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Hemostasis, transfusion medicine, vascular, laboratory medicine

Biopsy-based *KIT* D816V digital droplet PCR improves detection of residual disease after allogeneic hematopoietic cell transplantation in systemic mastocytosis

A. Stelmes[1], J. R. Passweg[1], J. P. Halter[1], F. Matteazzi[1], A. Tzankov[2], S. Dirnhofer[2], T. Menter[2], I. Bratic Hench[2], V. Perrina[2], M. S. Bader[1]

[1]Hematology, University Hospital Basel, Basel; [2]Pathology, University Hospital Basel, Basel

Key Points

- *KIT* D816V ddPCR testing on bone marrow biopsies reveals higher sensitivity for MRD detection in systemic mastocytosis after allogeneic hematopoietic cell transplantation compared to aspirates.
- Mast cell tissue residency may explain frequent discordance between biopsy and aspirate results.
- Biopsy-based ddPCR may improve post-transplant disease monitoring and warrants prospective validation.

Background

Systemic mastocytosis (SM) is a rare myeloid neoplasm, most frequently driven by the somatic *KIT* D816V mutation. Allogeneic hematopoietic cell transplantation (allo-HCT) is the only curative option in advanced SM. Measurable residual disease (MRD) remains challenging, as mast cells are tissue resident and often not aspirable, potentially limiting the sensitivity of molecular testing from bone marrow smears or peripheral blood.

Objective

To assess the concordance of *KIT* D816V digital droplet PCR (ddPCR) performed on formalin-fixed and EDTA-decalcified bone marrow biopsies versus aspirates in SM patients after allo-HCT and to evaluate the potential role of biopsy-based ddPCR result for MRD monitoring.

Methods

We retrospectively analyzed 20 bone marrow samples from 9 patients with advanced systemic mastocytosis who underwent allo-HCT at our institution between 2019 and 2025. Mast cell infiltration was assessed on bone marrow biopsies applying immunohistochemistry for mast cell tryptase and CD117. *KIT* D816V was quantified by ddPCR from aspirates and from DNA extracted from histological bone marrow biopsy sections.

Results

A clear discrepancy was observed between biopsy-based and aspirate-based *KIT* D816V detection. In nine paired analyses, the biopsy result remained positive while the corresponding aspirate was negative. No sample demonstrated the opposite pattern. This discordance between biopsy and aspirate results was statistically significant (exact McNemar's test, $P = 0.004$, **Fig. 1**).

		Bone marrow biopsy	
		negative	*positive*
Bone marrow aspirate	*negative*	5	9
	positive	0	6

Fig. 1: Overview of ddPCR results for *KIT* D816V

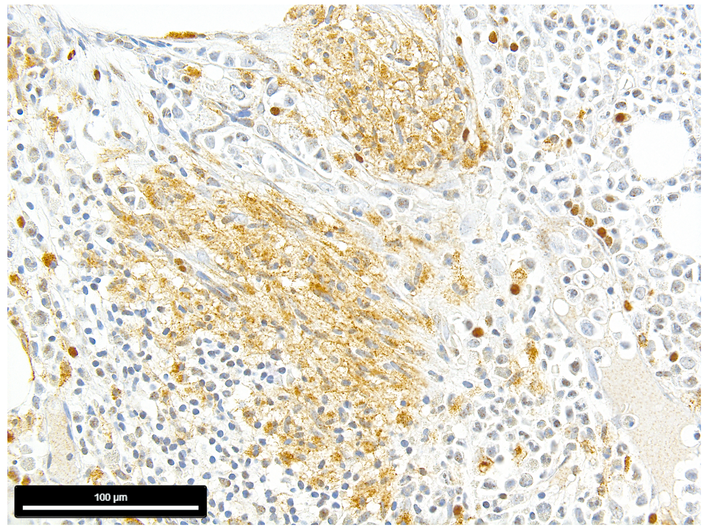

Fig. 2: Bone marrow biopsy highlighting pathological mast cell aggregates (CD25 immunostaining).

Conclusion

KIT D816V ddPCR testing on bone marrow biopsies appears more sensitive for MRD detection in SM after allo-HCT than analysis of aspirates, likely reflecting the poor aspirability of mast cell aggregates (**Fig. 2**). Biopsy-based molecular monitoring may therefore represent a valuable tool for post-transplant disease assessment and warrants prospective validation.

Contact
Anne Stelmes
Division of Hematology
University Hospital Basel, Switzerland
E-Mail: anne.stelmes@usb.ch

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