Familial Association of Mantle Cell Lymphoma: A Mini Meta-analysis

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Context

Mantle cell lymphoma (MCL) is an aggressive B-cell non-Hodgkin lymphoma characterized by the t(11;14)(q13;q32) translocation leading to overexpression of cyclin D1. Although typically considered sporadic, emerging evidence suggests a potential familial component to MCL, with several reports documenting familial clustering of lymphoid malignancies, including MCL. ATM, TP53 and CHEK are the most often discussed genes in relation to familial predisposition in MCL or related lymphomas.

Objective

To investigate and synthesize the current evidence on familial association of MCL and estimate the pooled prevalence of familial cases through a mini meta-analysis.

Methods

A comprehensive literature search was conducted in PubMed, EMBASE and Scopus databases for studies published up to February 2025, reporting familial occurrences of MCL. Eligible studies included case series, cohort studies, and case reports that documented at least two biologically related individuals with MCL or with MCL and another lymphoid malignancy. Data on familial prevalence, type of relatives affected, and co-occurrence with other hematologic malignancies were extracted. The pooled prevalence (with 95% confidence interval; CI) of familial MCL was calculated using a random-effects model.

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Results

A total of 12 studies met inclusion criteria, encompassing 47 familial cases of MCL across 31 families. Most cases involved first-degree relatives, with a 68% male predominance. Co-occurrence with other B-cell lymphomas such as chronic lymphocytic leukemia and diffuse large B-cell lymphoma was noted in 18% of families. The pooled prevalence of familial MCL among reported MCL cohorts was estimated at 1.6% (95% CI: 0.9–2.4%). No specific germline mutations were consistently identified, though several studies highlighted shared environmental and epigenetic influences as contributing factors.

Conclusions

Familial aggregation of MCL, although rare, is a recognized entity with implications for understanding lymphomagenesis and potential genetic predisposition. Current familial cases might reflect polygenic inheritance, shared environmental factors or yet-undiscovered low-penetrance variants. Our findings support the need for genetic counselling and consideration of family history in MCL patients. Further research into shared susceptibility loci and longitudinal studies of at-risk family members is warranted.

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