Mosaic Chromosomal Alterations and Risk of AIDS-Related Non-Hodgkin Lymphoma

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BACKGROUND

People with HIV (PWH) are living longer and are at elevated risk of numerous cancers that are associated with aging-related phenotypes such as mosaic chromosomal alterations (mCAs).

We evaluated whether the presence of detectable mCAs in blood-derived DNA is associated with increased odds of developing AIDS-defining non-Hodgkin lymphoma (NHL).

METHODS

Study population: We conducted a case-control study of 171 PWH with NHL and 654 PWH who did not have NHL as controls (1:4 case:control ratio), who are participants in the Multicenter AIDS Cohort Study (MACS) and the Women's Interagency HIV Study (WIHS) Combined Cohort Study (MWCCS).

Sample selection: Samples between 6 months and 5 years prior to NHL diagnosis were matched to controls within each study on draw date of the NHL case (within 12 months) and also on sex, age, smoking status, and CD4 cell count at the time of sample collection.

Detection of mCAs: Clonal hematopoiesis was detected utilizing genome-wide genotyping arrays to detect mosaic chromosomal alterations (mCAs).

Statistical approach: We used exact conditional matched-pair logistic regression to test for the association between having an mCA and the odds of developing NHL.

ADDITIONAL KEY INFORMATION

This research was supported by the Intramural Research Program of the National Institutes of Health (NIH). The contributions of the NIH author(s) were made as part of their official duties as NIH federal employees, are in compliance with agency policy requirements, and are considered Works of the United States Government. However, the findings and conclusions presented in this paper are those of the author(s) and do not necessarily reflect the views of the NIH or the U.S. Department of Health and Human Services.

Although we did not find strong evidence of an association between presence of mCAs and risk of NHL, there was some suggestion that mCAs may be more relevant closer to the time of NHL diagnosis.

RESULTS

- Median age of the study population was 40 years at specimen collection (**Table**).
- Among NHL cases, there were 7 (4.1%) with an mCA >2 MB in length and among controls there were 17 (2.5%). **Figure** (right) displays the chromosomal locations of those 24 mCAs.
- Additionally, there were 30 (14%) mCAs <2 MB among cases and 130 (17%) among controls.

Main analysis: The presence of an mCA was not significantly associated with and increased odds of developing NHL.
(odds ratio [OR]=1.71, 95% CI: 0.68, 4.31)

Table. Characteristics of selected non-Hodgkin lymphoma cases and specimen-matched controls according to study at the time of specimen collection, Multicenter AIDS Cohort Study (MACS) and Women's Interagency HIV Study (WIHS).

	MACS			WIHS		
Variable	Cases, N = 131	Controls, N = 481	p-value	Cases, N = 42	Controls, N = 169	p-value
Age	40 (34, 45)	39 (35, 45)	>0.9	39 (32, 43)	38 (34, 43)	>0.9
Race			0.041			0.005
Black	11 (8%)	64 (13%)		16 (38%)	89 (53%)	
White	117 (89%)	398 (83%)		16 (38%)	20 (12%)	
Another race	3 (3%)	19 (4%)		10 (24%)	60 (35%)	
Hispanic	13 (10%)	28 (6%)	0.10	9 (21%)	48 (28%)	0.4
Viral load			0.15			0.015
Below LLQ	6 (5%)	48 (10%)		4 (10%)	47 (28%)	
Detected	110 (95%)	432 (90%)		38 (90%)	122 (72%)	
Unknown	15	1				
CD4 (cells/mm^3)	334 (206, 491)	381 (228, 492)	0.063	251 (132, 423)	348 (150, 497)	0.2

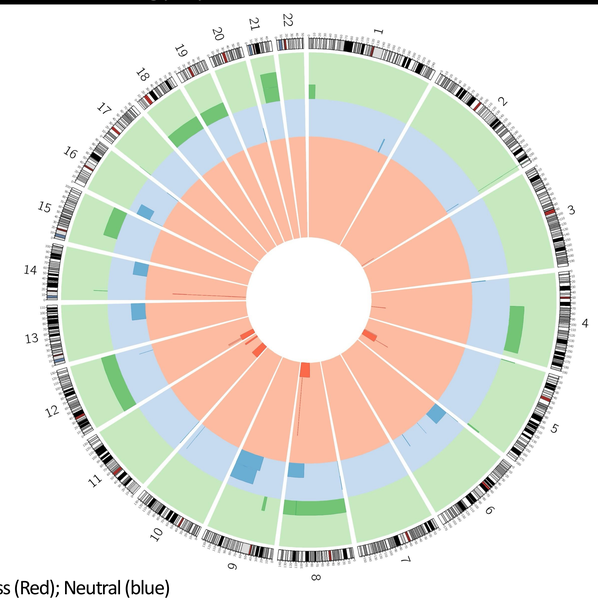
Post-hoc analysis
Among NHL cases, the median time between sample collection and NHL diagnosis was 2.25 years for those with an any mCA detected vs. 2.50 years for those without an mCA.

We further stratified according to time between sample collection and NHL diagnosis. For those whose sample was within 2.5 years from NHL diagnosis an mCA was associated with 1.86 greater odds of NHL (95%CI 0.91, 3.80) while for those whose samples collected between 2.5 and 5 years prior to NHL diagnosis the OR was 0.92 (95%CI 0.39, 2.15).

CONCLUSIONS

- In this relatively young population of PWH, mCAs were frequently detected.
- There was a suggestion that detection of an mCA is more relevant closer to time of NHL diagnosis.
- Further research is needed to understand the implications of mCAs with risk of age-related diseases among PWH.

Figure. Circos plot showing chromosomal position and size of autosomal mosaic chromosomal alterations among people with HIV.



Gain (green); Loss (Red); Neutral (blue)