HSCT in Chronic Inflammatory Demyelinating Neuropathy (CIDP)

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Duration of progressive phase

Percent of cases

GBS

CIDP

SIDP

Progressive phase weeks

0 4 8
Typical CIDP

- Chronically progressive, stepwise, or recurrent symmetric proximal and distal weakness and sensory dysfunction of all extremities, cranial nerves may be affected;
- > 2 months
- Absent or reduced tendon reflexes in all limbs
- Fulfillment of neurophysiological criteria
CIDP Prevalence Study in S-E England
Lunn 1999 JNNP 66 677

- Prevalence 0.5 - 1.25 per 100,000
- 46 patients in SE Thames
  - 54% had needed sticks
  - 13% still did
- Treatment received
  - 87% steroids
  - 46% azathioprine
  - 33% PE
  - 24% IVIG
- Still on treatment 54% (22% > 1)
Treatments

- Corticosteroids
- IVIg
- PE

- Immunosuppressive drugs
  - Broad spectrum
  - Resetting the immune system
  - Narrow spectrum
    - Against individual cell types
    - Against individual cytokines

- Immunomodulating drugs

All of proven benefit

None of proven benefit
CIDP and related disorders

- Without paraprotein
  - Symmetrical
  - Asymmetrical
  - MMN
- With paraprotein
  - MGUS
    - IgM and anti-MAG antibodies (DADS)
    - IgG or IgA coincidental
    - CANOMAD
  - POEMS
  - WM
  - Solitary myeloma/osteosclerotic myeloma
POEMS

Diagnostic criteria for POEMS syndrome require that all of the following be present:
- polyneuropathy
- a monoclonal plasma-cell proliferative disorder
- one or more of the following major criteria:
  - sclerotic bone lesions
  - Castleman's disease
  - elevated VEGF levels
POEMS

- one or more of the following minor criteria:
  - organomegaly (enlarged spleen, liver or lymph nodes)
  - extravascular volume overload (oedema, pleural effusion or ascites)
  - endocrinopathy (adrenal, pituitary, gonadal, parathyroid); diabetes or hypothyroidism alone are insufficient
  - skin changes
  - Papilloedema, thrombocytosis or polycythaemia
PBSCT in 16 patients with POEMS syndrome, and a review of the literature
Dispenzieri 2004 Blood 104 3400
Successful autologous PBSCT in CIDP

Vermeulen M and van Oers MH 2002 JNNP 127-8

- 48 year old male patient with symmetrical sensory and motor CIDP
- 10 year history needing IVIg every other week and prednisone 20 mg daily
- Improved post Cy Mobilisation stopped IVIg for 5 months until he relapsed.
- Given BEAM and then autologous SCT
- The response was maintained until five years post transplant before his symptoms recurred
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<tr>
<th>Patient</th>
<th>Age (years) Sex</th>
<th>Paraprotein</th>
<th>Disease duration years</th>
<th>Previous treatment</th>
<th>Months after transplant</th>
<th>Outcome</th>
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<td>42/M</td>
<td>IgA lambda</td>
<td>5</td>
<td>S, IVlg, PE, rituximab, cyclophosphamide</td>
<td>27</td>
<td>Improved</td>
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<td>52/M</td>
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<td>3</td>
<td>73/M</td>
<td>IgM</td>
<td>12</td>
<td>S, IVlg, PE, mycophenolate, Rituximab, aza, cyclophosphamide</td>
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<td>Worse</td>
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<td>4</td>
<td>29/F</td>
<td>None</td>
<td>21</td>
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Method

Immunosuppression stopped
exc steroids + IVIg

Mobilisation and harvest
- cyclophosphamide 2 g/m2 on 2 consecutive days
- then G-CSF 10 μg/kg/day sc for 5+ days
- then leukapheresis on day

Transplant
- cyclophosphamide 50 mg/kg + anti-thymocyte glob 2.5 mg/kg
- PBSCTs transfused under steroid, anti-H1 agent, anti-H2 agent and anti-emetic cover
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Walking limited to 10 m with a stick. Unable to dress.

Autologous PBSCT in May 2004: initial deterioration but then:

Steady improvement in strength and sensation and reduction in pain. Now walks a mile with a stick. Able to dress and do all his zips and buttons

Update now 8 years post transplant- Continued Remission
### Guy’s series case 2

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Progressive numbness and weakness of hands and feet despite treatment for 15 years. Severe flaccid areflexic tetraparesis with distal wasting and severe glove and stocking sensory loss. Inexcitable nerves but right ulnar (flexor carpi ulnaris) DML 39.8 ms. CSF protein 4700 mg/l. Nerve biopsy depletion of myelinated nerve fibres, onion bulbs and widely spaced myelin. CF antibody to nerve but negative immunoblot for to myelin proteins.
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February 2003 autologous PBSCT

At 3.5 years, previous progression arrested: symptomatically stronger

ONLS (disability) MRC sum score and ONLS unchanged

Update –Lost to long term FU after 4 years
### Guy’s series case 3

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**Aug 2005**  
autologous PBSCT: neutropenia - pneumonia - ventilation

Now even weaker but ONLS unchanged  
Update – Stable at 3 years post Transplant. Lost to long term FU
**Guy’s series case 4**

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Onset with GBS like illness age 8 with partial improvement. Then relapsing and remitting downhill course with partial responses to prednisolone, PE, IVIg, BIFN and mtx

Severe flaccid areflexic tetraparesis
Distal wasting and glove and stocking sensory loss

CSF protein 2800 mg/l
Median nerve MCV 9.5 m/s
Nerve biopsy onion bulb changes and T cell infiltration
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Maintained on IVIg 70 g 2 weekly, pred 20 mg alt die, mtx 15 mg weekly

June 2006 autologous PBSCT: neutropenia and pneumonia

Now off IVIg and mtx
Stronger, able to walk without knee brace and ankle splints which she has not done for 5 years.
ONLS unchanged.
Remission lasted for 18 months then relapsed with aggressive disease-coincided with revaccination.
10 metre walk time

NB - Patient 3 unable to walk before or after
Autologous peripheral blood stem cell transplantation for chronic acquired demyelinating neuropathy

Mohamed Mahdi-Rogers¹, Majid Kazmi², Rosalie Ferner¹, Richard AC Hughes¹

Susanne Renaud³, Andreas J. Steck³, Peter Fuhr³, Jörg Halter⁴, Alois Gratwohl⁴, Alan Tyndall⁵

Reported on total of 6 patients

- Two with features of POEMS syndrome improved; improvement was sustained in one but relapse required repeat transplant in the other.
- Two of the three with CIDP and one with an IgM paraprotein and antibodies to nerve improved.
- 1/6 globally weakened but stabilised.
- One relapsed after 18 months.
Conclusions

- CIDP - After PBSCT 5/6 patients improved to some extent.
- 1/6 - aged 73 at time of transplant had global weakness but 36 months post transplant remained stable. Lost to FU
- 1/6 - relapsed 18 months post transplant coinciding with revaccination.
- 4/6 remain well post transplant with significant improvement.
Acknowledgements

- Prof RAC Hughes/ Dr Mahdi-Rogers
- GSTT- HSCT team
- Prof A Steck, Prof Tyndall, Prof Gratwohl and HSCT team at Basel.