Topics

- Why do late effects matter?
- Risk factors & different kinds of late effects
- What is different in children?
- What is the patient perspective on late effects?
- Implications for nurses
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**Why do late effects matter?**

**Facts & Figures**

- Increased number of performed SCTs per year
- Broader indications
- Better options in alternative donor SCT
- Less death from relapse, infections, GvHD and other complications
- Improved supportive care measures
- Better HLA matching

**More and more SCT survivors!!!**
Why do late effects matter?

The problem

- Exposures before, during and after SCT potentially contribute to the development of late effects
- These late effects can...
  - impair the quality of life among SCT survivors
  - bring burden to the family of the patient
  - increase health care costs
  - cause morbidity
  - cause mortality

Burden of morbidity after SCT

Cumulative incidence (%) of late effects in 1022 patients graded by CTCAE (0-5)

Sun et al. 2010 Blood
Reasons for mortality among adult patients

- Causes of death in 1270 patients who had a survival ≥2 years after allogeneic SCT

Wingard J, et al. JCO 2011

Why do late effects matter?
The patient’s experience

Lasting impact on patients’ life

Worklife and financial issues: Wingard et al. (1991), Lee et al. (2001), Carey et al. (2012)
Social well-being & relationships/family life: Syrjala et al. (2009), Norkin et al. (2012)
Spiritual Well-being: Andrykowski et al. (2005), Sherman et al. (2009)
Emotional well-being: Gruber et al. (2003), Rusiewicz et al. (2008), Wingard et al. (2013), Sun et al. (2012)
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Time course of late effects

Early complications < 100 days after SCT

Delayed events Between 3 months and 2 years

Late events Between 2 and 10 years

Very late events > 10 years
**Multifactorial etiology of late effects**

- Bacteria
- Viral & fungal infections
- Acute or chronic GvHD (yes/no?)
- Engraftment
- Toxicity

### Kind of late effects

<table>
<thead>
<tr>
<th>Malignant late effects</th>
<th>Non-malignant late effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Solid cancers</td>
<td>Organ toxicity</td>
</tr>
<tr>
<td>(Lung, Breast, Skin, Brain, Gastro-intestinal)</td>
<td>/Organ dysfunctions</td>
</tr>
<tr>
<td>Secondary malignancies of the blood building system (AML, MDS, lymphoma)</td>
<td>Disease specific complications</td>
</tr>
<tr>
<td>Relapse</td>
<td>Psychosocial, sexual, fertility &amp; QoL issues</td>
</tr>
<tr>
<td></td>
<td>Chronic Graft versus Host Disease</td>
</tr>
<tr>
<td></td>
<td>Infections</td>
</tr>
<tr>
<td></td>
<td>Growth and development issues</td>
</tr>
</tbody>
</table>

**Organ toxicity /Late organ dysfunctions**

<table>
<thead>
<tr>
<th>Organ</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bone</td>
<td>Osteoporosis, avascular necrosis</td>
</tr>
<tr>
<td>Cardiovascular</td>
<td>Coronary artery disease, metabolic syndrome, cardiomyopathy</td>
</tr>
<tr>
<td>Eye</td>
<td>Sicca syndrome, cataracts</td>
</tr>
<tr>
<td>Endocrine</td>
<td>Hypothyroidism, growth disturbance</td>
</tr>
<tr>
<td>Neurologic</td>
<td>Cognitive dysfunction, neuropathy</td>
</tr>
<tr>
<td>Kidney</td>
<td>Chronic kidney disease</td>
</tr>
<tr>
<td>Liver</td>
<td>Iron overload, hepatitis</td>
</tr>
<tr>
<td>Oral</td>
<td>Xerostomia, caries</td>
</tr>
<tr>
<td>Pulmonary</td>
<td>Bronchiolitis obliterans</td>
</tr>
</tbody>
</table>

**Exposures with great impact on late organ dysfunctions**

- **TBI:**
  Coronary artery disease, caries, dry eye, cataracts, endocrine dysfunction

- **Corticosteroids/Cyclosporine:**
  Osteoporosis, kidney disease, myopathy

- **Chronic GVHD:**
  Dry eye, caries, xerostomia, bronchiolitis obliterans, genitourinary tissue problems
Chronic Graft versus Host Disease

- Allo-reactive response of donor T cells against normal recipient tissues after allogeneic SCT
- Pathogenesis poorly understood
- Occurs in 30%-70% of allogeneic SCT recipients
- Less often in children
- Symptoms similar like in autoimmune disorders
- Important risk factors:
  - Mismatched and unrelated SCT
  - Acute GVHD
  - Peripheral blood stem cells


Significance of GvHD
The heterogeneic picture of chronic GvHD

Eyes: Sicca syndrome
GI tract: Esophageal strictures, malabsorption,
Liver: Abnormal liver function
Muscles: Myositis
Lungs: Bronchiolitis obliterans
Oral: Sicca syndrome, lichenoid lesions, ulcerations
Skin & connective tissue: Rash (Poikiloderma or maculopapular), sclerosis, dyspigmentation, nail dystrophy, fasciitis
Other: Thrombocytopenia, serositis, vaginal stenosis, nephrotic syndrome, neuropathy


Case example:

• Ms. L, (58 years old), indication: AML
• 4 years after SCT
• Sclerosis of the skin, stretching problems of joints
• Sicca syndrome of the eyes
• Vaginal stenosis and dryness
• «Changed my life completely (...)»
• «Relationship with partner broke down (...) »
• «Re-evaluated what brings pleasure and joy to my life (...)»
Late infections

- Increased risk for infections in patients with delayed immune reconstitution in particular with chronic GVHD & prolonged steroid exposure
- Common infections:
  - Virus: Cytomegaly virus, Varicella zoster
  - Encapsulated bacteria: e.g. Hemophilus influenzae, Salmonella
  - Fungus: Aspergillus, Pneumocystis pneumonia

Recommendations for vaccinations in transplant recipients

Townsend (2012)

Case example:

- Mrs. S, (42 years old); mother of two boys (3 & 6 years), indication: MDS
- Had serious infection seasonal influenza 1 year after SCT, hospitalized
- Recovered well
- Now 2 years after SCT, she is fine, yet still intake of Immunosuppressants

- «I am afraid of the winter season(…)»
- «My family has to take so much care of me (…)»
- «Still a kind of social isolation (…)»
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What is different in children?

- Reason for late mortality in 228 allogeneic SCT recipient from Canada, all <20 years at time of SCT
- 85% overall survival at ten years after SCT
- Causes of death
  - Relapse (65%)
  - Infection (18%)
  - Organ failure (6%)
  - cGVHD (6%)
  - Unknown (6%)

Relapse main reason for mortality. Mortality rate due to infections, organ failure and cGVHD low

Schechter T, et al. BMT 2013
High burden of late effects after SCT in childhood

- Comprehensive single center study of 162 SCT survivors
- Median follow-up time 7.2 years (range 2.0-21.0 years)
- Cumulative incidence of late effects was 93%
- 25% of survivors had severe or disabling effects

Bresters D et al., BMT 2010

Specific kinds of late effects after childhood SCT

**Growth impairment**
- Incidence: 20-85%
- Major cause:
  - Conditioning with TBI
  - Growth hormone deficiency
- Contributing factors:
  - Underlying disease
  - Nutritional status
  - Thyroid function & pubertal delay
  - Steroid therapy

**Neurocognitive impairment**
- Limited evidence of neurocognitive and academic outcomes in pediatric SCT
- SCT seems to pose a low risk
- Higher risk for children of age <5 yrs at the time of SCT who received TBI

Case example:

• Mr. L, (18 years old) shows up for his 15th annual control after SCT at the follow-up clinic
• He is accompanied by his twin brother
• Mr. L has a height of 160 cm
• His brother has a height of 176 cm

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What is the impact of late effects from the patients perspective?

Preliminary results from a substudy of the multi-centre cross-sectional PROVIVO study, data collection in 2011/12

Patient sample & setting

- Including all patients who responded to experience late effects (N = 319 of 376, 1-33 years after SCT) from Basel & Zürich

Variables & Measurements

- Experience of late effects measured by adapted 9-item version of the Brief Illness Perception Questionnaire

1. Broadbent et al. 2006 Journal of psychosomatic research

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How much do late effects affect your life?

Valenta et al. Preliminary results from Master thesis under preparation
How long do you think the late effects will continue?

- A very short time (0-3): 10%
- Moderately (4-6): 20%
- Very long/Forever (7-10): 60%

How much do you think you have control over your late effects?

- No/little control (0-3): 30%
- Moderate control (4-6): 20%
- Under control (7-10): 50%
Reasons for late effects from patient perspective

TOP-4 Reasons from the patients perspective for the occurrence of late effects* in 376 patients (1-33 years after allo SCT)

<table>
<thead>
<tr>
<th>Reason</th>
<th>Percentage</th>
</tr>
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<tbody>
<tr>
<td>Medications</td>
<td>54%</td>
</tr>
<tr>
<td>Chemotherapy</td>
<td>45%</td>
</tr>
<tr>
<td>Radiation</td>
<td>41%</td>
</tr>
<tr>
<td>Psychological burden</td>
<td>36%</td>
</tr>
</tbody>
</table>

*Three responses per patient were possible

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Valenta et al. Preliminary results from Master thesis under preparation
What nurses can do....

- Support patient AND family/caring loved ones
- Being aware of follow-up guidelines
- Symptom management
- Patient education, training and skill training
- Promoting healthy behavior
- Increase patient's self management

Need for more innovative care models for long-term survivors

1. Majhail et al. 2012 Biol of Blood and Marrow Transplant

What can we recommend to patients? (1)

1. Discussing your needs with a healthcare professional at the end of treatment
2. Seeing a copy of your end-of-treatment assessment and care plan
3. Finding out who is your ongoing 'main contact'
4. Being aware of any post-treatment symptoms
5. Getting support with day-to-day concerns

http://www.cancerconsequences.org/10-tips-for-survivors.html
What can we recommend to patients? (2)

6. Talking about how you feel
7. Taking steps towards healthier living
8. Finding out more about what to look out for if you are worried about treatment side effects or the cancer coming back
9. Monitoring your own health and keeping up to date with ongoing check-ups
10. Making suggestions based on your experiences of treatment and care

http://www.cancerconsequences.org/10-tips-for-survivors.html

Thank you for your attention!

Monika.Kirsch@usb.ch