ALLOGENEIC STEM CELL TRANSPLANTATION IN A PATIENT WITH NASAL NK-T-CELL LYMPHOMA

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CASE REPORT

- Male patient
- 45 years
- First consultation in 04/2007
- ECOG 0
- First symptoms:
  - weight loss
  - local swelling, problems with breathing
  - palatal defect causing pain and dysphagia
Case Report (cont’d)

- **histology:**
  - ulcerous necrosis with lymphocytic infiltrate
  - CD2+, CD8+, partially CD56+
  - EBV+ in EBER ISH

- **Diagnosis:** NK-T-cell lymphoma, nasal type

- **Staging:** stage IV b
  - endoscopy: diffuse gastrointestinal infiltration
  - B-Symptoms (weight loss)
THERAPY

- **04/07**  
  Prephase treatment: vincristine 2mg single dose, prednisolone 100mg for 5 days; Start of donor search

- **04-07/07**  
  6 cycles of Gem/Dex/Ox  
  gemcitabine 1000 mg/m²  
  oxaliplatine 100 mg/m²  
  dexamethasone 40mg for 4 days

- Staging after 4 cycles of Gem/Dex/Ox:  
  Complete Remission
ALLOGENIC SCT

<table>
<thead>
<tr>
<th>Conditioning regime</th>
<th>Day</th>
<th>Drug</th>
<th>Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>-7</td>
<td>Thiotepa</td>
<td>6 mg/kg</td>
</tr>
<tr>
<td></td>
<td>-5, -4</td>
<td>Cyclophosphamide</td>
<td>20 mg/kg</td>
</tr>
<tr>
<td></td>
<td>-5, -4</td>
<td>Fludarabin</td>
<td>30 mg/m²</td>
</tr>
<tr>
<td></td>
<td>-6, -3, -2</td>
<td>ATG (rabbit Fresenius)</td>
<td>20 mg/kg</td>
</tr>
</tbody>
</table>

- 09.08.2007: allogenic, unrelated, HLA-Cw-mismatch, blood-group-identical SCT (7.9 x 10⁶ CD34+ cells/kg bw)

- Engraftment: leucocytes d+15, platelets d+18
**POST ALLOGENIC SCT**

- No acute or chronic GvHD
- No severe infections
- 12/07 termination of immunosuppressive therapy

- 01/10: thrombopenia after respiratory infection
  - platelet count: 25/nl
  - bone marrow aspiration: immune thrombocytopenia
  - steroid-sensitive

- Current status (5 years post allogenic SCT):
  - Continuing complete remission
  - No signs of GvHD,
  - 82 kg, ECOG 0
  - persisting palatal defect
  - platelet count 60/nl
NK-T-CELL-LYMPHOMA

- Predominantly male patients (ratio 3:1)
- Peak in the 5th decade of life
- More frequent in Asia and Latin America than in western countries
  \[
  3\text{-}9\% \text{ of all NHL} < 1\%
  \]

MDR phenotype (resistance to anthracyclines and vinca alkaloids):
- Chemotherapy with L-asparaginase, ifosfamide and/or MTX
NK-T-CELL-LYMPHOMA (CONT´D)

- EBV-associated
  - EBV DNA measurement in the serum allows monitoring response and relapse

![Graph showing survival probability versus time since inclusion (months)](image)

Jaccard, Curr Opin Oncol. 2011
## Upfront Therapy

### Newly diagnosed, Stage I/II (cont'd)

<table>
<thead>
<tr>
<th>Treatment</th>
<th>patients</th>
<th>ORR(%)</th>
<th>CR (%)</th>
<th>OS (%)</th>
<th>PFS (%)</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>RT (45Gy) + CHOP</td>
<td>17</td>
<td>58</td>
<td>58</td>
<td>3y: 59</td>
<td>nA</td>
<td>Isobe et al 2006</td>
</tr>
<tr>
<td>Concurrent RT (55 Gy) + CMED</td>
<td>202</td>
<td>92</td>
<td>91</td>
<td>5y: 85</td>
<td>5y: 91</td>
<td>Aviles et al 2013</td>
</tr>
<tr>
<td>Concurrent RT (50 Gy) + 2/3 DeVIC</td>
<td>27</td>
<td>81</td>
<td>77</td>
<td>2y: 78</td>
<td>2y: 67</td>
<td>Kim et al 2001</td>
</tr>
<tr>
<td>Concurrent RT (40 Gy)/cisplatin + VIPD</td>
<td>30</td>
<td>83</td>
<td>80</td>
<td>3y: 86</td>
<td>3y: 85</td>
<td>Yamaguchi et al 2009</td>
</tr>
<tr>
<td>sandwich RT(56 Gy) + LVP</td>
<td>26</td>
<td>89</td>
<td>81</td>
<td>2y: 89</td>
<td>2y: 81</td>
<td>Kim et al 2009</td>
</tr>
<tr>
<td>sandwich RT(56 Gy) + GELOX</td>
<td>27</td>
<td>96</td>
<td>74</td>
<td>2y: 86</td>
<td>2y: 86</td>
<td>Yamaguchi et al 2012</td>
</tr>
</tbody>
</table>

### Chemotherapy:

- **CHOP:** cyclophosphamide, doxorubicin, vincristine, prednisolone
- **CMED:** cyclophosphamide, methotrexate, etoposide, and dexamethasone
- **2/3 DeVIC:** dexamethasone, etoposide, ifosphamide, carboplatine
- **VIDP:** etoposide, ifosphamide, cisplatine, dexamethasone
- **LVP:** L-asparaginase, vincristine, prednisolone
- **GELOX:** Gemcitabine, E. coli L-asparaginase, Oxaliplatin
## Upfront Therapy
Stage III/IV or relapse/refractory stage

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Patients</th>
<th>ORR(%)</th>
<th>CR (%)</th>
<th>OS (%)</th>
<th>PFS (%)</th>
<th>reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMILE</td>
<td>38</td>
<td>79</td>
<td>45</td>
<td>1y: 55</td>
<td>2y: 86</td>
<td>Jiang et al 2013</td>
</tr>
<tr>
<td>SMILE + sandwich RT (50 Gy) (all stages)</td>
<td>87</td>
<td>81</td>
<td>66</td>
<td>5y 50</td>
<td>4y DFS: 64</td>
<td>Kwong et al, 2012</td>
</tr>
<tr>
<td>Asp/Met/Dex (relapsed/refractory)</td>
<td>19</td>
<td>77</td>
<td>61</td>
<td>Median survival 12.2 mos</td>
<td>Median PFS 12.2 mos</td>
<td>Jaccard et al, 2011</td>
</tr>
</tbody>
</table>

**Chemotherapy:**

SMILE: steroid (dexamethasone), methotrexate, ifosfamide, L-asparaginase, etoposide  
Asp/Met/Dex: L-asparaginase, metotrexate, dexamethasone
Role of autologous SCT in NK-T-cell lymphoma

- Few data available, no prospective clinical trial
- Outcome and prognostic factor of autologous HSCT (n=57):

![Graph showing overall survival (OS) of patients with different response categories. CR1, first CR; CR2, second CR; R1, first untreated relapse; R2, second untreated relapse.]

Kwong Y-L: High-dose chemotherapy and hematopoietic SCT in the management of natural killer-cell malignancies; Bone Marrow Transplant. 2009 Dec;44(11):709-14
ROLE OF ALLOGENIC SCT IN NK-T-CELL LYMPHOMA

- Retrospective analysis over 13 years
- N=28 (all NK-lineage neoplasms, ENKL=22)
- Death by disease progression 28% (n=8), TRM 28% (n=8)

Overall survival was 40% at 2 years after allogeneic haematopoietic stem cell transplantation. Broken lines indicate 95% confidence intervals. The median follow-up was 34 months.

TREATMENT ALGORITHM