MultipleMyelomaHub

Patients eligible for transplant

New imaging methodology enables rapid assessment of transplant success in hematologic malignancies

Appitha Eakin | Apr 25, 2018

The primary treatment option for younger Multiple Myeloma (MM) patients is a hematopoietic stem cell transplant (HSCT), and although this is now a routine process, it still involves the invasive process of bone marrow (BM) biopsies. Such biopsies are used to monitor the success of transplant in terms of engraftment, but this is painful for patients and carries a high risk of infection. This poses a challenge to the task of investigating and following the engraftment process, but recent developments in imaging modalities could circumvent this.

Kirsten M. Williams, from the Children's Research Institute, Children's National Health System, Washington, USA, and colleagues, carried out a pilot study in which they investigated the use of 18F-fluorothymidine (^{18}F-FLT) imaging during HSCT to visualize early cellular proliferation and subsequent engraftment. The results of the study were published in the Lancet Haematology in January 2018.

Study design:

- Eligibility of patients (pts): 18–55 years of age; high-risk acute leukemia (n = 21); chronic myeloid leukemia (n = 1); myelodysplastic syndrome (n = 1)
    - Drug administration: myeloablative conditioning (1200 cGy total-body irradiation); cyclophosphamide (120 mg/kg) with infusion of human leukocyte antigen (HLA); calcineurin inhibitor and mini-methotrexate regimen at 10 mg/m² on day 1 and at 5 mg/m² on days 3, 6, and 11 after HSCT for graft-versus-host disease (GvHD) prophylaxis
- Imaging schedule included:
    - ^{18}F-FLT PET and CT (PET/CT) scanning: 1 and 5, or 9, 28 days, and 1 year after HSCT
    - ^{18}F-FDG scanning: 28 days and 1-year post-HSCT
    - Sites analyzed: thorax (thoracic spine 1–12), lumbar region (lumbar spine 1–5), cervical region, bilateral pelvic wings, bilateral iliac crests, bilateral humeri, and femurs, sternum, spleen, liver, and fat
- Engraftment defined as 'the first day of 3 consecutive days with an absolute neutrophil count ≥ 0.5 × 10^9/L after hematopoietic stem cell transplantation (HSCT)'

Key Findings:

- N = 23 pts; Median age (years) = 33.7 (26.9–39.4)
- Median follow-up after HSCT (years) = 4.3
- Median time to engraftment: peripheral blood stem cell (PBSC) grafts = 15 days (IQR 13–19) and BM grafts = 20 days (17–22)
- ^{18}F-FLT imaging revealed:

- Subclinical engraftment after HSCT
- Improved BM visualization compared to ^{18}F-FDG
- BM uptake from day 5 post-HSCT, with a consistent pattern of BM activation
- Pronounced initial uptake in the thoracic spine, followed by the remainder of the axial skeleton, sternum and extremities
- Increase in standardized uptake values (SUV) at the BM site as a 'function of time from transplantation'
- Higher uptake at day 28 post-infusion in comparison to day 1 pre-infusion ($P < 0.0001$)
- Uptake is associated with the rate of cellular recovery
- An association between thoracic spine SUV and time to engraftment: pts with a median thoracic spine SUVs ≥ 1.4 had a shorter time to engraftment than those with SUVs < 1.4 (< 8 days *vs* 14 days, $P = 0.0075$)
- Unchanged uptake in fat over time ($P = 0.96$)
- Uptake in BM is suggestive of site-specific cellular expansion, as it was much higher than the uptake in the peripheral blood ($P < 0.0001$)
- A sequence of hemopoietic engraftment occurs after HSCT over time: uptake in the liver and the spleen peaked on days 5–6 post-HSCT (followed by parts of the spine, the sternum and then arms and legs)
- Uptake in the spleen exceeded the background circulation of unbound ^{18}F-FLT early after HSCT
- A mean extremity SUV of 6.72 (SD = 3.81) at day 28 and 3.64 (SD = 2.13) at 1-year ($P = 0.0078$), n = 8 pts

- Tissue samples were assessed from 2 patients to identify whether increased ^{18}F-FLT uptake is representative of donor hemopoiesis:
  - 99% of hemopoietic cells in the spleen were of donor origin
  - CD34-positive cells and cells of donor origin were found in the liver

This study showed that the characterization and quantification of subclinical HSC homing and repopulation after HSCT were possible with the use of the radiolabeled tracer ^{18}F-FLT. The tracer also detected early hematopoietic cell proliferation in the BM and revealed an association between the intensity of ^{18}F-FLT uptake and the pace of engraftment. Given that ^{18}F-FLT was well-tolerated with no associated adverse events, the authors suggest the potential use of ^{18}F-FLT as a biomarker of hemopoiesis, and this could potentially replace BM biopsies to test for transplant success.

References

1. Williams KM. *et al.* Imaging of subclinical haemopoiesis after stem-cell transplantation in patients with haematological malignancies: a prospective pilot study. The Lancet. Haematology. January 2018. DOI: 10.1016/S2352-3026(17)30215-6