Optical genome mapping (Bionano - Saphyr®) for AML associated with cryptic chromosomal recurrent abnormality

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SUMMARY

Here, we report the diagnostic work-up of a thirty-three-year-old woman presenting with 77% bone marrow myeloid blasts. Conventional cytogenetic did not show any recurrent abnormality but four mutations were found in three genes: *FLT3, CEBPA* and *IDH1*. This AML was considered "AML with CEBPA mutation" (2022 WHO classification) with an intermediate prognosis according to the 2022 ELN recommendations. On top of that, the newly described Optical Genome Mapping (OGM) technology was used to search for a potential structural variant. Using this assay, we detected a *NUP98::NSD1* fusion in the bone marrow cells. This infrequent but recurrent translocation was subsequently confirmed by specific FISH and RNA-sequencing (Archer®). It is associated with high induction failure and poor survival in AML. In summary, the OGM approach can efficiently detect cryptic chromosomal aberrations in AML, which could change the prognosis and guide the patient's treatment.

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INTRODUCTION

Acute leukaemia now requires comprehensive genetic analysis to determine prognosis and select the best available treatment options. Classifications schema, such as those proposed by the WHO or the ELN network, establish prognosis or guide the best treatment choice offered to the patient.[1,2] It is depending on the detection of recurrent chromosomal abnormalities such as structural variants (SV), hyper or hypodiploidy and copy number variant (CNV) of genes.[1,2]

Detection of cryptic anomalies not disclosed by standard karyotype could change the prognosis of patients and modify their induction and consolidation therapy. This is why, a pangenomic analysis with high resolution of chromosomal structure assessment is needed but it is not done by classical conventional cytogenetic assays.

Optical Genome Mapping (OGM) is a new technology using long fragments of DNA to detect SV and CNV with a high resolution. Briefly, the principle of this technique requires "Ultra High Molecular Weight DNA (UHMW)", obtained by DNA isolation using magnetic disks. This UHMW DNA is then labelled using an enzyme that links fluorescent labels to a 6bps sequence motif. The result is a uniquely identifiable genome-specific label patterns that is captured on the Saphyr system. Data are analysed after bioinformatics treatment following various pipelines, using the Access program. Comparison of patient genome with reference genome can lead to detection of CNV, SV and aneuploidy.

OGM allows in a one-step comprehensive assay to identify cryptic chromosomal anomalies potentially missed when conventional cytogenetic techniques are used.

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