Stem Cell Transplantation

The origin of epithelial neoplasms after allogeneic stem cell transplantation

We analyzed five women, who have developed epithelial neoplasms after sex-mismatched stem cell transplants. Using in situ hybridization for sex chromosome-specific DNA probes and immunohistochemistry we identified the origin of the tumor cells. We conclude that none of the non-hematologic malignancies was of donor origin.

Table 1. Female patients with non-hematologic malignancies after sex-mismatched stem cell transplantation (SCT).

<table>
<thead>
<tr>
<th>Patient’s sex</th>
<th>Patient’s age at SCT</th>
<th>Indication for SCT</th>
<th>Donor-type</th>
<th>Conditioning for SCT</th>
<th>CD3+ cells left in the graft (&lt;x10^5/kg)</th>
<th>GVHD acute/chronic</th>
<th>Interval SCT-diagnosis carcinoma (years)</th>
<th>Histological diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>47</td>
<td>NHL</td>
<td>HLA-id</td>
<td>TBI plus CPM</td>
<td>0.74</td>
<td>0/0</td>
<td>1.5</td>
<td>Moderately differentiated invasive ductal carcinoma</td>
</tr>
<tr>
<td>F</td>
<td>52</td>
<td>MM</td>
<td>HLA-id</td>
<td>Ida plus TBI plus CPM</td>
<td>0.74</td>
<td>I / L</td>
<td>5</td>
<td>Well differentiated invasive ductal carcinoma</td>
</tr>
<tr>
<td>F</td>
<td>51</td>
<td>RAEB-t</td>
<td>HLA-id</td>
<td>Ida plus TBI plus CPM</td>
<td>0.72</td>
<td>I / 0</td>
<td>8.5</td>
<td>Poorly differentiated ductal carcinoma in situ</td>
</tr>
<tr>
<td>F</td>
<td>56</td>
<td>MM</td>
<td>HLA-id</td>
<td>TBI plus CPM</td>
<td>0.72</td>
<td>II / 0</td>
<td>3</td>
<td>Basocellular carcinoma</td>
</tr>
<tr>
<td>F</td>
<td>54</td>
<td>RA</td>
<td>HLA-id</td>
<td>TBI plus CPM</td>
<td>0.70</td>
<td>I / L</td>
<td>10</td>
<td>Lobular carcinoma in situ</td>
</tr>
</tbody>
</table>

1NHL: Non-Hodgkin’s lymphoma; MM: multiple myeloma; RAEB-t: refractory anemia with an excess of blasts in transformation; RA: refractory anemia; HLA-id: HLA-identical brother; TBI: total body irradiation 9 Gy; CPM: cyclophosphamide 120 mg/kg; Ida: idarubicin 42 mg/m²; I chronic GVHD: limited chronic graft-versus-host disease.
endothelial cells. The endothelium within the tumor showed mixed chimerism, which is at least partially the
result of neo-angiogenesis. In contrast, other studies have repeated shown that post-transplant lymphoprolifera-
tive disorders after SCT are mostly derived from donor
cells.\(^6\,7\) This was expected since SCT can fully replace the
hematopoietic system, including lymphopoiesis. Solid
tumors arise after SCT even more often,\(^8\) but until now
studies into the origin of the tumor cells have not been
reported.

The present findings show that none of the epithelial
malignancies after SCT was of donor origin. This is in
contrast with the experimental model of Houghton and
Wang.\(^3\) The major difference is that the Helicobacter-assoc-
ated gastric cancer in their model arises after continued
inflammation and tissue repair. The tumors we describe
are not related to chronic inflammation and no such cases
were present in our relatively large series with a median
follow-up of 10 years. Of course we cannot exclude the
rare occurrence of donor-derived cancers, but the mecha-
nism by which most transplantation-associated cancers
arise might be different from that in an experimental
model. We conclude that the investigated non-hematol-
ogic malignancies are derived from recipient rather than
donor epithelial cells.

Mary J. Smith,* Patricia H.J. van Cleef,*
Anton V.M.B. Schattenberg,* Johan H.J.M. van Krieken*
Departments of Pathology* and Haematology,* Radboud University
Nijmegen Medical Center, The Netherlands

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Correspondence: Johan H.J.M. van Krieken, Department of
Pathology, Radboud University Nijmegen Medical Centre,
Nijmegen, the Netherlands, P.O. Box 9101, 6500 HB Nijmegen,
the Netherlands. Phone: international +31.24.3614314. Fax: inter-
national +31.24.3540520. E-mail: J.vanKrieken@pathol.umcn.nl

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New malignancies after blood or marrow stem-cell transplanta-

Figure 1. Invasive ductal carcinoma without bone marrow-derived
tumor cells. Immunohistochemical staining of tumor tissue for
CAM 5.2 (purple) with \textit{in situ} hybridization for Y chromosome-spe-
cific DNA probe (brown dots), counterstained by nuclear fast red.
The tumor sample was taken from a 48-years/old female patient,
1.5 years after a stem cell transplant. Y chromosome positive
cells were present, but no double positivity for both CAM 5.2 and
Y chromosome was detected. Magnification is 200x, and 400x
(insert).