Complexities in cell populations chimerism testing interpretation. A case example.

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Background

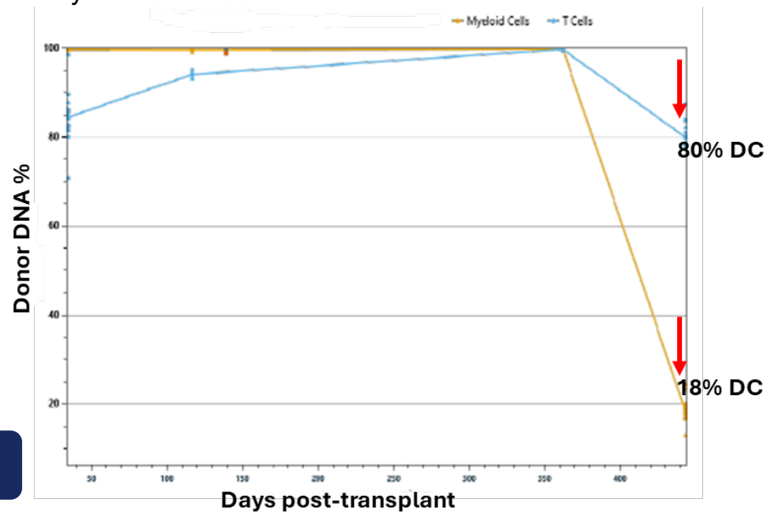
Chimerism analysis is essential to monitor engraftment success, detect disease relapse, and guide clinical interventions after allogeneic hematopoietic stem cell transplantation (HSCT).
Testing isolated cell populations is more sensitive than testing whole blood, particularly for relapse prediction in malignancies. Specific cellular markers are used to isolate different cell populations.

Case

A patient diagnosed with T-cell acute lymphoblastic leukemia (T-ALL) received a HSCT and relapsed 14 months after.
Chimerism percentages in samples from 117 and 363 days post-transplant were 99% donor chimerism for myeloid and T-cells populations.
Cell counts from a peripheral blood sample from 443 days post-transplant showed 96% of circulating blast in the CBC. Hence, low donor chimerism was expected.

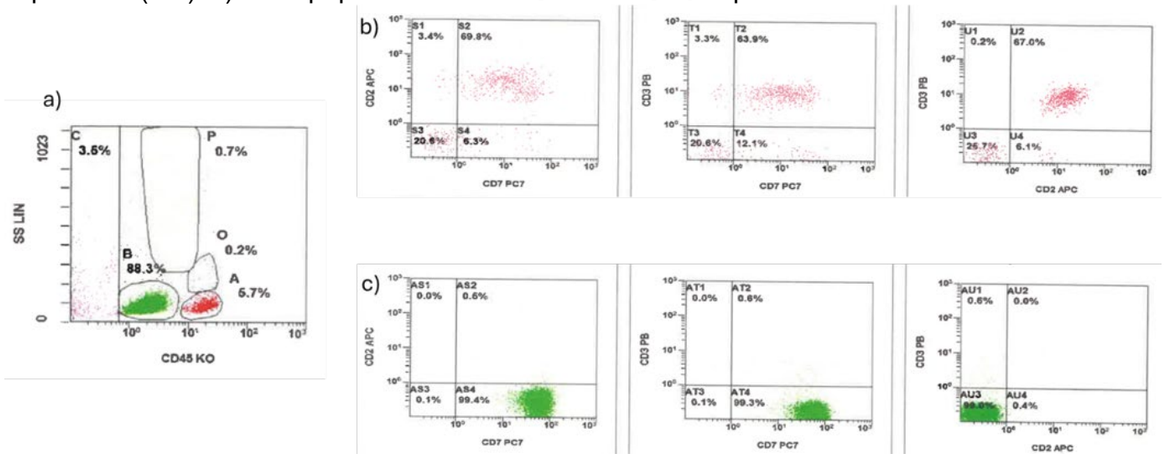
Case (Cont.)

Figure 1. Graph of donor chimerism (DC) percentage for myeloid and T cell fractions.



Correlating with this expectation, there was 18% donor chimerism for the myeloid fraction but 80% percent of T cell donor chimerism (Figure 1).
Examination of the flow cytometry results using various cellular markers revealed that about 80% of the patient's T cells had aberrant expression of lineage markers, including lack of expression of CD2 and CD3 markers (Figure 2).
These same markers are used to isolate the T cell fraction and to assess its purity for chimerism testing.

Figure 2. a) CD45 vs side scatter flow cytometric plot showing the normal lymphocyte population in red and the blast population with dim CD45 in green. b) Lymphocyte population with normal CD2 and CD3 expression (red). c) Blast population without CD2 and CD3 expression.



Hence, we realized that the only T cells captured by our isolation process were the 20% of remaining donor cells in circulation, which did not accurately represent the percentage chimerism for this cell fraction.
We recommended using chimerism results from either the myeloid fraction and/or unfractionated cells to have a more accurate estimation of the donor chimerism levels present.
The myeloid fraction accurately represents the actual percentage of donor chimerism (18%), which correlates with the approximate 20% of non-malignant cells remaining, while the rest 80% of the cells would correspond to relapsed cancer cells.

Conclusions

- Chimerism along with flow cytometry results helped to conclusively diagnose relapse.
- This case illustrates the importance of interpreting chimerism results in the context of the specific disease and clinical developments.
- It also demonstrates the importance of correlating questionable results with other testing to provide accurate assessments.