Clonal Hematopoiesis in Breast Cancer: Underrecognized Predictor of Anthracycline Cardiotoxicity Reviewing Prevalence, Mechanisms, and Prognostic Implications

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INTRODUCTION

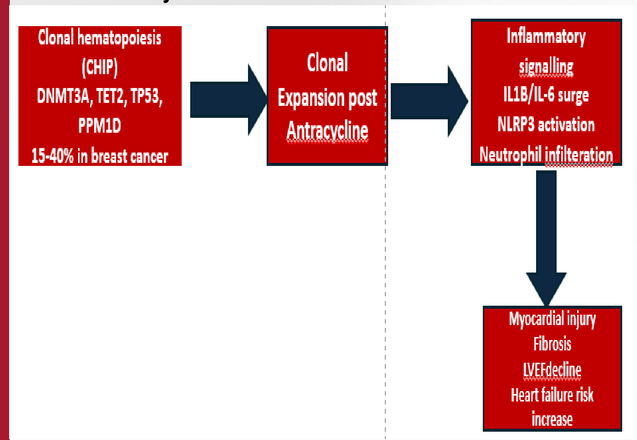
Clonal hematopoiesis of indeterminate potential (CHIP) is a somatic mutation in hematopoietic stem cells without cytopenia or malignancy, and is a common age-related finding, present in 10–20% of adults over 70 and up to 40% of older women with breast cancer. Cytotoxic therapies, especially anthracyclines and alkylating agents, further enrich high-risk clones such as TP53 and PPM1D. Beyond hematologic risk, CHIP is a strong independent predictor of cardiovascular disease, conferring a 2–4-fold increase in CAD, MI, and HF.

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METHODS

We performed a narrative review of published articles (through June 2025), including studies evaluating CHIP prevalence, mutation profiles, cardiovascular outcomes, or anthracycline-induced cardiotoxicity in breast cancer.

CHIP- anthracycline- inflammation pathway leading to cardiotoxicity



RESULTS

CHIP mutations (DNMT3A, TET2, ASXL1, TP53, PPM1D) were detected in 15–40% of breast cancer patients, with TP53 and PPM1D showing post-anthracycline expansion. CHIP carriers had a 25-100% higher risk of HF/MI, driven largely by TET2 and ASXL1 mutations. Mechanistically, CHIP activated IL-1β and the NLRP3 inflammasome, promoting myocardial injury and fibrosis. In prospective data, CHIP conferred an 8-fold increased risk of symptomatic HF or LVEF decline independent of age and anthracycline dose. Evidence is limited by small cohorts and inconsistent CHIP definitions

CONCLUSION

CHIP is a common, age-related genomic alteration with significant cardiovascular implications in breast cancer patients, especially those treated with anthracyclines. Despite emerging evidence linking CHIP to AIC, it remains absent from current risk stratification models. Prospective, breast cancer–specific studies are needed to validate CHIP as a predictive biomarker and inform its integration into personalized cardio-oncology management strategies

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