Application of liquid biopsy and STR-profiling to detect latent aberrations at 1p32 locus in multiple myeloma

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INTRODUCTION

Multiple myeloma (MM) is characterized by pronounced spatiotemporal heterogeneity of tumor clones [1, 2]. Traditional assessment of chromosomal aberrations in selected bone marrow cells (BM) (CD138+) has limitations due to the focal nature of the BM tumor lesions [3, 4]. Previously, it was shown that short tandem repeat (STR) profiles in paired samples of BM and circulating free plasma DNA (cfDNA) may differ, suggesting anatomical dissociation of the subclones [5]. Deletion at the 1p32 locus (biallelic or in combination with other high-risk aberrations) is known as an independent predictor of poor prognosis [6, 7].

AIM

To evaluate the effectiveness of the developed STR panel for screening aberrations at the 1p32 locus on various types of biomaterial in patients with MM.

MATERIALS AND METHODS

The study included 37 newly diagnosed MM patients, lacking 1p32 deletion, and one patient with 1p32 deletion confirmed by FISH on selected BM cells as a positive control. DNA was isolated from three fractions: selected CD138+ BM plasmocytes, plasma cfDNA, and peripheral blood cells for control. For multiplex 1p32 loci STR profiling 4 pairs of primers were used: F1 (FAM-cagatcagactgttaacagtggt), R1 (catcttgatctcccctctcgaa); F2 (FAM-cctgggtaacagagtgagact), R2 (tggagacagccagtggatca); F3 (FAM- caatcctaaatttgtatgcacat), R3 (cagtgaaaccatctaggcatga); and F4 (FAM-gcagcaatcagagggcctca), R4 (accctggctggtcctgatgt).

RESULTS

Stable amplification of fragments ranging in length from 103 to 324 nucleotide pairs was observed on all types of samples, including cfDNA. Loss of heterozygosity (LOH) in BM cells from 4 (10.5%) out of 38 patients (including one FISH-positive) was found. In another 9 (23.7%) patients, LOH at the 1p32 locus was found exclusively in plasma cfDNA samples. In no patient was 1p32 LOH detected in both sources simultaneously; thus, LOH was found in 13 (34.2%) of 38 patients, in either BM cells or plasma cfDNA but never in both (Fig.1).

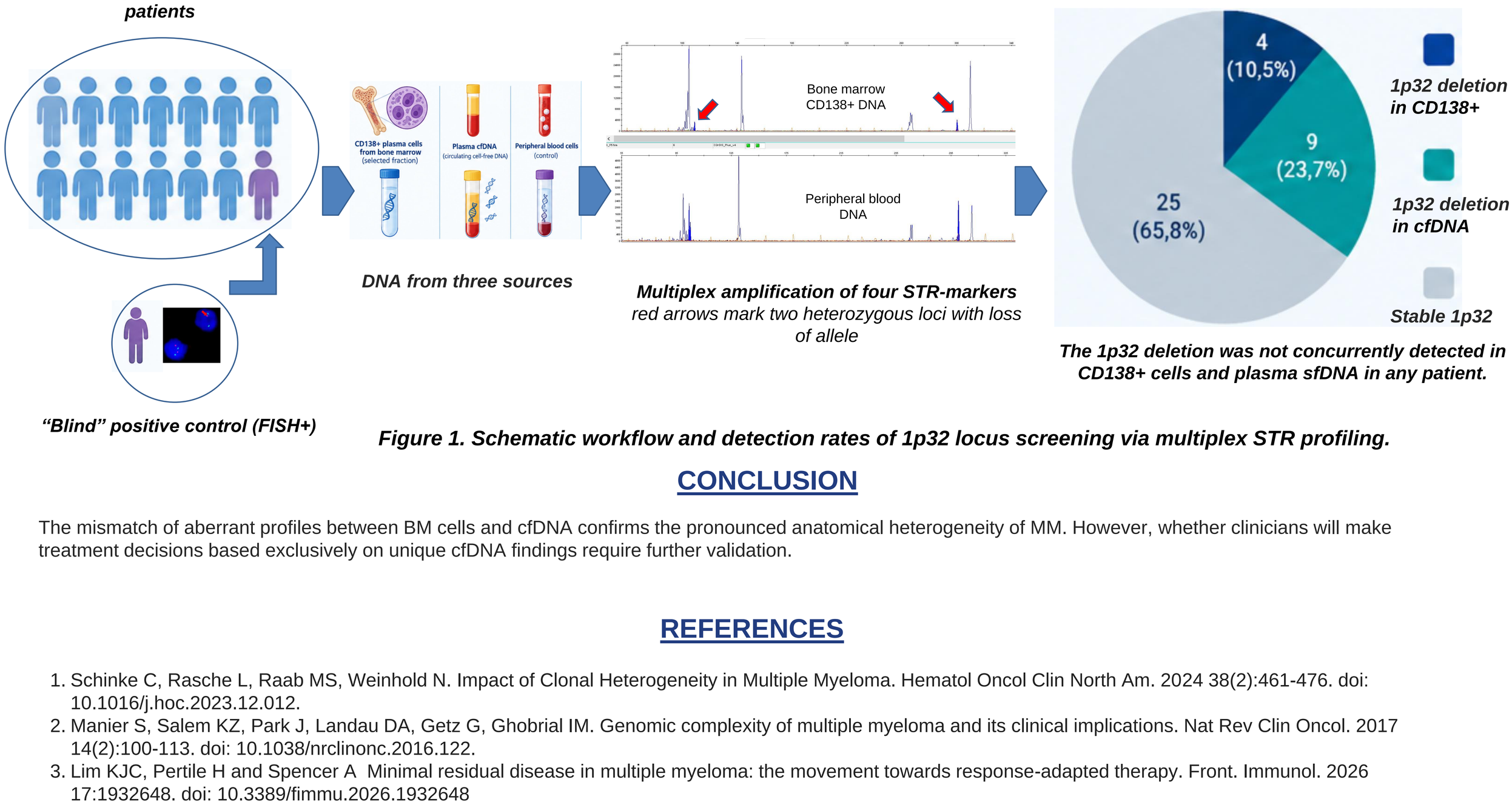


Figure 1. Schematic workflow and detection rates of 1p32 locus screening via multiplex STR profiling.

CONCLUSION

The mismatch of aberrant profiles between BM cells and cfDNA confirms the pronounced anatomical heterogeneity of MM. However, whether clinicians will make treatment decisions based exclusively on unique cfDNA findings require further validation.

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