Clonal Hematopoiesis in Solid Tumor Survivors: A Retrospective Literature Review on an Emerging Precursor to Therapy-Related Hematologic Malignancies

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Context:

- Clonal hematopoiesis (CH), defined as the expansion of hematopoietic stem or progenitor cells harboring somatic mutations in the absence of cytopenias or hematologic malignancy, has recently emerged as a significant biomarker of future myeloid transformation.
- It is most commonly age-associated but is also increasingly recognized in patients exposed to cytotoxic cancer therapies.
- In solid tumor survivors, CH may reflect subclinical genomic stress resulting from radiation, platinum-based chemotherapy, or immunotherapy and is believed to increase the risk of therapy-related myeloid neoplasms, particularly myelodysplastic syndromes (MDS) and acute myeloid leukemia (AML).

Objective:

- Evaluate the prevalence, mutation profile, clinical significance, and progression risk of CH in adult survivors of solid tumors.

Design:

- Retrospective literature review. PubMed, EMBASE, and Scopus were searched (2000–2025) using relevant terms.
- Inclusion criteria were cohort or registry studies involving adult patients with solid tumors and reporting on CH prevalence, mutation types, and outcomes.

Setting:

- Multi-institutional cancer centers, large genomic profiling databases (eg, MSK-IMPACT, Foundation Medicine, UK Biobank), and prospective registry cohorts

Participants:

- Solid tumor survivors aged ≥18 years with post-treatment sequencing data or follow-up for secondary hematologic malignancies.
- Cancer types included lung, breast, prostate, bladder, and testicular.

Interventions:

- Prior exposure to systemic chemotherapy (eg, platinum agents, etoposide), radiation therapy, or immune checkpoint inhibitors

Main Outcome Measures:

- Prevalence of CH, dominant mutations (TP53, PPM1D, DNMT3A, TET2), time to therapy-related MDS/AML, and risk factors for clonal expansion

Results:

- CH was present in 10–25% of solid tumor survivors, with higher rates in older individuals and those exposed to chemotherapy or radiation.
- Therapy-associated CH mutations, especially TP53 and PPM1D, were enriched in patients treated with platinum agents and radiation.
- In some studies, pre-existing CH mutations predicted subsequent therapy-related MDS/AML with a hazard ratio of up to 12.
- Higher variant allele frequency (VAF ≥2%) and multiple co-mutations were associated with faster progression.
- No guidelines currently exist for CH surveillance.

Conclusions:

- CH is common in solid tumor survivors and can act as a molecular harbinger of hematologic malignancy.
- Surveillance of high-risk mutations and integration of CH monitoring into survivorship care warrants prospective evaluation to mitigate late-onset hematologic toxicity.

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