POEMS Syndrome

Maite Cibeira
Amyloidosis and Myeloma Unit
Hospital Clinic of Barcelona
POEMS Syndrome

Also known as...
Osteosclerotic Myeloma
Crow-Fukase syndrome
and Takatsuki syndrome
- Polyneuropathy
- Organomegaly
- Endocrinopathy
- Monoclonal protein
- Skin changes
Clinical Features*

- N = 99 patients
- Median age: 51 years
- Male gender in 63% pts
- Neuropathy is the dominant characteristic
- Only 29 patients had a “complete” POEMS syndrome
- 18 patients developed new manifestations over time
- Infrequent progression to overt MM

*Dispenzieri et al, Blood 2003
## POEMS Diagnostic Criteria*

| Mandatory major criteria | 1. **Polyneuropathy**  
<table>
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<tr>
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<th>2. <strong>Monoclonal PC proliferative disorder</strong></th>
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| Major criteria           | 3. Sclerotic bone lesions  
|                          | 4. Castleman disease  
|                          | 5. Increased levels of VEGF-α |
| Minor criteria           | 6. **Organomegaly or lymphadenopathy**  
|                          | 7. Extravascular volume overload  
|                          | 8. **Endocrinopathy**  
|                          | 9. **Skin changes**  
|                          | 10. Papilledema  
|                          | 11. Thrombocytosis/polycythemia |

**Required:**
- both mandatory major criteria
- 1 major criteria
- and at least 1 minor criteria

**Diabetes and thyroid abnormalities** by itself are not enough as endocrinopathy

Other Symptoms and Signs

- Clubbing
- Weight loss
- Hyperhidrosis
- Pulmonary hypertension / restrictive lung disease
- Thrombotic diathesis
- Diarrhea
Mandatory Major Diagnostic Criteria

- Sensorymotor peripheral neuropathy  
  (typically demyelinating with axonal loss)

- Monoclonal plasmaproliferative disorder  
  (almost always lambda, usually IgA-lambda, and BMPC <10%)

Biopsy of an sclerotic lesion is not imperative in the proper clinical context
Utility of VEGF in POEMS*
(both serum or plasma levels)

- **Differential diagnosis** with other plasma cell dyscrasias, neuropathic processes and multisystem diseases
  - Chronic inflammatory desmyelinating polyradiculoneuropathy (CIDP ≠ POEMS also by nerve conduction study/EMG**)
  - MGUS neuropathy
  - AL neuropathy
  - Castleman’s disease variant of POEMS syndrome (no PC dyscrasia, little/no PN, but several of the minor criteria)

- **Monitoring disease activity** after treatment (correlates with clinical improvements better than hematologic response)

* D'Souza A et al (Mayo Clinic), Blood 2011.
** Mauermann ML et al (Mayo Clinic), J Neurol Neurosurg Psychiatry 2012.
Assessment of Response / Progression (after ASCT)*

<table>
<thead>
<tr>
<th></th>
<th>Response</th>
<th>Progression/relapse</th>
</tr>
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<tbody>
<tr>
<td>Clinical</td>
<td>Any objective improvement</td>
<td>Any objective worsening</td>
</tr>
<tr>
<td>Hematologic</td>
<td>= MM</td>
<td>= MM</td>
</tr>
<tr>
<td>VEGF (if baseline ≥ 200 pg/mL)</td>
<td>↓ at least 50%</td>
<td>↑ to ≥ 200 pg/mL</td>
</tr>
<tr>
<td>PET</td>
<td>↓ at least 50%</td>
<td>Definite ↑ in size or FDG avidity or new lesions (FDG+)</td>
</tr>
</tbody>
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* D’Souza et al, Blood 2012;120:56-62
Treatment Options: “Localized” Disease

- 1 or 2 (3) osteosclerotic lesions without BM involvement
  → **LOCAL RADIATION THERAPY** 40 to 50 Gy
  (>50% NRL responses within months/years and can be curative)

Dispenzieri A et al, Blood 2012 (How I treat); Humeniuk et al, Blood 2013
## Treatment Options: Widespread Disease

- Widespread disease (i.e., BM involvement or >2 bone lesions) or progression 3-6 months after completing radiation therapy → **SYSTEMIC THERAPY** needed
  +/- RADIATION of a large bone lesion

<table>
<thead>
<tr>
<th>Regimen</th>
<th>Response Rate</th>
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<tbody>
<tr>
<td>MP</td>
<td>44%</td>
</tr>
<tr>
<td>VAD or Cy-based</td>
<td>27%</td>
</tr>
<tr>
<td>Prednisone or dexta alone</td>
<td>15%</td>
</tr>
<tr>
<td>HDM/SCT in younger patients (Dispenzieri et al, Blood 2004)</td>
<td>Response in 14 of 16 patients, but with significant morbidity (TRM 1/16)</td>
</tr>
</tbody>
</table>
ASCT in POEMS Syndrome: First reports

Dramatic improvement of POEMS syndrome following autologous haematopoietic cell transplantation

M. Rovira, E. Carreras, J. Bladé, F. Graus, J. Valls, F. Fernández-Avilés and E. Montserrat
Department of Haematology and Neurology, BMT Unit, Postgraduate School of Haematology Farreras-Valenti, Institut d’Investigacions Biomèdiques August Pi i Sunyer, Hospital Clinic, University of Barcelona, Barcelona, Spain

Received 28 March 2001; accepted for publication 15 May 2001

Case report

Successful treatment of POEMS syndrome with autologous hematopoietic progenitor cell transplantation

WJ Hogan, MQ Lacy, GA Wiseman, RD Fealey, A Dispenzieri and MA Gertz

1Division of Hematology and Internal Medicine, 2Section of Nuclear Medicine, and 3Department of Neurology, Mayo Clinic, Rochester, Minnesota, USA
Long-term outcomes after ASCT in POEMS syndrome*

- N=59, treated at a single institution (Mayo Clinic, Rochester)
- Median follow-up: 45 months
- Response rate:
  - Hematologic PR or better: 78% (CR 57%)
  - Clinical improvement: 92%
- 5-yr PFS: 75%
  - Most common progression events: Rx > ↑VEGF
    (rare symptomatic progression)
  - Risk factors for progression: Age ≤ 50 years
    IgG-lambda
    PET-avid lesions at baseline
    Lack of hematologic CR
- 5-yr OS: 94%

* D’Souza et al, Blood 2012;120:56-62
ASCT in POEMS Syndrome

Concerns

- Graft failure (10%): PBSC back-up
- Engraftment syndrome (50%): avoid G-CSF
- Pulmonary complications: need for ICU
- TRM: 3%
ASCT in POEMS Syndrome

EBMT Long-term Results*

- Study period: 1997-2010 (mFU: 48 mos)
- No. of patients: 127
- Median age: 50 yrs. (range: 26-69)
- Median time from dx to ASCT: 7.5 mos.
- Engraftment syndrome: 23% pts
- Hem RR (PR or better): 69.3% (CR in 48.5%)
- 5yr-PFS: 74%, 5yr-OS: 89%

*Cook G et al (EBMT), Haematologica 2017;102(1):160-7
POEMS and New Drugs

- **Thalidomide/Dex**: anecdotic responses (12 pts), not recommended as first line due to risk of neuropathy

- **Lenalidomide/Dex**: promising responses (>60 pts reported)

- **Bortezomib**: anecdotic responses (5 pts), used alone or in combination

- **Bevacizumab (anti-VEGF-A MoAb)**: anecdotic responses (7 out of 11 pts), two early deaths and two progressions despite normal VEGF

Lenalidomide* in POEMS Syndrome

- Prospective, open-label, pilot study
- \(N=18\) patients (13 pre-treated, 5 newly diagnosed but ineligible for HDM)
- Lenalidomide (25 mg/d x 21d) + dexa (40 mg weekly) until progression or intolerance
- Hem RR: 13/18 pts (72%)
- NRL response: 9/18 pts (50%)
- Median FU: 39 months -> 3yr-PFS: 59%
- No discontinuations due to toxicity

*Nozza et al (Italy), Br J Haematol 2017 (in press)
POEMS Syndrome
Mayo Clinic Long-term Results*

- Study period: 1974-2014
- No. of patients: 291
- Median age: 51 yrs. (range: 19-83)
- Dx after 2003 (n=146):
  - POEMS features
  - ASCT (49% vs. 8%)
  - CR rate (41% vs. 25%)
- OS at 10 yrs: 62%

OS for 291 patients with POEMS syndrome*

OS for 291 patients with POEMS syndrome*

OS according to first line treatment

OS according to depth of hematologic response

POEMS syndrome: prognostic features at multivariate analysis*

- Younger age
- Serum albumin > 3.2 g/dL
- CR

Daratumumab in POEMS?

Muchas gracias