DISCORDANCE OF CHIMERISM IN THE BLOOD AND BONE MARROW AS A POSSIBLE SIGN OF ADVERSE OUTCOME AFTER ALLO-HSCT

Olga Dubova[1], Natalya Risinskaya[2], Anna Yushkova[2], Firuza Shikhveledova[2], Mikhail Drokov[2], Larisa Kuzmina[2], Hunan Julhakyan[2], Andrey Sudarikov[2]

[1]Sechenov University, [2]National Research Center for Hematology, Moscow, Russia

soho22 TENTH ANNUAL MEETING

SECHENOV UNIVERSITY

Abstract

Chimerism analysis is one of the main methods to monitor the bone marrow engraftment after stem cells transplantation.

Background

DNA isolated from bone marrow (BM) or peripheral blood (PB) of the patients receiving allogeneic hematopoietic stem cell transplantation (allo-HSCT) is used to assess hematopoietic chimerism. Both sources are presumably equivalent for this purpose. Here we report several allo-HSTC cases with BM chimerism not matching that of PB and vice versa.

Objective

To investigate the possible association between disparity of chimerism in paired PB and BM samples and the disease features in post-transplant AML patients.

Materials & Methods

This study includes an analysis of the STR profiles in the DNA of paired archival BM and PB samples of 43 patients who received allo-HSCT in the National Medical Research Center for Hematology (Moscow, Russia) from 2016 to 2022. Paired BM and PB samples were collected with a time difference of one day or less. Chimerism was assessed by STR-PCR. STR - profiles were evaluated by PCR with COrDIS Plus multiplex kit (Gordiz Ltd, Russia). Inclusion criteria: presence of mixed hematopoietic chimerism at certain time points during monitoring.

Results

- In eight patients out of 43 (18.6%) disparity of chimerism between PB and BM samples was found *(figure 1).*
- In three patients (7%) at the early stages after allo-HSC chimerism measured in PB sample was twice or more times higher than in BM *(figure 2).*
- In 5 (11.6%) patients, the proportion of recipient DNA in BM was twice as high as in PB. In two patients, this phenomenon might be due to donor lymphocytes transfusion before chimerism measuring. For three patients, no simple explanation for this phenomenon is evident so far. However, all five relapsed. Four patients died from the progression of the disease, one underwent a second transplant and maintains remission.

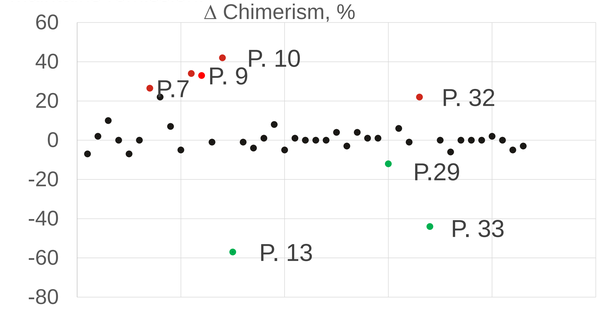


Figure 1. *Graph of delta values of chimerism in bone marrow and peripheral blood (Δ=BM-PB). Green dots - negative Δ in patients who have the proportion of the recipient in the mixed chimera in the PB is ≥ 50% than in the BM. Red dots are positive Δ values in patients who have the proportion of host in mixed chimera in BM is ≥ 50% than chimerism in PB. Blue dots - Δ does not exceed 10%. We did not include patients with chimerism ≤5%, as discordance in this case is comparable to the measurement error*

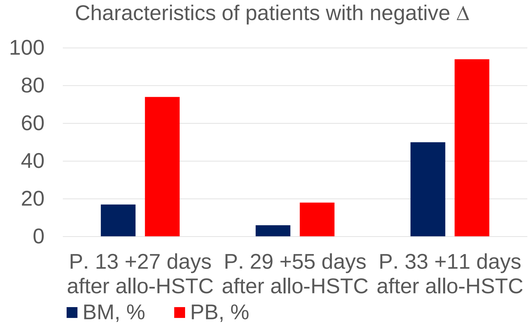


Figure 2. Characteristics of patients with negative Δ

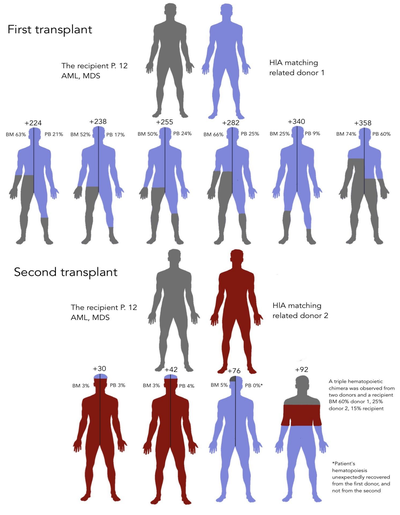


Figure 3*. Patient #12 blood and bone marrow chimerism monitoring presentation*

Case #12

In P. 12, the phenomenon of chimerism discordance between BM and PB was observed at 6 time points after allo-HSCT from the first related donor. After recurrence, P. 12 underwent retransplantation from another fully matched related donor, and no difference in chimerism in BM and PB was observed. After a while, the patient's hematopoiesis unexpectedly recovered from the first donor, and not from the second. Later, a triple hematopoietic chimera was observed from two donors and a recipient. The patient died from infections. *(Figure 3).*

Summary

The predominance of recipient DNA in PB sample compared to BM, noted at the early stages after allo-HSCT, may not correspond to the real picture due to delayed hematopoietic reconstitution. The study of chimerism in sorted cell populations might provide explanation for host predominance in BM over the PB. Probably, such patients relapsing at early stages after allo-HSCT could have chimerism split between certain cell lineages. Further studies of chimerism in paired PB and BM samples on extended cohorts of post-transplant patients are required.

References

1. Systematic comparison of donor chimerism in peripheral blood and bone marrow after hematopoietic stem cell transplantation. Bach C, Steffen M, Roesler W, et al. Blood Cancer J. 2017;7 (6):e566. doi:10.1038/bcj.2017.42
2. The practical application of chimerism analyses in allogeneic stem cell transplant recipients: blood chimerism is equivalent to marrow chimerism. Rauwerdink, Cocav et al. Experimental and molecular pathology 93 3 (2012): 339-44
3. Quantitative PCR-based chimerism in bone marrow or peripheral blood to predict acute myeloid leukemia relapse in high-risk patients: results from the KIM-PB prospective study. Gambacorta V, Parolini R, Xue E, et al. Haematologica. 2020; 106(5):1480-1483. doi:10.3324/haematol.2019.238543