Petechiae, Purpura and Vasculitis

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Purpuras

• Caused by leakage of red blood cells out of vessels into skin or mucous membranes.
• Varies in size and ranges in color related to duration.
Purpuras

• Either Non-Palpable or Palpable Purpura
  – Non-palpable (flat): Petechiae (less than 3mm), Ecchymoses (more than 5mm)
  – Palpable: Elevated Purpuras
Purpura

• 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)
Non-Palpable Purpura: Ecchymoses

- A discoloration of the skin or mucous membranes resulting from extravasation of blood with color change over time with a characteristic transition of color ranging from blue-black, brown-yellow, or green.
Non-Palpable Purpura: Petechiae

- Petechiae: Small 1-2 mm, non-blanchable purpuric macules resulting from tiny hemorrhages.
Petechiae
Palpable Purpura

- Palpable Purpura: Raised and palpable red or violaceous discoloration of skin or mucous membranes due to vascular inflammation in the skin and extravasation of red blood cells.
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 in order to distinguish 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
Diascopy: Purpura

- Looking through a glass slide as pressure is placed.
- By definition: true purpuric lesions do not blanch as blood is fixed in the skin.
Examples of Purpura

Petechia

Ecchymosis
Examples of Purpura

Ecchymoses

Petechiae
Case One
Case One: History

- HPI: 42-year-old man 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: without stable housing, 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: Skin Exam

- Perifollicular petechiae
- Keratotic plugging of hair follicles
Case One: Exam

- hemorrhagic gingivitis
Case One, Question 1

Which of the following is the most likely diagnosis?

a. Drug hypersensitivity reaction
b. Nutritional deficiency
c. Rocky mountain spotted fever
d. Urticaria
e. Vasculitis
Case One, Question 1

Answer: b

- Which of the following is the most likely diagnosis?
  a. Drug hypersensitivity reaction (typically without purpuric lesions)
  b. **Nutritional deficiency**
  c. Urticaria (would expect raised edematous lesions, not purpura)
  d. Vasculitis (purpura would not be perifollicular and would be palpable)
  e. Rocky mountain spotted fever (no history of travel or tick bite)
Vitamin C Deficiency - Scurvy

• Scurvy results from insufficient vitamin C intake (e.g., fat diet, alcoholism), increased vitamin requirement (e.g., certain medications), and increased loss (e.g., dialysis)

• Vitamin C is required for normal collagen structure and its absence leads to skin and vessel fragility
Vitamin C Deficiency - Scurvy

- 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
Vitamin C Deficiency - Scurvy
Case Two
Case Two: History

- **HPI:** 19-year-old man who was admitted to the hospital with a headache, stiff neck, high fever, and 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 history:** last vaccination as a child
- **Family history:** non-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
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 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

Answer: a

- In addition to fluid resuscitation, what is the most needed treatment at this time?
  a. IV antibiotics (may be started before lumbar puncture)
  b. IV corticosteroids (not unless suspicion for pneumococcal meningitis is high)
  c. Pain relief with oxycodone (not the patient’s primary issue)
  d. Plasmapheresis (not unless suspecting diagnosis of thrombotic thrombocytopenic purpura – TTP)
Sepsis and DIC

- Patient’s clinical picture is concerning for meningococccemia with disseminated intravascular coagulation (DIC)
- Presence of petechial or purpuric lesions in the patient with meningitis should raise concern for sepsis and DIC
- Neisseria meningitidis is a gram negative diplococcus that causes meningococcal disease
  - Most common presentations are meningitis and meningococcemia
- DIC may be initiated by: hypoxemia, acidosis, malignancies, chemotherapy, antiphospholipid antibody syndrome, SLE, leukemia
Meningococcemia
Meningococcemia
Disseminated Intravascular Coagulation

• Skin lesions may be the initial manifestation
• Wide spread petechiae, ecchymoses, ischemic necrosis of the skin, and hemorrhagic bullae
• Purpura fulminans may supervene and progress to symetrical gangrene
• DIC results from unregulated intravascular clotting resulting in depletion of clotting factors and bleeding
  • The primary treatment is to treat the underlying condition
Purpura Fulminans - DIC
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.

Initially 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.
Rocky Mountain Spotted Fever
Rocky Mountain Spotted Fever
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 (e.g., von Willebrand disease)
  - Use of drugs and medications (e.g., aspirin, warfarin) that may affect platelet function and coagulation
  - Medical conditions (e.g., 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**
  - Abnormal platelet function
  - DIC and infection
  - Increased intravascular venous pressures
  - Thrombocytopenia
    - Idiopathic
    - Drug-induced
    - Thrombotic
  - Some inflammatory skin diseases

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

- Palpable purpura results from inflammation of small cutaneous vessels (i.e., 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 or large)
- Clinical morphology correlates with the size of the affected blood vessels
  - **Small vessel**: palpable purpura (urticarial lesions in rare cases, e.g., urticarial vasculitis)
  - **Small to medium vessel**: subcutaneous nodules, purpura and FIXED livedo reticularis (also called livedo racemosa). Ulceration and necrosis may be present in medium-vessel vasculitis.
  - **Large vessel**: claudication, ulceration and necrosis
- Diseases may involve more than one size of vessel
- Systemic vasculitis may involve vessels in other organs
Vasculitides According to Size of the Blood Vessels

- Small vessel vasculitis (leukocytoclastic vasculitis)
  - Henoch-Schönlein purpura
  - Other:
    - Idiopathic
    - Malignancy-related
    - Rheumatologic
    - Infection
    - Medication
  - Urticarial vasculitis
Vasculitides According to Size of the Blood Vessels

- Predominantly Mixed (Small + Medium)
  - ANCA associated vasculitides
    - Churg-Strauss syndrome
    - Microscopic polyangiitis
    - Wegener granulomatosis
  - Essential cryoglobulinemic vasculitis
- Predominantly medium sized vessels
  - Polyarteritis nodosa
- Predominantly large vessels
  - Giant cell arteritis
  - Takayasu arteritis
Clinical Evaluation of Vasculitis

- 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** (helps 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
Case Three: History

- **HPI:** 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:** no major illnesses or hospitalizations
- **Medications:** none, up to date on vaccines
- **Allergies:** none
- **Family history:** no history of clotting or bleeding disorders
- **ROS:** cough and runny nose a few weeks ago
Case Three: Skin 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. CBC
  b. ESR
  c. HIV test
  d. Skin biopsy
  e. Urinalysis
Case Three, Question 1

Answer: d

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

- 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. Disseminated intravascular coagulation
- b. Henoch-Schönlein Purpura
- c. Idiopathic thrombocytopenic purpura
- d. Sepsis
- e. Urticaria
Case Three, Question 2

Answer: b

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

- Henoch-Schönlein Purpura (HSP) is the most common form of systemic vasculitis in children
  - Characterized by palpable purpura (vasculitis), arthritis, abdominal pain and kidney disease
- 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 (streptococcal pharyngitis) infection
- Other bacterial infections, drugs, food and lymphoma may cause HSP
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* \textit{IgA deposition} (the \textit{diagnostic} feature of HSP)
- Rule out streptococcal infection with an ASO or throat culture
HSP: Evaluation and Treatment

- It is 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
HSP
Case Four
Case Four: History

- 45-year-old man who was admitted to the hospital five weeks ago with acute bacterial endocarditis. After an appropriate antibiotic regimen was started and patient 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.
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 pedal edema
- Labs: normal CBC, PT, PTT, INR
- ANA < 1:40
- Negative ANCA, cryoglobulins
- HIV negative, negative hepatitis serologies (except for HBVsAb positive)
Case Four, Question 1

Which of the following is the most likely cause of skin findings?

a. DIC secondary to sepsis
b. Leukocytoclastic vasculitis secondary to antibiotics
c. Septic emboli with hemorrhage from undiagnosed bacterial endocarditis
d. Urticarial vasculitis
Case Four, Question 1

Answer: b

- Which of the following is the most likely cause of Mr. Burton’s skin findings?
  - a. DIC secondary to sepsis (history and skin exam are less concerning for sepsis. In DIC, coagulation studies are abnormal)
  - b. Leukocytoclastic vasculitis secondary to antibiotics
  - c. Septic emboli with hemorrhage (these lesions tend to occur on the distal extremities)
  - d. Urticarial vasculitis (presents with a different morphology, which is urticarial)
Case Four, Question 2

A skin biopsy confirmed LCV. What else should be done at this time?

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

Answer: a & c

- What else should be done at this time?
  a. **Obtain a urinalysis** (detection of renal involvement will impact treatment)
  b. Start systemic steroid (typically used when vasculitis is systemic or severe)
  c. **Stop the IV antibiotics and replace with another** (remove the offending agent)
  d. All of the above
LCV: Etiology

- Acute infection – *beta-hemolytic Streptococcus group A*, and rarely *Mycobacterium tuberculosis*
- Lymphoproliferative neoplasms
- Solid tumors: *lungs, colon, prostate and breast*
- Connective Tissue Disease
LCV: Evaluation

- CBC
- Urinanalysis
- ASO titer
- ANA
- Hepatitis serology
- ANCA
- Serum cryoglobulins
- Skin biopsy
LCV: Treatment

• Patients with normal UA and clinically well – nonaggressive treatment: rest, elevation of the leg, analgesics, avoidance of trauma and treat underlying cause

• NSAIDs,

• Colchicine, dapsone for chronic vasculitis

• Systemic corticosteroids for serious systemic manifestations or necrotic lesions
Leukocytoclastic vasculitis

- Palpable hemorrhagic papules coalescing into plaques, bilateral on the lower extremities
Leukocytoclastic Vasculitis
Case Five
Case Five: History

- **HPI:** 34-year-old previously healthy woman who was admitted to the hospital with a 5-day history of fever, weight loss, joint pain/swelling, paresthesias (both feet), and painful skin nodules
- **PMH:** mild normocytic anemia
- **Medications:** OCP, Malarone (malaria prophylaxis)
- **Allergies:** sulfa
- **Family history:** no autoimmune disease
- **Social history:** worked in Haiti one month prior to admission; no animal contacts
- **Health-related behaviors:** no tobacco, alcohol, or drug use
- **ROS:** reports no photosensitivity, malar rash, mucosal ulcers, dry eyes/mouth, sore throat, abdominal pain, or dysuria
Case Five: Exam

- Vitals: febrile
- Gen: well-appearing, very thin female
- HEENT: clear, no ulcers noted
- No lymphadenopathy
- Normal cardiac, respiratory, abdominal exams
- Neurologic exam: decreased sensation and reflexes in bilateral legs
- Joint exam: warmth/swelling at hands, feet, ankles, knees
- Skin: lower extremities with multiple 6x8mm tender, erythematous subcutaneous nodules
Case Five: Exam continued

- Swelling of feet
- Erythematous nodule
Case Five: Labs

- CBC: **anemia**
- ESR: **60 [0-15]**; CRP: **46.8 [<6.3]**
- Normal liver function, BUN/Cr
- UA: trace hemoglobin, trace protein
  - 24 hour urine: **increased protein**
  - Urine sediment: **RBCs, WBCs, tubular casts**; no dysmorphic RBCs
- CXR: negative
- ANCAs: negative
- ANA: negative
- Blood/urine cultures: negative
- Infectious work-up for parasites, bacteria, and viruses: negative
- Work-up for hematologic malignancy and hypercoagulability: negative
Case Five: Skin Biopsy

- A skin biopsy obtained from a subcutaneous nodule on leg reveals inflammation of a medium-sized artery of the skin
Case Five, Question 1

What is the most likely diagnosis?

a. Henoch-Schönlein Purpura
b. Erythema nodosum
c. Polyarteritis nodosa
d. Takayasu arteritis
e. Urticaria
Case Five, Question 1

Answer: c

- What is the most likely diagnosis?
  
  a. Henoch-Schönlein Purpura *(affects small vessels)*
  
  b. Erythema nodosum *(panniculitis on biopsy)*
  
  c. **Polyarteritis nodosa** *(affects medium-sized arteries)*
  
  d. Takayasu arteritis *(affects large vessels)*
  
  e. Urticaria *(presents with a different morphology, which is urticarial)*
Polyarteritis Nodosa

Polyarteritis Nodosa (PAN) is a potentially systemic disorder of necrotizing vasculitis of medium-sized arteries
  • Characterized by painful subcutaneous nodules, which can ulcerate
  • Patients may also present with livedo reticularis

Unknown etiology; may affect any organ (most often skin, peripheral nerves, kidneys, joints, and GI tract)

PAN has been associated with HBV, HCV, HIV, parvovirus B19, Crohn’s disease, strep and TB infections and medications (minocycline)
Polyarteritis Nodosa-Cutaneous

- ESR – the only laboratory abnormality
- P-ANCA may be present
- Most patients respond to aspirin, NSAIDs, prednisone
- In childhood – antibiotics may be used, since streptococcal infection is common
Polyarteritis Nodosa

- Several hyperpigmented nodules along medium-sized vessels
Polyarteritis Nodosa
Systemic PAN

- Key diagnostic features of this case
  - Fever
  - Leukocytosis with neutrophilia, trombocytosis
  - Skin nodules with medium-sized artery inflammation on biopsy
  - Renal involvement
  - Paresthesias, decreased sensation and reflexes (i.e., mononeuritis multiplex)
Diagnosis: PAN

It is important to differentiate between cutaneous and systemic PAN to help guide therapy

- Cutaneous PAN
  - Skin involvement +/- polyneuropathy, arthralgias, myalgias, fever
  - More common in children (may follow a strep infection)
  - Chronic benign course

- Systemic PAN
  - Neurological involvement common: mononeuritis multiplex, stroke
  - Renal: hypertension
  - Joint, Heart, GI, Liver also may be affected
  - Orchitis in patients with HBV
Management: PAN

- Chronic course (months-years); exacerbations/remissions
- Local wound care to any skin ulcerations
- Patients without cutaneous PAN may be treated with systemic corticosteroids alone
- For patients with cardiac, gastrointestinal, neurological, or renal involvement (i.e., systemic PAN):
  - Specialty consultation for involved organs (especially nephrology and neurology)
  - Adjunctive therapy with cyclophosphamide
- Treat any underlying infections (e.g., HBV)
Pigmentary Purpuric Eruptions

• Presents on lower extremities with several clinical patterns
• The most common variant — Schamberg’s disease
• The other variants:
  – purpura anularis telangiectoides (Majocchi’s disease)
  – Gougerot-Blum syndrome (pigmented purpuric lichenoid dermatitis)

• Ducas and Kapetanakis pigmented purpura
• Lichen aureus
Schamberg’s Disease

- Typical lesions: thumb-print sized and composed of aggregates of pinhead-sized petechiae resembling grains of cayenne pepper along with golden-brown hemosiderin staining
- The lesions begin on the lower legs with slow proximal extension
- The favored sites: lower shins and ankles
Schamberg’s Disease - Treatment

- Topical steroids for 4-6 weeks
- Pentoxifyline 400mg three times a day for 2-3 weeks
- Oral rutoside 50 mg twice a day and ascorbic acid 500mg twice a day
- Support stocking in settings of venous stasis
Schamberg’s Disease
Purpura
Annularis
Telangiectoides
Majocchi’s disease
Gougerot-Blum Syndrome
Lichen Aureus
Summary: Petechiae and Purpura

• The term purpura is used to describe red-purple lesions that result from extravasation of the blood into the skin or mucous membranes
• Purpura may be palpable and non-palpable
• Purpura does not blanch with pressure
• Purpura may result from hyper- and hypocoagulable states, vascular dysfunction and extravascular causes
• 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
Summary: Palpable Purpura

- 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 usually necessary for the diagnosis of vasculitis