Sarcoidosis

• Inflammatory disorder of unknown origin
  – Environmental factors and genetic factors

• > 90% pulmonary involvement

• 2-5% granulomatous inflammation in the nervous system (“neurosarcoidosis”)

Sarcoidosis

Granulomatous inflammation
Neurosarcoidosis

- Granulomatous inflammation within the nervous system:
  - Brain
  - Meninges
  - Spinal cord
  - Peripheral and cranial nerves
Peripheral nervous system

- (Poly-)radiculopathy

- Polyneuropathy
  - Axonal
  - Demyelinating
  - Large vs small fiber

- Multiple mononeuropathies
Many diverse presentations...
Granulomatous inflammation in common
Neurosarcoidosis treatment

• Aimed to suppress inflammation
  
  • prednison
  • Methotrexaat
  • azathioprine
  • anti-TNF
Neurosarcoidosis

• Diagnosis

Patients diagnosed with active sarcoidosis:

versus

Patients not known with sarcoidosis
Sarcoidosis

• Inflammatory disorder of unknown origin
  – Environmental factors and genetic factors

• > 90% pulmonary involvement

• 2-5% granulomatous inflammation in the nervous system ("neurosarcoidosis")
Sarcoïdose

• Presentation and course show a wide variation

• Often continuing pain and fatigue
I have no clue what’s wrong…The car appears well

“I guess you will have to learn to live with the noise jack….”
Symptoms

often continuing after signs of inflammation have dissolved

• Pain
• Dry eyes and mouth
• “flushes”
• Sheet intolerance
• Hyper/hypohidrosis
• Difficulties with urination
• Diarrhea/obstipation
• Sexual dysfunction
• Fainting
Small fiber neuropathy
Peripheral nervous system

Large (Aβ) nerve fibers
- Motor function
  - muscle control
- Sensory function
  - position and movement sensation

Small (Aδ/C) nerve fibers
- Sensory function
  - pain and temp. sensation
- Autonomic function
  - basal physiology

Polyneuropathy
- EMG

Small fiber neuropathy (SFN)
Diagnosis of SFN

• Physical examination usually normal
• EMG usually normal

• Possible diagnostic tests
  – Temperature threshold testing (TTT)
  – Skin biopsy
  – Skin wrinkling
  – The Neuropad®
  etc
Temperature Threshold Testing (TTT)

Sarcoidosis population (n=74):
69% abnormal warmth and/or cold sensation

Psychophysical test

Skin and sweat gland innervation
Skin biopsy
Skin biopsy

IENFD controls: 12.3 (7.6 - 15.6)
IENFD sarcoidosis: 5.1 (3.9 - 6.7)

(p=0.003)

Hoitsma et al. Lancet 2002; 359: 2058-6
Skin Biopsy (IENFD)

188 healthy controls and 72 sarcoidosis patients

33% of sarcoidosis patients with SFN symptoms had abnormal skin biopsy

– Objective;
– However, not widely available
– Sensitivity?

Skin wrinkling

35 SFN patients vs 61 healthy controls

Both hands 30 min in water at 40 °C

Mechanism:
– local vasoconstriction after disturbed electrolytes in sweat glands

Abnormal = absence of wrinkling

The Neuropad®

an adhesive pad impregnated with blue cobalt

When cobalt gets in contact with water (sweat) its color changes from blue to pink

Abnormal = no colour change

Papanas et al. *Diabetes Educ* 2007; 33:257-8
It appears rather primitive here.
### Value of these tests

<table>
<thead>
<tr>
<th>Study</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>TTT</td>
<td>40-82%</td>
<td>83%</td>
</tr>
<tr>
<td>Skin biopsy</td>
<td>33-81%</td>
<td>64-97%</td>
</tr>
<tr>
<td>Skin wrinkling</td>
<td>66%</td>
<td>70%</td>
</tr>
<tr>
<td>The Neuropad®</td>
<td>27%</td>
<td>93%</td>
</tr>
</tbody>
</table>

**Advantage:** cheap and simple
“I have found the cause:
The wires are not working well… and I know more and more how to test these wires…”

…Huh.? How does that come? Is it dangerous? How can we fix them?...
Small Fiber Neuropathy in sarcoidosis

Therapy

- Prednison/MTX not effective

- Neuropathic pain medication
  - Antidepressants/ anti-epileptic drugs
  - Effective in 1/3 to reach 50% pain reduction
  - Side effects…

A need for better therapy
Hit the road jack....!
.....And don’t you come back no more....!