Purpura, Petechiae and Vasculitis

UCSF Dermatology

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Module Instructions

- The following module contains a number of green, underlined terms which are hyperlinked to the dermatology glossary, an illustrated interactive guide to clinical dermatology and dermatopathology.
- We encourage the learner to read all the hyperlinked information.
Goals and Objectives

- The purpose of this module is to help medical students develop a clinical approach to the initial evaluation and treatment of patients with petechiae and purpura.

- After completing this module, the medical student will be able to:
  - Identify and describe the morphology of petechiae and purpura
  - Outline an initial diagnostic approach to petechiae or purpura
  - Recognize patterns of petechiae that are concerning for life-threatening conditions
  - Recognize palpable purpura as the hallmark lesion of leukocytoclastic vasculitis
  - Name the common etiologies of vasculitides according to size of vessel affected
Purpura: The Basics

- The term **Purpura** is used to describe red-purple lesions that result from the extravasation of blood into the skin or mucous membranes.
- Purpura may be palpable or non-palpable (flat/macular).
- Macular purpura is divided into two morphologies based on size:
  - **Petechiae**: small lesions (< 3 mm)
  - **Ecchymoses**: larger lesions (>5 mm)
- The type of lesion present is usually indicative of the underlying pathogenesis:
  - Macular purpura is typically non-inflammatory
  - Palpable purpura is a sign of vascular inflammation (**vasculitis**)
Purpura: The Basics

- All forms do not blanch when pressed
  - Diascopy refers to the use of a glass slide to apply pressure to the lesion, which can be useful in distinguishing erythema secondary to vasodilation (blanchable with pressure), from erythrocyte extravasation (retains its red color)
- Purpura may result from hyper- and hypo-coagulable states, vascular dysfunction and extravascular causes
Examples of Purpura

- Petechia
- Ecchymosis
Examples of Purpura

Ecchymoses

Petechiae
Case One

Mr. Chad Fields
Case One: History

- **HPI:** Mr. Fields is a 42 year-old gentleman who presents to the ER with a 2-week history of a rash on his abdomen and lower extremities.
- **PMH:** hospitalization 1 year ago for community acquired pneumonia
- **Medications:** none
- **Allergies:** none
- **Family History:** unknown
- **Social History:** marginally housed, no recent travel or exposure to animals
- **Health Related Behaviors:** smokes 10 cigarettes/day, drinks 3-10 beers/day, limited access to food
- **ROS:** easy bruising, bleeding from gums, overall fatigue
Case One: Exam

Perifollicular petechiae
Keratotic plugging of hair follicles
Case One: Exam

Mr. Fields also has hemorrhagic gingivitis
Case One, Question 1

Which of the following is the most likely diagnosis?

a. drug hypersensitivity reaction
b. urticaria
c. vasculitis
d. rocky mountain spotted fever
e. nutritional deficiency
Case One, Question 1

Answer: e

Which of the following is the most likely diagnosis?

a. drug hypersensitivity reaction (typically without purpuric lesions)

b. urticaria (would expect raised edematous lesions, not purpura)

c. vasculitis (purpura would not be perifollicular and would be palpable)

d. rocky mountain spotted fever (no history of travel or tick bite)

e. nutritional deficiency
Scurvy results from insufficient vitamin C intake (i.e. fad diet, alcoholism), increased vitamin requirement (i.e. certain medications), and increased loss (i.e. dialysis).

Vitamin C is required for normal collagen structure and its absence leads to skin and vessel fragility.

Characteristic exam findings include:
- perifollicular purpura
- large ecchymoses on the lower legs
- intramuscular and periosteal hemorrhage
- keratotic plugging of hair follicles
- hemorrhagic gingivitis (when patient has poor oral hygiene)

Remember to take a dietary history in all patients with purpura.
Case Two

Mr. Andrew Thompson
Case Two: History

- **HPI:** Andrew is a 19 year-old gentleman who was admitted to the hospital with a headache, stiff neck, high fever, and a rash. His symptoms began 2-3 days prior to admission when he developed fevers with nausea and vomiting.
- **PMH:** splenectomy 3 years ago after a snowboarding accident
- **Medications:** none
- **Allergies:** none
- **Vaccination hx:** last vaccination as a child
- **Family history:** not contributory
- **Social history:** attends a near-by state college, lives in a dormitory
- **Health related behaviors:** reports occasional alcohol use on the weekends with 2-3 drinks per night, plays basketball with friends for exercise.
- **ROS:** as mentioned in HPI
Case Two: Exam

Vitals: T 102.4 °F, HR 120, BP 86/40, RR 20, O2 sat 96% on room air

Gen: ill-appearing male lying on a gurney

HEENT: PERRL, EOMI, + nuchal rigidity

Skin: petechiae and large ecchymotic patches on upper (not shown) and lower extremities = Purpura fulminans
Case Two: Initial Labs

- WBC count: 14,000 cells/mcL
- Platelets: 100,000/mL
- Decreased fibrinogen
- Increased PT, PTT
- Blood Culture: gram negative diplococci
- Lumbar puncture: pending
Case Two, Question 1

- In addition to fluid resuscitation, what is the most needed treatment at this time?
  a. Plasmapheresis
  b. IV antibiotics
  c. Pain relief with oxycodone
  d. IV corticosteroids
Case Two, Question 1

Answer: b

- In addition to fluid resuscitation, what is the most needed treatment at this time?
  
a. Plasmaphoresis (not unless suspecting diagnosis of TTP)

  b. **IV antibiotics** (may be started before lumbar puncture)

  c. Pain relief with oxycodone (not the patient’s primary issue)

  d. IV corticosteroids (not unless suspicion for pneumococcal meningitis is high)
Sepsis and DIC

- Andrew’s clinical picture is concerning for meningococcemia with disseminated intravascular coagulation (DIC)
- Presence of petechial or purpuric lesions in the patient with meningitis should raise concern for sepsis and DIC
- Neisseria meningitis is a gram negative diplococcus that causes meningococcal disease
  - Most common presentations are meningitis and meningococcemia
- DIC results from unregulated intravascular clotting resulting in depletion of clotting factors and bleeding
  - The primary treatment is always to treat the underlying condition
Another life-threatening diagnosis to consider in a patient with a petechial rash is Rocky Mountain Spotted Fever (RMSF).

The most commonly fatal tickborne infection (caused by *Rickettsia rickettsii*) in the US.

A petechial rash is a frequent finding that usually occurs several days after the onset of fever.

Initial appearance of the rash is characterized by faint macules on the wrists or ankles. As the disease progresses, the rash may become petechial and involves the trunk, extremities, palms and soles.

Majority of patients do not have the classic triad of fever, rash and history of tick bite.
Clinical Evaluation of Purpura

- A history and physical exam is often all that is necessary
- Important history items include:
  - Family history of bleeding or thrombotic disorders (i.e. von Willebrand disease)
  - Use of drugs and medications (i.e. aspirin, warfarin) that may affect platelet function and coagulation
  - Medical conditions (i.e. liver disease) that may result in altered coagulation
- Complete blood count with differential and PT/PTT are used to help assess platelet function and evaluate coagulation states
Causes of Non-Palpable Purpura

- **Petechiae**
  - Thrombocytopenia
    - Idiopathic
    - Drug-induced
    - Thrombotic
  - DIC and infection
  - Abnormal platelet function
  - Increased intravascular venous pressures
  - Some inflammatory skin diseases

- **Ecchymoses**
  - External trauma
  - DIC and infection
  - Coagulation defects
  - Skin weakness/fragility
  - Waldenstrom hypergammaglobulinemia purpura
Palpable Purpura

- Palpable purpura results from inflammation of small cutaneous vessels, ie vasculitis
- Vessel inflammation results in vessel wall damage and in extravasation of erythrocytes seen as purpura on the skin
- Vasculitis may occur as a primary process or may be secondary to another underlying disease
- Palpable purpura is the hallmark lesion of leukocytoclastic vasculitis (small vessel vasculitis)
Vasculitis Morphology

- Vasculitis is classified by the vessel size affected (small, medium, mixed size or large)
- Clinical morphology correlates with the size of the affected blood vessels
  - Small vessel: palpable purpura (urticarial lesions in rare cases, i.e., urticarial vasculitis)
  - Small-to medium-sized vessels: subcutaneous nodules, purpura and FIXED livedo reticularis (also called livedo racemosa)
  - Large-vessel disease: claudication, ulceration and necrosis
- Diseases may involve more than one size of vessel
- Systemic vasculitis may involve vessels in other organs
Vasculitides: Size of the Blood Vessel

- Small vessel vasculitis (leukocytoclastic vasculitis)
  - Henoch-Schonlein purpura
  - Urticarial vasculitis
  - Other:
    - Idiopathic
    - Malignancy-related
    - Rheumatologic
    - Infection
    - Medication
Vasculitides: Size of the Blood Vessel

- **Predominantly Mixed (Small + Medium)**
  - ANCA associated vasculitides
    - Churg-Strauss syndrome
    - Wegener granulomatosis
    - Microscopic polyarteritis
  - Essential cryoglobulinemic vasculitis

- **Predominantly medium sized vessels**
  - Polyarteritis nodosa

- **Predominantly large vessels**
  - Takayasu arteritis
  - Giant cell arteritis
The following laboratory tests may be used to evaluate patient with suspected vasculitis:

- CBC with platelets
- ESR (systemic vasculitides tend to have sedimentation rates > 50)
- ANA (a positive antinuclear antibody test suggests the presence of an underlying connective tissue disorder)
- ANCA (help diagnose Wegener granulomatosis, microscopic polyarteritis, drug-induced vasculitis, and Churg-Strauss)
- Complement (low serum complement levels may be present in mixed cryoglobulinemia, urticarial vasculitis and lupus)
- Urinalysis (helps detect renal involvement)

Also consider ordering cryoglobulins, an HIV test, HBV and HCV serology, occult stool samples, an ASO titer and streptococcal throat culture
Case Three

Jenny Miller
Case Three: History

- **HPI:** Jenny is a 9 year-old girl with a 4-day history of abdominal pain and rash on the lower extremities who was brought to the ER by her mother. Her mother reported that the rash appeared suddenly and was accompanied by joint pain of the knees and ankles and aching abdominal pain. Over 3 days the rash changed from red patches to more diffuse purple bumps.
- **PMH:** normal birth history, no major illnesses or hospitalizations
- **Medications:** none, up to date on vaccines
- **Allergies:** none
- **Family History:** no history of clotting or bleeding disorders
- **Social History:** happy child when feeling well, attends school, takes ballet
- **ROS:** cough and runny nose a few weeks ago
Case Three: Exam

Non-blanching erythematous macules and papules on both legs and feet sparing the trunk, upper extremities and face, diffuse petechiae.
Case Three, Question 1

- In this clinical context, what test will establish the diagnosis?
  a. HIV test
  b. CBC
  c. ESR
  d. Urinalysis
  e. Skin biopsy for routine microscopy and direct immunofluorescence
Case Three, Question 1

Answer: e

- In this clinical context, what test will establish the diagnosis?
  a. HIV test
  b. CBC
  c. ESR
  d. Urinalysis
  e. Skin biopsy for routine microscopy and direct immunofluorescence
A skin biopsy obtained from a new purpuric lesion reveals a leukocytoclastic vasculitis of the small dermal blood vessels.

Direct immunofluorescence demonstrates perivascular IgA, C3 and fibrin deposits.

A skin biopsy is often necessary to establish the diagnosis of vasculitis.
Case Three, Question 2

- What is the most likely diagnosis?
  a. Urticaria
  b. Disseminated intravascular coagulation
  c. Henoch-Schönlein Purpura
  d. Idiopathic thrombocytopenic purpura
  e. Sepsis
Case Three, Question 2

Answer: c

- What is the most likely diagnosis?
  a. Urticaria
  b. Disseminated intravascular coagulation
  c. Henoch-Schonlein Purpura
  d. Idiopathic thrombocytopenic purpura
  e. Sepsis
Henoch Schonlein Purpura

- Henoch Schonlein Purpura (HSP) is the most common form of systemic vasculitis in children
- Primarily a childhood disease (between ages 3-15), but adults can also be affected
- HSP follows a seasonal pattern with a peak in incidence during the winter presumably due to association with a preceding viral or bacterial infection
- Characterized by palpable purpura (vasculitis), arthritis, abdominal pain and kidney disease
HSP: Diagnosis and Evaluation

- Diagnosis often made on clinical presentation +/- skin biopsy
- Skin biopsy shows leukocytoclastic vasculitis in postcapillary venules (small vessel disease)
  - Immune complexes in vessel walls contain IgA deposition (the diagnostic feature of HSP)
- Rule out streptococcal infection with an ASO or throat culture
HSP: Evaluation and Treatment

- Also important to look for systemic disease:
  - Renal: Urinalysis, BUN/Cr
  - Gastrointestinal: Stool guaiac
  - HSP in adults may be a manifestation of underlying malignancy

- Natural History: most children completely recover from HSP
  - Some develop progressive renal disease (more common in adults)

- Treatment is supportive +/- prednisone
Case Four

Mr. Matthew Burton
Case Four: History

- Hospital Course: Mr. Burton is a 45 year-old gentleman who was admitted to the hospital five weeks ago with acute bacterial endocarditis. After an appropriate antibiotic regimen was started and Mr. Burton was stable, he was transferred to a skilled nursing facility to finish a six-week course of IV antibiotics. On week #5, the patient developed a rash on his lower extremities. The dermatology service was consulted to evaluate the rash.
Case Four: History Continued

- PMH: history of community-acquired pneumonia 2 years ago, history of multiple skin abscesses requiring incision and drainage (last abscess 2 months ago)
- Medications: IV Vancomycin
- Allergies: none
- Social history: lives by himself in an apartment
- Health-related behaviors: history of IV drug use
- ROS: no current fevers, sweats or chills
Case Four: Skin Exam

- Normal vital signs
- General: appears well in NAD
- Skin exam: palpable hemorrhagic papules coalescing into plaques, bilateral and symmetric on lower extremities
- Also with bilateral and symmetric pedal edema
- Labs: normal CBC, PT, PTT, INR
- ANA < 1:40
- Negative ANCA, cyroglobulins
- HIV negative, Negative hep serologies except for HBVsAb positive
Case Four, Question 1

- Which of the following is the most likely cause of Mr. Burton’s skin findings?
  
a. Leukocytoclastic vasculitis secondary to antibiotics
b. Septic emboli with hemorrhage
c. Urticarial vasculitis
d. DIC secondary to sepsis
Case Four, Question 1

Answer: a

- Which of the following is the most likely cause of Mr. Burton’s skin findings?
  
  a. Leukocytoclastic vasculitis secondary to antibiotics
  
  b. Septic emboli with hemorrhage (these lesions tend to occur on the distal extremities)
  
  c. Urticarial vasculitis (presents with a different morphology, which is more nodular and less diffuse)
  
  d. DIC secondary to sepsis (in DIC, coagulation studies are abnormal)
What is the most important next step?

a. Stop the IV antibiotics and replace with another
b. Obtain a urinalysis
c. Start systemic steroid
d. a & b
e. a & c
Case Four, Question 2

**Answer: d**

- What is the most important next step?
  
  - a. Stop the IV antibiotics and replace with another (remove the offending agent)
  
  - b. Obtain a urinalysis (detection of renal involvement will impact treatment)
  
  - c. Start systemic steroid (typically used when vasculitis is systemic or severe)
  
  - d. a & b
  
  - e. a & c
Take Home Points: Petechiae & Purpura

- The term purpura is used to describe purpuric lesions that result from extravasation of blood into the skin or mucous membranes.
- Purpura may be palpable and non-palpable.
- Purpura does not blanch with pressure.
- Various life-threatening conditions present with petechial rashes including meningococcemia and RMSF.
- The presence of petechial or purpuric lesions in a septic patient should raise concern for DIC.
- Purpura may result from hyper- and hypocoagulable states, vascular dysfunction and extravascular causes.
Take Home Points: Vasculitis

- Palpable purpura results from underlying blood vessel inflammation (vasculitis)
- Palpable purpura is the hallmark lesion of leukocytoclastic vasculitis
- The various etiologies of vasculitis may be categorized according to size of vessel affected
- A skin biopsy is often necessary for the diagnosis of vasculitis
End of Module