AMERICAN COLLEGE OF EMERGENCY PHYSICIANS
SCIENTIFIC ASSEMBLY
1999

Cutaneous Signs of Systemic Illness

Many serious systemic diseases are manifested at least in part with skin signs, such as meningococcal meningitis or Kawasaki's disease. This presentation will cover illnesses from inflammatory bowel disease to sepsis, with a focus on their cutaneous signs.

- Recognize the skin signs of Kawasaki's disease, acute rheumatic fever, inflammatory bowel disease, AML, sepsis, and many others.
- Discuss the initial management.
- Discuss the appropriate disposition and referral.

MO-56
Monday, October 11, 1999
5:00 PM - 5:55 PM
Room # N250
Las Vegas Convention Center

FACULTY

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Carl M. Ferraro, MD

I. Introduction

Patients commonly present to the ED because of rashes and other skin complaints. These skin lesions, exanthems, or eruptions may be caused by a variety of agents or illnesses, and may range from being transient curiosities to heralding life-threatening diseases. Familiarity with not only typical skin changes but accompanying signs and symptoms will aid the ED physician in the diagnosis and management of these problems.

II. Approach to Patients

A. History and Physical

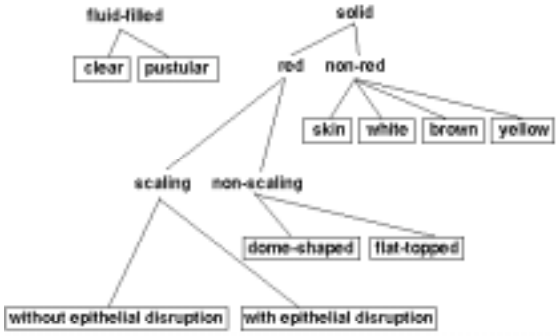
1. History: not to be neglected!
   a) Usual chief complaint, HPI, past history, ROS
   b) Remember occupation, hobbies, and sexual history
2. Physical
   a) Expose
   b) Visualize with adequate light
   c) Palpate with gloved hand

B. Ancillary Tests

1. Bedside
   a) side lighting
   b) Wood's light
   c) diascopy - compression with glass slide
   d) manipulation of lesions
2. Others
   a) slides - Gram stain, KOH, Tzanck smear
   b) skin biopsy

C. Classification Schemes

1. Algorithmic approach of Lynch
   - provides 95% diagnostic accuracy
   - 65 common illnesses in 10 major groups



(Adapted from Lynch and Edminster, Annals Emerg Med, 13:8 August 1984)

2. Other algorithms based on broad categories such as eczematous, maculopapular, papular, etc. [see Pediatric Emergency Medicine by Ludwig and Fleischer and others]

III. Life-Threatening Rashes

A. Meningococcemia

1. Presentation

a. may begin as URI/influenza-like illness
   - coryza, pharyngitis, tonsillitis, or laryngitis
   - fever, malaise, headache, vomiting, myalgia/arthralgia

b. skin findings - hours to days
   - diffuse mottling, morbiliform
   - petechiae (50-60% of patients)
   - purpuric lesions

c. hypotension, oliguria, renal failure
   - usually fatal

d. poor prognostic factors
   1. petechiae for less than 12 hours
   2. systolic pressure < 70 mmHg
   3. < 20 WBC/mm^3 in CSF
   4. WBC < 10,000/mm^3
   5. ESR < 10 mm/hr

e. diagnosed by gram stain, culture, or CIE

2. Treatment

a. cultures and antibiotics
   - Penicillin G / chloramphenicol
   - broad-spectrum (such as ceftriaxone)

b. close monitoring

c. supportive therapy
   - ? heparin for DIC
   - ? steroids

3. Prophylaxis of contacts

a. Who?
   - household members
   - certain hospital personnel
   - nursery school contacts

b. How?

	adults	children
- rifampin	600mg q12 x 4 doses	10mg/kg q12 x 4 doses (1-12 yrs)
or		5mg/kg q12 x 4 doses (3 mo - 1 yr)
- ceftriaxone	250mg IM	125mg IM
or		
- ciprofloxacin	500mg PO	

B. Staphylococcal Scalded Skin Syndrome

1. Etiology: toxigenic strains of *Staphylococcus aureus*
   - produce epidermolytic toxin
   - acts at granular layer of epidermis (intraepidermal)
2. Various names - spectrum of severity
   - Ritter disease / pemphigus neonatorum - neonates
   - toxic epidermal necrolysis (TEN) / Lyell disease - older children
   - bullous pemphigus
3. Site of infection: conjunctivitis, abrasions, nasopharynx, umbilicus, circumcision, urinary tract, endocarditis, blood
4. Sudden fever and irritability with cutaneous tenderness
5. Flaccid blisters, erosions, easy disruption of skin (Nikolsky's sign)

6. Secondary flaky desquamation
7. Loss of normal integument
    - fluid and electrolyte loss
    - heat loss
    - portal of secondary infection
8. Treatment
    - systemic antibiotics: parenterally
    - supportive care
    - do not use steroids
    - topical preparations of no benefit

C. Erythema Multiforme

- there is no consensus in the literature as to what this entity is

1. Describes a spectrum of illnesses including (from mild to severe):
    - Erythema Multiforme Minor
    - Erythema Multiforme Major
        - Stevens-Johnson Syndrome (mucous membranes)
        - Toxic Epidermal Necrolysis (widespread blistering)

2. Mortality of about 10%
    - from sepsis and fluid/electrolyte deficits

3. Causes / Precipitants
    a) exact cause unknown; suspected to be immunologic reaction to foreign antigen
    b) common causes
        1) Herpes Simplex infection
        2) Mycoplasma infection
        3) drug reaction
            - anticonvulsants (phenytoin, carbamazepine)
            - sulfonamides
            - NSAIDs
            - other antibiotics (cephalosporins, penicillin)
            - allopurinol
        4) others
            - collagen vascular diseases, malignancies, other infections

4. Clinical manifestations
    a) Prodromal symptoms
        - malaise, fever, myalgias, arthralgias, headache, diffuse pruritus or burning
    b) Hallmark: target or "iris" lesions and symmetric erythematous macules or plaques on extensor surfaces
    c) variable; evolve during course
        - lesions become papules, vesicles, or bullae
    d) mucous membranes / genitalia
        - painful superficial ulcerations

5. Treatment
    - *No definite consensus on optimal management*
    a) Supportive / Symptomatic
        - mainstay of therapy

b) Discontinue all new drugs (unless life threat itself)
c) Admit if: greater that 10% TBSA involved with blisters
or severe mucous membrane or ocular involvement
d) Wound care
- dressings, isolation (just like burns)
e) IV fluids
- volume, electrolytes, nutritional support
f) Steroids
- controversial
- if used; short course (5-10 days)

IV. Erythrodermas

A. Toxic Shock Syndrome

1. Etiology

This clinical syndrome of hypotension, fever, rash, and multi organ system involvement is thought to be caused by toxins produced by *Staphylococcus aureus*. About 90% of cases occur in menstruating women using tampons. Cases not associated with menstruation have been related to cutaneous staph infections and with nasal packing.

2. Case Definition

Major Criteria
a) Fever - temp > 102°F
b) Rash - erythroderma (localized or diffuse) followed by desquamation
c) Mucous membrane - hyperemia of oral, vaginal or conjunctiva
d) Hypotension - history of dizziness, orthostatic changes, or hypotension

Multisystem manifestations

Diagnosis requires all four major and three or more systems

3. Clinical Course

This syndrome is acute in onset, and may present in a variety of ways depending upon the organ systems involved. Characteristically there is a fever greater than 102°, hypotension (systolic BP < 90 mmHg), and an erythroderma. Patients may have myalgias, abdominal pain, weakness, headache, confusion, vomiting, or diarrhea. Similarly, there may be multiple laboratory abnormalities.

4. Treatment

Restoration of intravascular volume is essential. A focus of infection must be sought and addressed - tampons removed, etc. Although antistaph agents are recommended, no effect on outcome is proven. Most patients improve within 48 hours of initiation of therapy.

B. Kawasaki Syndrome

1. Etiology

Generalized vasculitis, unknown - suspected to be viral, children < 5.

2. Presentation

The diagnosis is made by the presence of fever and at least 4 of 5 principal clinical features:

a) Extremity changes
b) Polymorphous exanthem
c) Bilateral conjunctival injection
d) Lip and oral changes
e) Cervical lymphadenopathy

3. Complications

Include coronary artery aneurysms and myocardial inflammation/ischemia.

4. Treatment

Gamma globulin therapy within 10 days and high dose aspirin.

V. Infectious Diseases

A. Lyme Disease

1. General

a) Tick-borne infection caused by *Borrelia bergdorferi*, a spirochete, and transmitted by the *Ixodes* ticks
b) Case definition: presence of erythema migrans rash $\geq$ 5 cm diameter or lab confirmation of infection with *B. burgdorferi* and at least one objective sign of musculoskeletal, neurologic, or cardiovascular disease
c) Multisystem illness with myriad manifestations
d) Serologic testing is of limited value (timing and specificity)

2. Clinical Presentation

a) Dermatologic

1) Erythema migrans (erythema chronicum migrans)
- present in 50-83% of cases
- begins 2-30 days after tick bite
- starts as red macule or papule at bite site
- expands forming an erythematous annular lesion with central clearing
- average size: 15 cm
- if untreated, lasts about a month; resolves within days of treatment
- secondary/multiple/metastatic erythema migrans lesions can appear within days to weeks after the primary

2) Borrelia lymphocytoma
- 1% of cases in Europe
- firm red nodule or plaque
- earlobe in children; nipple/areola in adults

3) Acrodermatitis chronica atrophicans
- biphasic pattern
  - early (inflammatory): erythematous / violaceous discoloration in doughy and swollen skin

- weeks to years (atrophic): glistening skin [cigarette-paper] with prominence of blood vessels

4) others: benign lymphocytic infiltration, anetoderma, morphea, allergic reactions

b) Neurologic
- begins months after initial presentation
- up to 15% of cases
- common manifestations: meningitis, encephalitis, cranial neuropathies (Bell's), radiculopathies, myelitis
- later: paresthesias, organic brain syndrome, spastic paraparesis, dementia

c) Cardiac
- 8-10% of cases
- varying degrees of AV block
- myocarditis, pericarditis

d) Musculoskeletal
- arthralgias and myalgias
- arthritis of large joints

3. Treatment
- shortens duration and prevents later illness
- duration of treatment dependent on severity of symptoms

a) Oral regimens
doxycycline 100 mg BID
or amoxicillin 500 mg TID
for 10-21 days up to 1 month (for arthritis or Bell's)

b) Parenteral
ceftriaxone 2 g/day
or penicillin G 20-24 million units/day
IV for 14-21 days

B. Rocky Mountain Spotted Fever

1. Etiology / Pathogenesis
- etiologic agent: *Rickettsia rickettsii*
coccobacillus, obligate intracellular bacteria
- vector-borne disease transmitted by certain ticks:
wood tick (*Dermacentor andersoni*)
dog tick (*Dermacentor variabilis*)
- widespread; most cases from south Atlantic coastal and south central states
- organism spreads from portal of entry (bite) to all body organs resulting in increased vascular permeability and vasculitis

2. Clinical Manifestations
a) General
- incubation of about 7 days (2-14 range)
- initial symptoms nonspecific: fever, malaise, severe frontal headache myalgias, nausea/vomiting/anorexia, abdominal pain, photophobia

b) Cutaneous
- maculopapular rash (3-5 days)
- becomes more defined and petechial
- begins on extremities (wrists and ankles), spreads centrally to trunk;
- involves palms and soles; +/- face

c) Gastrointestinal
- nausea, vomiting, abdominal pain, diarrhea
- mistaken for acute abdomen
- hepatomegaly, splenomegaly, clinical jaundice, pancreatitis (mild)

d) Pulmonary
- cough, dyspnea, non-cardiogenic pulmonary edema, infiltrates on CXR, hypoxemia

e) Neurologic
- rickettsial encephalitis (grave prognosis)
- confusion, delirium, ataxia, coma, seizures
- papilledema, hearing loss, SIADH

f) Renal
- elevated BUN (prerenal azotemia)
- acute tubular necrosis from hypovolemic shock

g) Cardiac
- mild effect on myocardium
- abnormal EKG (consistent with myocarditis; arrythmias)

3. Treatment
- early appropriate treatment decreases mortality from 25% to 5% or less
- Adults: doxycycline 100 mg BID for 5-7 days
- Children: doxycycline 2.2 mg/kg BID [stains teeth]
  or (if under 8 years of age) chloramphenicol 100 mg/kg/day IV in 4 divided doses [hematologic side effects]
- fluid and electrolyte replacement

C. Acute Rheumatic Fever

1. Diagnostic Criteria:

Major Manifestations	Minor Manifestations
Carditis	Clinical findings
Polyarthritis	Arthralgia
Chorea	Fever
Erythema Marginatum	Laboratory findings
Subcutaneous Nodules	Elevated acute phase reactants
	ESR
	C-reactive protein
	Prolonged PR interval

Supportive Evidence of Antecedent Group A Streptococcal Infection
Positive throat culture or rapid streptococcal antigen test
Elevated or rising streptococcal antibody titer

2. Erythema Marginatum

a. due to Streptococcal disease

b. rash:
- pink, pale centers with rounded or serpiginous borders
- vary in size
- mainly on trunk and proximal extremities (not on face)
- evanescent, transient and migratory

3. Subcutaneous Nodules
    a. firm and painless
    b. overlying skin is not inflamed
    c. typical locations:
        1) extensor surfaces, particularly elbows knees and wrists
        2) occipital region
        3) over the spinous processes (thoracic or lumbar vertebrae)

4. Treatment
    a. with penicillin if ongoing infection suspected (rare)
    b. aspirin for antiinflammatory effects

VI. Inflammatory Bowel Disease - Crohn's Disease and Ulcerative Colitis

A. Pyoderma Gangrenosum
1. Occurrence
    a. Also in rheumatoid disease, leukemias, myeloma, and in healthy individuals
    b. "Significantly associated" but numbers vary by study
        - 1/3 to 1/2 with PG have IBD
    c. Can be the presenting finding of IBD
2. Typical lesions
    a. Begins as a pustule that enlarges and ulcerates
    b. Discreet ulcer with a necrotic base usually with blood and exudate
    c. Undermined, violaceous margin
    d. Most common on lower extremity
    e. Prominent pain
3. Treatment
    a. Usually resolve with treatment of the bowel
    b. Corticosteroids - systemic or intralesional
    c. Others: periactin, dapsone, cyclosporine

B. Erythema Nodosum
1. Occurs during flare ups
    - relation is questionable; possibly drug induced
2. Erythematous, tender, non-ulcerative subcutaneous nodules
3. Treatment aimed at IBD
    a. NSAIDs / analgesia
    b. possibly steroids

C. Other Lesions
- Aphthous ulcers
- Granulomata
- many others

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