Myeloid Neoplasms with Isolated Deletion 5q and Myeloproliferative Neoplasm Driver Mutations: A Systematic Review of Clinicopathological Features and Therapeutic Outcomes

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Introduction

Myeloid neoplasms harboring both an isolated deletion of chromosome 5q (del(5q)) and a driver mutation in JAK2, CALR, or MPL represent a diagnostically and therapeutically ambiguous subgroup, blending myelodysplastic syndrome (MDS) and myeloproliferative neoplasm (MPN) features (Figure 1).

Despite growing recognition of these cases, their classification, optimal management, and prognostic implications remain poorly defined due to limited aggregated data.

This study explores clinicopathological characteristics, treatment responses, and disease outcomes from published cases to better understand their position within the MDS/MPN spectrum.

Objectives

To describe the clinicopathologic features of del(5q) myeloid neoplasms with JAK2/CALR/MPL mutations.

To summarize treatments (esp. lenalidomide) and outcomes, including AML transformation.

Methods

A systematic review was conducted following PRISMA guidelines, encompassing PubMed and Google Scholar searches for cases of myeloid neoplasms with isolated del(5q) (with ≤1 additional cytogenetic abnormality excluding −7/del(7q)) and confirmed JAK2, CALR, or MPL mutations.

Data extraction included demographics, laboratory/cytogenetic/molecular findings, treatment details, and outcomes.

Descriptive statistics were used for analysis given the heterogeneity of case-level data.

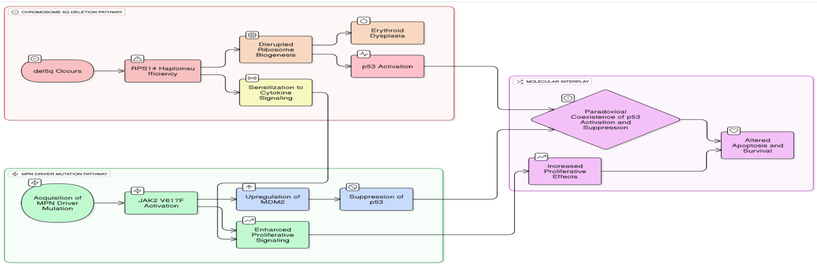


Figure 1. Molecular interplay of del(5q) and MPN driver mutations

Results

From 20 publications (2006–2021), 24 patients were identified (median age 70.5 years; 17/24 [70.8%] female).

Hybrid MDS/MPN features were universal: thrombocytosis (median platelets 735×10³/μL), macrocytic anemia (median hemoglobin 9.6 g/dL, MCV 108 fL), megakaryocytic hyperplasia (16/17 [94.1%] cases), universal dysplasia (20/20 [100%] assessable cases), and marrow fibrosis (10/14 [71.4%] cases).

JAK2 V617F predominated (22/24 [91.7%] cases; median VAF 24.8%).

Lenalidomide induced hematologic responses in 15/17 [88.2%] patients (14/17 [82.4%] complete) and cytogenetic responses in 14/16 [87.5%] patients (8/16 [50.0%] complete), though JAK2 clearance occurred in only 4/13 [30.8%] cases.

Transformation to acute myeloid leukemia occurred in 5/24 [20.8%] patients (median 3 years).

Comparative analysis of four retrospective cohorts revealed a 5–15% prevalence of JAK2 mutations in del(5q) MDS, with variable lenalidomide efficacy (43–100%) and AML progression risk (0–20%)(Table 1).

Table. Retrospective studies of del(5q) with MPN driver mutations

Study	Cohort Size	Key Findings	Clinical Implications
Ingram et al. (2006) [1].	6 del[5q]+JAK2 (of 97)	Proliferative BM (↑PLT, megakaryocytic hyperplasia)	JAK2+ defines a distinct MDS subset
Wong et al. (2009)[2]	3 del[5q]+JAK2 (of 10)	Low risk of leukemic transformation	Risk stratification
Patnaik et al. (2010)[3]	5 del[5q]+JAK2, 3 del[5q]+MPL, 1 del[5q]+JAK2+MPL (of 190)	Low risk of leukemic transformation JAK2+ linked to worse OS (HR 2.1, p=0.04)	Risk stratification
Sangiorgio et al. (2020)[4]	6 del(5q)+JAK2(of 47)	Fibrosis in 70%; 20% AML progression	Monitor for MPN progression

Conclusions

This first case-level systematic review highlights that myeloid neoplasms with isolated del(5q) and MPN driver mutations exhibit consistent clinicopathological overlap between MDS and MPN, high but heterogeneous sensitivity to lenalidomide, and significant progression risk.

While these findings provide preliminary insights, the rarity of cases and retrospective nature of available data underscore the need for prospective, multicenter collaboration to define diagnostic and therapeutic paradigms for this patient subset.

Acknowledgments

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