TAFI in plasma confers a significant risk of acute CAD. Thus, functional TAFI plasma levels above the 126% cut-off increased the risk of acute CAD almost 4-fold. To our knowledge, this is the first case-control study that unequivocally establishes that high levels of functional TAFI are associated with an increased risk of acute CAD in patients under the age of 80 years. We hypothesize that high functional TAFI levels may represent a significant thrombotic biomarker for the risk of acute CAD. Knowledge of the pathophysiological role of functional TAFI should lead to a better understanding of the mechanism of thrombotic disease.

Aknowledgments. We are indebted to Professor WH Stone for his encouragement in this study. We are grateful to the physicians, nurses, and all staff at The Royal Marsden Hospital. For their consistent participation in the study.

Key words: TAFI, arterial, thrombosis, coronary artery disease, atherosclerosis, clinical outcome.

References

Stem Cell Transplantation

High-dose granulocyte colony-stimulating factor mobilizes a higher proportion of early CD34+CD33- hematopoietic progenitors in children receiving treatment for solid tumors

A relationship between dose of granulocyte colony-stimulating factor (G-CSF) and maturational stage of the progenitors mobilized in healthy adult donors has been suggested. In this study we characterize the progenitors mobilized by 2 different dosages of G-CSF in children receiving autologous peripheral blood progenitor cells (PBPC) transplant as intensive chemotherapy to the first harvest session was performed on the 5th day. If an insufficient number of CD34+ cells was harvested (<2.5x10^6 CD34+ cells/Kg), the patient received a 5th dose of G-CSF on that day and a second harvest session was performed on the 6th day. Overall, a second harvest was performed in 45 cases. In addition, 24 patients received priming with cyclophosphamide (1.5 mg/Kg) prior to mobilization with G-CSF. The average time from the last course of chemotherapy to the first harvest session was 28±23.9 days.

Conditioning regimens included melphalan (33 cases), busulphan plus melphalan (10), thiotepa plus etoposide (2), carboplatin alone (9), and carboplatin plus melphalan (1). Endpoints for this study were: numbers of CD34+ cells harvested, CD34+CD33- and CD34+CD33+ cells harvested, and time to neutrophil and platelet engraftment and influence of harvest timing and cyclophosphamide priming on the maturation stage of these progenitors. High doses of G-CSF appear to mobilize a higher proportion of early CD34+CD33- progenitors.

The most relevant data on the qualitative contents of harvests are shown in Table 1. There were no significant differences in overall number of CD34+ or CD34+CD33- cells harvested after mobilization with either 5 or 10 µg/Kg of G-CSF. However, the percentage of CD34+CD33- cells within the CD34+ population was significantly (p<0.05) higher in patients receiving 10 mg/Kg of G-CSF. A similar dose-dependent effect has been reported in healthy adult donors. A possible explanation is that high doses of G-CSF...
Table 2. Influence of priming with cyclophosphamide and harvest timing (before or after 14 days from the last course of chemotherapy) on the contents of total CD34+ cells, CD34+ CD33- cells and in the percentage of CD33- cells within the overall CD34+ population. Cell counts are expressed as x 10^9/Kg.

<table>
<thead>
<tr>
<th>Cyclophosphamide priming</th>
<th>&lt; 14 days</th>
<th>&gt; 14 days</th>
</tr>
</thead>
<tbody>
<tr>
<td>CD34+</td>
<td>5.1±7.5</td>
<td>4.7±5.0</td>
</tr>
<tr>
<td>CD34+CD33-</td>
<td>2.8±3.8</td>
<td>4.0±4.4</td>
</tr>
<tr>
<td>% CD33-</td>
<td>51.3±32.0</td>
<td>74.7±12.0</td>
</tr>
</tbody>
</table>

might stimulate earlier forms of progenitors with a lower density of receptors for G-CSF on their surface.

Early mobilization (within the first two weeks) after the last block of chemotherapy mobilizes a higher proportion of CD34+CD33- cells. Harvests collected earlier than 14 days after the last course of chemotherapy had significantly (p<0.04) higher overall percentages of CD34+CD33- cells, while the CD33- yields were not significantly different. Priming with cyclophosphamide did not produce significant differences. Values corresponding to these analyses are detailed in Table 2. These results are consistent with early reports of mobilization of CFU-GM after chemotherapy in children. Grafts containing high proportions of early progenitors may provide faster multi-lineage hematopoietic reconstitution.

Neither CD34+ cell dose nor dose of CD34+CD33- early progenitors seemed to influence neutrophil or platelet recovery. However, children receiving grafts containing >75% of early progenitors had a non-significant (p<0.06) tendency towards earlier platelet engraftment (25.1±24.3 vs. 57.3±54.4 days, respectively). Moreover, children receiving 10 µg/Kg of G-CSF for mobilization had significantly (p<0.02) faster platelet recovery (18.1±15.6 days in children mobilized with 10 µg/Kg and 47.9±62.1 in children mobilized with 5 mg/Kg). These results suggest that the reinfusion of an earlier, pluripotent progenitor could allow faster multi-lineage hematopoietic reconstitution.

In conclusion, doses of G-CSF of 10 mg/Kg seem to mobilize an earlier type of hematopoietic progenitor than doses of 5 mg/Kg in children receiving treatment for solid tumors. These early progenitors could provide faster multi-lineage hematopoietic reconstitution. These results should be confirmed in prospective, randomized studies.

References

Stem Cell Transplantation

Polymorphism of the α4-subunit of VLA-4 integrin and bone marrow transplantation

Integrin α4β1 is an important homing molecule on stem cells. Two genetic variants of this integrin are known, α4-mas and α4-tex. We assessed the potential influence of this polymorphism in 37 patients undergoing allogeneic bone marrow transplantation. None of the constellations of variants influenced the outcome, as determined by the recovery of leukocytes or platelets, hospitalization time, and the development of graft-versus-host disease.

Regarding neutrophil engraftment, the most relevant differences occurred in mas/tex on tex/tex pairs compared to both tex/tex on tex/tex pairs (p=0.0519) and tex/tex on