Normal Recipient Hematopoiesis Mimicking Relapse in Lineage-Specific Chimerism After Allogeneic Stem Cell Transplantation

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BACKGROUND

- Lineage-specific STR chimerism is central to monitoring engraftment and detecting early relapse after allogeneic HSCT.
- A falling donor fraction is usually interpreted as impending relapse.
- Interpretation relies on a pre-transplant recipient reference, typically blood that may be dominated by the malignant clone.

Aim: describe how recovery of normal recipient hematopoiesis mimicked relapse, and how it was resolved.

CASE PRESENTATION

60-year-old man with a myelodysplastic/myeloproliferative neoplasm (MDS/MPN)

Pre-HSCT marrow: hypercellular with granulocytic dysplasia and a complex myeloid mutational profile; cytogenetics non-informative

Donor: matched related donor (his daughter), 10/10 HLA-matched

Table 1. HLA typing of recipient and donor

Locus	Recipient	Donor (daughter)	Match
A*	02:01 · 26:01	02:01 · 26:01	✓
B*	51:01 · 57:03	51:01 · 57:03	✓
C*	07:01 · 14:02	07:01 · 14:02	✓
DRB1*	07:01 · 15:01	07:01 · 15:01	✓
DQB1*	02:02 · 06:02	02:02 · 06:02	✓

10/10 match at HLA-A, -B, -C, -DRB1 and -DQB1

STR CHIMERISM INVESTIGATION

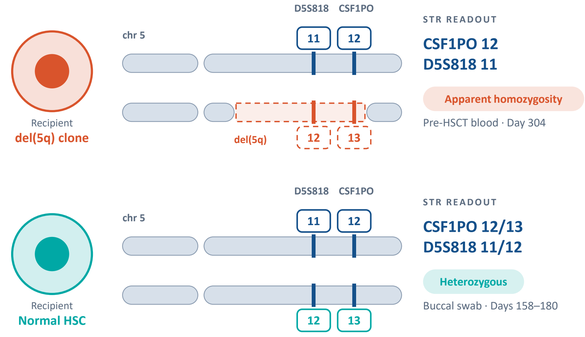
Methods: myeloid and lymphoid fractions analyzed by STR-PCR and capillary electrophoresis; donor % quantified at the informative locus D21S11. References: donor blood, recipient pre-HSCT blood and recipient buccal swab (non-hematopoietic germline).



Figure 1. Schematic GeneMapper-style electropherograms (peak heights modeled from allele dosage and measured chimerism; not raw instrument output). Post-HSCT rows show the myeloid fraction. Pre-HSCT blood showed apparent homozygosity at both chr 5q loci, whereas the buccal swab revealed germline heterozygosity, which re-emerged during the false-relapse period and was lost again at true relapse.

PROPOSED MECHANISM

Figure 3. Two recipient-derived myeloid populations with different chromosome 5 genotypes



POST-SUBMISSION UPDATE

~Day 300 (Day 304): frank relapse with clinical and hematological evidence of disease.

	Days 158–180 False relapse	Day 304 True relapse
Myeloid donor	7% → 2%	0%
Lymphoid donor	89% → 90%	82%
CSF1PO (recipient)	12/13 · HET	12 · HET lost
D5S818 (recipient)	11/12 · HET	11 · HET lost
Clinical status	Remission	**Frank relapse**

Loss of 5q heterozygosity coincided with true relapse, further confirming that the early donor decline reflected normal recipient hematopoiesis, not relapse.

CLINICAL COURSE

Day 0 — HSCT
Allogeneic HSCT from his 10/10 HLA-matched daughter

Day 30 — Engrafted
Trilineage marrow regeneration; whole-blood chimerism 92% donor

Day 158 — False relapse
Whole blood 19% donor (myeloid 7%, lymphoid 89%); new recipient alleles at CSF1PO & D5S818, yet in clinical remission

Day 180 — False relapse
Myeloid 2%, lymphoid 90% donor; same alleles. Buccal swab confirms germline heterozygosity at both 5q loci

Day 304 — True relapse
Frank relapse (clinical & hematological); myeloid 0%, lymphoid 82% donor; 5q heterozygosity lost

LINEAGE CHIMERISM

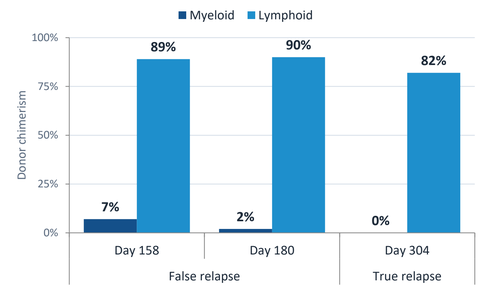


Figure 2. Donor chimerism by lineage. Myeloid donor levels were similarly low in the false- and true-relapse periods; percentages alone could not tell them apart.

STR ALLELE COMPOSITION

Table 2. Alleles detected in each sample

Sample	D21S11 chr 21 · informative	CSF1PO chr 5q	D5S818 chr 5q
Donor daughter	29, 33.2	12, 12	11, 12
Recipient · blood pre-HSCT	29, 30	12, 12	11, 11
Recipient · buccal non-blood (germline)	29, 30	12, 13	11, 12
Post-HSCT false relapse (D158–180)	29, 30/33.2	12, 13	11, 12
Post-HSCT true relapse (D304)	29, 30/33.2	12, 12	11, 12†

30 = recipient-specific and 33.2 = donor-specific allele at the informative locus. **Coral**: apparent homozygosity / heterozygosity lost; **teal**: heterozygous 5q alleles. †Allele 12 at relapse is donor-derived.

CONCLUSIONS

1. Normal recipient hematopoiesis can mimic relapse when lineage chimerism is interpreted in isolation.
2. A presumed 5q deletion in the malignant clone masked germline alleles in the pre-HSCT blood reference; a buccal swab revealed the true genotype.
3. Integrating lineage chimerism, STR locus location, disease biology and clinical status prevented unnecessary intervention.
4. Heterozygosity at LOH-prone loci acted as a clonal marker: restored in benign recipient recovery, lost at true relapse.

For patients: an alarming result is not always relapse; careful investigation can spare unnecessary, harsh treatment. Continuous monitoring remains essential.