to several years
- Rule out underlying malignancy
Histopathology

- Neutrophilic dermatosis
- Leukocytoclasis
- No vasculitis
- May have secondary bullae and panniculitis
Pyoderma Gangrenosum
Clinical

- Erythematous pustule or nodule which progresses to become a necrotic ulcer with an undermined and violaceous edge
- Variable size as (~20 cm)
- Satellite lesions
- Lower extremities, trunk, and occasionally head and neck
- Pathergy
Histopathology

- Variable changes depending upon site of biopsy and age of lesion
- Early lesions may show neutrophilic dermatosis
- Possible role of folliculitis
- DX of exclusion: Rule out infection
Acute Generalized Exanthematous Pustulosis
Clinical

- Occurs within 2 days of drug exposure
- Numerous small, mostly nonfollicular pustules arising on an erythematous base
- Fever (38C)
- Blood neutrophil count >7000/mm3
- Acute evolution with spontaneous resolution of pustules in less than 15 days (average 9-10 days)
Histopathology

- Intraepidermal or subcorneal pustules associated with dermal edema with focal necrosis of the keratinocytes
Behcet’s syndrome
Dr. Hulusi Behçet

Thursday, May 23, 13
Clinical

- Mucocutaneous lesions (oral ulcers - recurrent, at least three times per year)
- Patients must also meet two of the following four criteria:
  - Recurrent genital ulcerations
  - Eye lesions (uveitis or retinal vasculitis)
  - Positive pathergy test (trauma induced lesions)
  - Skin lesions as diagnostic of Behcet's disease
Histopathology

- Neutrophilic dermatosis
- May have leukocytoclastic vasculitis
- Panniculitis change mimics erythema nodosum or erythema induratum
TRAPS
(Tumor necrosis factor receptor–

Tumor Necrosis Factor Receptor–Associated Periodic Syndrome A Novel Syndrome With Cutaneous Manifestations Jorge R. Toro, MD; Ivona Aksentijevich, MD; Keith Hull, MD; Jane Dean, MSN; Daniel L. Kastner, MD, PhD

Table 1. Clinical Findings in 25 Patients With TRAPS*

<table>
<thead>
<tr>
<th>Findings</th>
<th>No. (%) of Patients</th>
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<tbody>
<tr>
<td>Cutaneous</td>
<td></td>
</tr>
<tr>
<td>Erythematous patches†</td>
<td>21 (84)</td>
</tr>
<tr>
<td>Erythematous plaques</td>
<td>10 (40)</td>
</tr>
<tr>
<td>Ecchymotic lesions</td>
<td>9 (36)</td>
</tr>
<tr>
<td>Conjunctivitis and/or periorbital edema</td>
<td>11 (44)</td>
</tr>
<tr>
<td>Associated</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>25 (100)</td>
</tr>
<tr>
<td>Myalgia</td>
<td>20 (80)</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>22 (88)</td>
</tr>
<tr>
<td>Pleuritic chest pain</td>
<td>10 (40)</td>
</tr>
<tr>
<td>Arthralgia</td>
<td>13 (52)</td>
</tr>
<tr>
<td>Headache</td>
<td>17 (68)</td>
</tr>
<tr>
<td>Amyloidosis</td>
<td>2 (8)</td>
</tr>
</tbody>
</table>

*TRAPS indicates tumor necrosis factor–associated periodic syndrome.
†Sometimes serpiginous and annular lesions.
Pathogenesis

- Prolonged episodes of periodic fever and localized inflammation and dominantly inherited mutations in *TNFRSF1A*, the gene encoding the 55-kDa tumor necrosis factor receptor
Histopathology

- Normal epidermis
- Superficial and deep perivascular and interstitial infiltrate of lymphocytes and monocytes
- Scattered neutrophils
- Slightly more dermal edema in papules and plaques
- CD8 and CD68 positive cells
<table>
<thead>
<tr>
<th></th>
<th>TRAPS</th>
<th>FMF</th>
<th>HIDS</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Inheritance</strong></td>
<td>Autosomal dominant</td>
<td>Autosomal recessive</td>
<td>Autosomal recessive</td>
</tr>
<tr>
<td><strong>Gene</strong></td>
<td><strong>TNFRSF1A</strong></td>
<td><strong>MEFV</strong></td>
<td><strong>MVK</strong></td>
</tr>
<tr>
<td><strong>Protein</strong></td>
<td>p55, CD120a</td>
<td>Pyrin/marenostrin</td>
<td>Mevalonate kinase</td>
</tr>
<tr>
<td><strong>Disease locus</strong></td>
<td>12p13.3</td>
<td>16p13.3</td>
<td>12q24</td>
</tr>
<tr>
<td><strong>Typical ethnic backgrounds</strong></td>
<td>Diverse ethnic groups</td>
<td>Armenian, Arab, Jewish, or Turkish</td>
<td>Dutch, French, or other European</td>
</tr>
<tr>
<td><strong>Duration of attack, d</strong></td>
<td>7-21</td>
<td>1-3</td>
<td>3-7</td>
</tr>
<tr>
<td><strong>Fever</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Abdominal pain</strong></td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Arthralgia</strong></td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>Chest pain</strong></td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>Myalgia</strong></td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Lymphadenopathy</strong></td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td><strong>Amyloidosis</strong></td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td><strong>Elevated IgD level, %</strong></td>
<td>10</td>
<td>10</td>
<td>95</td>
</tr>
<tr>
<td><strong>Conjunctivitis and/or peri orbital edema</strong></td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td><strong>Eruption</strong></td>
<td>Common</td>
<td>Common</td>
<td>Common</td>
</tr>
<tr>
<td><strong>Distribution</strong></td>
<td>Generalized</td>
<td>Lower leg</td>
<td>Extremities</td>
</tr>
<tr>
<td><strong>Morphological characteristics</strong></td>
<td>Large erythematous migratory patches or plaques; serpiginous, annular, or ecchymotic lesions</td>
<td>Erysipelatiforme</td>
<td>Small erythematous macules, papules, urticaria, and nodules</td>
</tr>
<tr>
<td><strong>Histologic characteristics</strong></td>
<td>Perivascular lymphocytes and monocytes</td>
<td>Dermal neutrophilic infiltrate</td>
<td>Mild vasculitis; other Sweet-like or cellulitislike</td>
</tr>
<tr>
<td><strong>Other dermatologic lesions</strong></td>
<td></td>
<td>HSP, PAN</td>
<td>HSP, EED</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td>Corticosteroids, etanercept†</td>
<td>Colchicine</td>
<td>NSAIDs or corticosteroids (for arthritis)†</td>
</tr>
</tbody>
</table>

*TRAPS indicates tumor necrosis factor receptor–associated periodic syndrome; FMF, familial Mediterranean fever; HIDS, hyperimmunoglobulinemia D syndrome; plus sign, present; minus sign, absent; HSP, Henoch-Schönlein purpura; PAN, polyarteritis nodosa; EED, erythema elevatum diutinum; and NSAIDs, nonsteroidal anti-inflammatory drugs.

†Investigational.
Treatment

- Respond rapidly to corticosteroid and NSIADS
- Poor response to colchicine
- Etanercept, bioengineered fusion protein of the p75 soluble TNF receptor (TNFR:Fc or Enbrel)
Familial Mediterranean fever
Clinical

- Mediterranean ancestry, especially non-Ashkenazi (Sephardic) Jews, Armenians, and Arabs
- Begin between ages 5-15.
- Inflammation in the lining of the abdominal cavity, chest cavity, skin, or joints occurs
- High fevers usually peak in 12 to 24 hours
- Attacks vary in severity of symptoms
- Usually symptom free between attacks
Histopathology

- Non-specific
- Skin may show sparse neutrophil infiltrate
- Kidney: massive amyloid infiltration of the blood vessels and of the endothelial side of the glomerular basement membrane
- Rectum: Submucosal amyloid in blood vessels
Bowel Bypass Syndrome
Clinical and Histopathology

- Jejunoileal bypass for morbid obesity
- Influenza-like illness with increased temperature, chills, polyarthralgia and myalgia
- Inflammatory papules and pustules
  - 2 to 4 mm in diameter
  - Extremities and upper trunk
- Neutrophilic dermatosis

Thursday, May 23, 13
Rheumatoid Neutrophilic Dermatosis
Clinical and Histopathologic

- Rare
- Severe RA
- Symmetric erythematous papules, plaques, and rarely vesicles on extensor skin
- Occ. urticarial plaques
- Occ. asymptomatic

- Neutrophilic dermatosis
- Papillary neutrophilic microabscesses
- Spongiotic intraepidermal blisters and subepidermal bullae
"RA-associated Intravascular Histiocytopathy"

- Palisading and/or diffuse interstitial granulomatous inflammation
- Variable collagen necrobiosis
- Interstitial neutrophilia
- Vasculitis
