Cutaneous vasculitis: clinical images and practical approach

Prof. Dr. Petra De Haes
Dermatology
1. When to think of it?

2. How to diagnose?

3. Required evaluations?
1. When to think of it?
   Clinical presentation

2. How to diagnose?

3. Required evaluations?
CUTANEOUS VASCULITIS: CLINICAL PRESENTATION

= HETEROGENEOUS!
Clinical morphology correlates with predominant vessel-size involved

**Small, superficial vessels**
- < 50 micrometer
- Postcapillary venules, capillaries, nonmuscular arterioles
- Superficial + mid-dermis

**Medium, deep vessels**
- 50 – 150 micrometer
- Arteria with muscular wall
- Deep dermis + subcutis
Small vessels
Medium-sized vessels
Clinical morphology correlates with predominant vessel-size involved

<table>
<thead>
<tr>
<th>Small</th>
<th>Medium</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Palpable) Purpura</td>
<td>Subcutaneous nodules</td>
</tr>
<tr>
<td>Vesiculobullous</td>
<td>Livedo</td>
</tr>
<tr>
<td>Superficial ulcerations</td>
<td>Ulcerations (deep ulcers)</td>
</tr>
<tr>
<td>Persistent urticarial</td>
<td>Digital cyanosis + necrosis</td>
</tr>
</tbody>
</table>
CUTANEOUS VASCULITIS: CLINICAL PRESENTATION

Predominant small-vessel involvement

1. Palpable purpura
+/- hemorrhagic bullae/superficial ulcerations

2. Persistent urticarial lesions
Palpable purpura (+/- hemorrhagic bullae/superficial ulcerations) + vasculitis superficial small vessels

- ASSOCIATED DIAGNOSIS ACCORDING TO CHCC2012
  - Infection-associated vasculitis
  - Drug-induced vasculitis
  - IgA-vasculitis (systemic or skin dominant)
  - Cryoglobulinemic vasculitis (systemic or skin dominant)
  - IgG/IgM-vasculitis (skin restricted)
  - Vasculitis associated with systemic disease
    (SLE, Sjögren, DM, RA, ....)
  - Vasculitis associated with other autoimmune disease (e.g. IBD)
  - ANCA-associated vasculitis

‘Idiopathic cutaneous small-vessel vasculitis’?
Predominant small-vessel involvement

1. Palpable purpura
   +/- hemorrhagic bullae/superficial ulcerations

2. Persistent urticarial lesions
Persistent urticarial lesions

+ vasculitis superficial small vessels

ASSOCIATED DIAGNOSIS ACCORDING TO CHCC2012

• Normocomplementemic urticarial vasculitis (skin restricted)

• Hypocomplementemic urticarial vasculitis (HUV)
  (=anti-C1q vasculitis)
  skin dominant
  systemic (HUV syndrome)
**CUTANEOUS VASCULITIS: CLINICAL PRESENTATION**

Clinical morphology correlates with predominant vessel-size involved

<table>
<thead>
<tr>
<th>Small</th>
<th>Medium</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Palpable) Purpura</td>
<td>Subcutaneous nodules</td>
</tr>
<tr>
<td>Vesiculobullous</td>
<td>Livedo</td>
</tr>
<tr>
<td>Superficial ulcerations</td>
<td>Ulcerations (deep ulcers)</td>
</tr>
<tr>
<td>Persistent urticarial</td>
<td>Digital cyanosis + necrosis</td>
</tr>
</tbody>
</table>
Predominant medium-size vessel involvement

1. Subcutaneous nodules

2. Livedo racemosa

3. Necrotic ulcerations

4. Digital cyanosis +/- necrosis
Nodules, livedo, ulceration, necrosis
+ vasculitis deep medium-sized vessels

**ASSOCIATED DIAGNOSIS ACCORDING TO CHCC2012**

- Polyarteritis nodosa (systemic or skin dominant)
- ANCA-associated vasculitits
- Drug-induced vasculitis
- Vasculitis associated with systemic disease
  (SLE, Sjögren, DM, RA, ...)
- Cryoglobulinemic vasculitis (systemic or skin dominant)
1. When to think of it?

2. How to diagnose?

3. Required evaluations?
CUTANEOUS VASCULITIS: DIAGNOSIS

BIOPSY

LIGHTMICROSCOPY (H&E)

DIRECT IMMUNOFLUORESCENCE (DIF)
CUTANEOUS VASCULITIS: DIAGNOSIS

BIOPSY – LIGHTMICROSCOPY

CONFIRM VASCULITIS

Exclude non-vasculitic (pseudo-vasculitic) disorders
In **SMALL vessels** (venules, arterioles sup. dermis):

2 out of 3 criteria:

- Angiocentric and/or angioinvasive inflammatory (predominant neutrophilic) infiltrate
- Disruption and/or destruction of vessel walls by the inflammatory infiltrate
- Fibrinoid necrosis of vessel wall
In MEDIUM-SIZED vessels (arteries, veins deep dermis/subcutis):

Both criteria:

• Inflammatory (predominant neutrophilic) infiltrate infiltrating the muscular vessel wall
• Fibrinoid necrosis
Clinical suspicion of vasculitis should be confirmed histologically (cfr criteria)

= clear scientific statement/conclusion

= often frustrating in daily practice....
HISTOLOGIC PATTERN = DYNAMIC !!!

1. TIMING

Lesions 24 - 48h

> 48 h: non-specific infiltrate (lymphocytes, histiocytes)

< 24 h: no clear vessel wall damage
LIGHT MICROSCOPY VASCULITIS

HISTOLOGIC PATTERN = DYNAMIC !!!

2. LOCATION + DEPTH

- PP, UV: lesional; punch ≥ 4/0
- Nodules: lesional + deep (!); wedge biopsy
- Ulcerations: border of ulcer + deep; wedge biopsy
- Livedo: within pale center of rings (± purple part of rings) + deep; wedge biopsy
- (Infarcted digits: no biopsy...)

HISTOLOGIC PATTERN DEPENDS ON TIMING + LOCATION OF BIOPSY

REPEETIVE BIOPSIES OFTEN NECESSARY BEFORE CLEAR HISTOLOGIC DIAGNOSIS OF VASCULITIS
CUTANEOUS VASCULITIS: DIAGNOSIS

BIOPSY

- LIGHTMICROSCOPY (H&E)
- DIRECT IMMUNOFLUORESCENCE (DIF)
DIRECT IMMUNOFLUORESCENCE VASCULITIS

- In setting of **palpable purpura or urticarial lesions**
- **Fresh** biopsy!
- **Lesions < 24h**
  - Rapid degradation of immune deposits
- Identify **perivascular immunoreactants**
  - (complement and/or Ig)
DIRECT IMMUNOFLUORESCENCE VASCULITIS

**Negative DIF ≠ exclude vasculitis**

**Positive DIF ≠ diagnosis of vasculitis**

**Perivascular IgA?**
- IgA vasculitis
- Renal involvement!

Perivascular IgM: cryoglobulinemia? RA vasculitis?

DIF perivascular AND BMZ: vasculitis + SLE

Negative DIF + H&E vasculitis pattern: pauci-immune (PAN or ANCA) vasculitis?
1. When to think of it?

2. How to diagnose?

3. Required evaluations?
CLINICAL MORPHOLOGY SUGGEST VASCUITIS

BIOPSY CONFIRMS VASCUITIS

UNDERLYING CAUSE?

SYSTEMIC VASCUITIS?
CUTANEOUS VASCULITIS

UNDERLYING CAUSE?

• Infections (15-20%)
  (Strep pyogenes, HCV, HBV, HIV)
• Medications (10-15%)
• Connective tissue dis (10-15%)
  (SLE, Sjögren, RA,...)
• Malignancy (5%)
  (Hematologic>solid)
• Primary systemic vasculitis (< 4%)
  (PAN; ANCA-associated)
• Idiopathic (40-60%)

SYSTEMIC VASCULITIS?

• Renal
• Pulmonary
• Neurologic
• Gastro-intestinal
FOR ALL PATIENTS PROVEN VASCULITIS

THOROUGH HISTORY
Infection signs
Medications (+ stimulant drugs)
Review of all systems
• Interval first exposure – vasculitis variable!
  i.e. hours to years...
  in cutaneous small vessel vasculits: usually days - weeks

• Check Drug-eruption data banks + literature
  antibacterial, NSAID, diuretics (hydralazine), anticonvulsants,
  GMCS factor, propylthiouracil, TNF-α antagonist, interferon β,
  levamisole-containing cocaine
  ...

MEDICATION INTAKE
SYSTEM REVIEW

• Constitutional: fever, weight loss, fatigue, night sweats, chills
• Musculoskeletal: arthralgias/arthritis, myalgias
• Renal: hematuria (dark urine?)
• Gastroenterologic: abdominal pain, diarrhea, bloody stools/melena
• Neurologic: numbness, paresthesias, weakness
• Cardiopulmonary: dyspnea, chest pain, cough, hemoptysis, asthma
• Ear/nose/throat: sinusitis, nose bleeding, sore throat
**CUTANEOUS VASCULITIS: INVESTIGATIONS**

First episode with
- clear inciting factor and/or
- no suggestion of systemic involvement

**MINIMAL LAB**
- Complete blood count + differential
- Liver function test
- Creatinine
- CRP + sedimentation rate
- Urinalysis (hematuria? proteinuria?)
CUTANEOUS VASCULITIS: INVESTIGATIONS

Recurrent disease with unclear cause
and/or
Suggestion underlying systemic involvement

EXTENSIVE LAB
±
OTHER TESTS BASED ON SPECIFIC SIGN/SYMPTOMS
CUTANEOUS VASCULITIS: INVESTIGATIONS

EXTENSIVE LAB

±
OTHER TESTS BASED ON SPECIFIC SIGN/SYMPTOMS
EXTENSIVE LAB

- Complete blood count with differential
- Creatinine
- CRP + sedimentation rate
- Liver function tests
- Urinalysis
- Hep B and C serology
- HIV antibody
- Serum complement levels (total, C4, C3; C1 and anti C1q for HUV)
- ANF + dsDNA + ENA/....
- RF
- ANCA
- Serum protein electrophoresis and immunofixation
- Cryoglobulins (difficult lab procedure!)
CUTANEOUS VASCULITIS: INVESTIGATIONS

OTHER TESTS

No global guideline

Depends on symptoms/signs/lab results

Pulmonary symptoms: chest X-ray (infection? vasculitis? malignancy?,...)

GI symptoms: FOB, colonoscopy, culture, ...

Neurologic symptoms: EMG, MRI brain,...

General weight loss, night sweating, fatigue: hematologist, PET-CT,...
CONCLUSION

• **Clinical image** depends on affected vessel size

• **Confirm diagnosis by biopsy (H&E)**
  
  histologic pattern = dynamic
  
  timing and location/depth of biopsy is important
  
  repetitive biopsies sometimes necessary

• **In proven vasculitis:**
  
  search for possible cause and/or systemic vasculitis

  Thorough history!
  
  Minimal or extensive lab
  
  (depends on clinical image and history)
Cutaneous vasculitis: clinical images and practical approach

Prof. Dr. Petra De Haes
Dermatology

No more stress when you think of vasculitis 😊