Treatment small vessel cutaneous vasculitis: PRESENT

Prof. Dr. Petra De Haes
Dermatology
CUTANEOUS SMALL VESSEL VASCULITIS (CSVV): TREATMENT
Key questions guiding treatment

1. Isolated cutaneous versus systemic involvement?

2. Can a cause be identified + eliminated?

3. In isolated cutaneous SVV
   - First episode versus recurrent/chronic?
   - Severity of cutaneous involvement?
CSVV: TREATMENT

Thorough history + LAB (with urinalysis!)

- SKIN RESTRICTED VASCULITIS
- + EXTRACUTANEOUS VASCULITIS
  - Kidney!
  - Joints, GI, lung

Multidisciplinary approach
CSVV: TREATMENT

Key questions guiding treatment

1. Isolated cutaneous versus systemic involvement?

2. Can a cause be indentified + eliminated?

3. In isolated cutaneous SVV
   
   First episode versus recurrent/chronic?

   Severity of cutaneous involvement?
ISOLATED CSVV: TREATMENT

REMOVE/TREAT INCITING CAUSE?

- Infection
- Medication
- Connective tissue diseases
  - SLE, Sjögren, RA,…
- Cryoglobulinemia
- ANCA-associated vasculitis
- Malignancy

> 50 % NO CLEAR UNDERLYING CAUSE!
1. Isolated cutaneous versus systemic involvement?

2. Can a cause be identified + eliminated?

3. In isolated cutaneous SVV

   First episode versus recurrent/chronic?

   Severity of cutaneous involvement?
ISOLATED CSVV: TREATMENT

FIRST EPISODE + MILD CUTANEOUS INVOLVEMENT

SYMPTOM ALLEVIATION!
Relative rest + leg elevation
Compression stocking
Topical potent Cs
NSAID (if no contra-indications)
  *Indomethacine: few case reports/series with specific effect in CSVV
Antihistamines if itchy
FIRST EPISODE + SEVERE CUTANEOUS INVOLVEMENT

Widespread AND severely symptomatic
OR
Hemorrhagic bullae and/or necrosis

Consider short taper of systemic corticosteroids

- Prednisone: start (60) 40 mg/d
- Methylprednisolone: start (40) 32 mg/d
- Taper: over ± 6 weeks
ISOLATED CSVV: TREATMENT

RECURRENT/CHRONIC + MILD TO MODERATE SEVERITY

ANTI-INFLAMMATORY DRUGS TARGETING NEUTROPHILS

• Colchicine
• Dapsone
  + colchicine
  + pentoxifylline
• (Tetracyclines?)
TREATMENT CSVV: COLCHICINE

Herbal remedy since Egyptians

Colchicine isolated begin 1800

Only 2009 FDA approval for FMF and gout

Colchicum autumnale
TREATMENT CSVV: COLCHICINE

- Efficacy in CSVV reported in multiple case-reports/series

- 1 prospective RCT
  
  41 pts
  
  Colchicine 0.5 mg/d versus topical emollients
  
  NO significant effect
  
  BUT: small group, low dose, 3/41 pts complete response with recurrence after stop

Considered first-line R/ in chronic CSVV expert reviews
• **Dose:** 1 – 2 mg/day
  start: 2 x 0.5 mg/d ➞ 3 x 0.5 mg/d ➞ 2 x 1 mg/d

• **Side-effects at recommended dosage:**
  GI problems: diarrhea!, nausea, vomiting, abd pain
  Hematologic: myelosuppression
  Myotoxicity: in combination with other risk factors (e.g. statins)

• **Safe long-term profile**
**BEWARE:**

- Toxic at high doses (40 mg in adults); no antidote available!
- Drug interactions (CYP 3A4 inhibitors and P-gp inhibitors)
  - e.g. cyclosporine, macrolides, itraconazole, anti-retroviral drugs, verapamil, ....
- SEVERE hepatic dysfunction
- SEVERE renal impairment (creat clearance < 30mL/min)

> increased risk colchicine toxicity!
TREATMENT CSVV: DAPSONE

• Efficacy in CSVV reported in multiple case-reports/series
• NO placebo-controled trials

Diaminodiphenylsulfone:

• 50 mg/d → 100-150 mg/d → (200 mg/d)
• Check for G6PDH deficiency before start!
• Regular lab controls for:
  myelosuppression
  hemolysis – methemoglobinemia
  hepatic dysfunction
Dapsone + colchicine
  safe combination
  sometimes more effective than either agent alone

Dapsone + pentoxifylline
  more effective than dapsone alone
  Nurnberg W et al. Lancet 1994
  dapsone 100mg/d + PTX 1200 mg/d
TREATMENT CSVV: TETRACYCLINES

- In literature: only induction of vasculitis by minocycline!

- Based on well-known anti-neutrophilic effects: tetracyclines are theoretically a possible R/

- **Personal use in recurrent mild isolated CSVV:**
  - Doxycycline 2 x 100 mg/d in pts not tolerating colchicine
  - Doxycycline 2 x 100 mg/d + colchicine 2 x 0.5 mg/d if colchicine alone is not efficient
CHRONIC/RECURRENT
MILD TO MODERATE SEVERITY

Doxycycline
2 x 100 mg/d

Colchicine
2 x 0.5 – 2 x 1 mg/d

Dapsone
50 – 150 (200) mg/d

Dapsone +
Colchicine
Pentoxyfylline
(Doxycycline)

Compression stockings!
ISOLATED CSVV: TREATMENT

RECURRENT/CHRONIC + SEVERE CUTANEOUS INVOLVEMENT

NO CHRONIC MONOTHERAPY SYSTEMIC CS!

IMMUNOSUPPRESSIVE/CS-SPARING DRUGS

• Mycophenolate mofetil
  2 (-3) g daily, divided doses
• Azathioprine
  2 - 2.5 mg/kg daily if no TPMT mutations
• Methotrexate
  10 - 20 mg weekly (but: may cause cutaneous vasculitis)
**SYSTEMIC Cs: dose as low as possible (tapering!) +**

**IMMUNOSUPPRESSIVE/CS-SPARING DRUGS**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Choice based on:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mycophenolate mofetil</td>
<td>Patient’s co-morbidities</td>
</tr>
<tr>
<td>Azathioprine</td>
<td>Patient’s tolerance/preference</td>
</tr>
<tr>
<td>Methotrexate</td>
<td>Physician’s experience</td>
</tr>
<tr>
<td></td>
<td>No comparing studies in CSVV</td>
</tr>
</tbody>
</table>
ISOLATED CSVV: TREATMENT

RECURRENT/CHRONIC + SEVERE CUTANEOUS INVOLVEMENT

2nd LINE IMMUNOSUPPRESSIVE R/
- Cyclosporine
- Cyclophosphamide

Intravenous Ig
2 g/kg monthly, divided over 2 – 4 days
Expensive!!!
ISOLATED CSVV: TREATMENT

OTHER DESCRIBED TREATMENT OPTIONS

• Hydroxychloroquine
  - Urticarial vasculitis
  - Cutaneous vasculitis in context of SLE

• Potassium iodide
  For nodular vasculitis: moderate evidence for efficacy

• (Omega-3 fatty acids)
  1 case report: Barnadas MA, Case Rep Dermatol 2016