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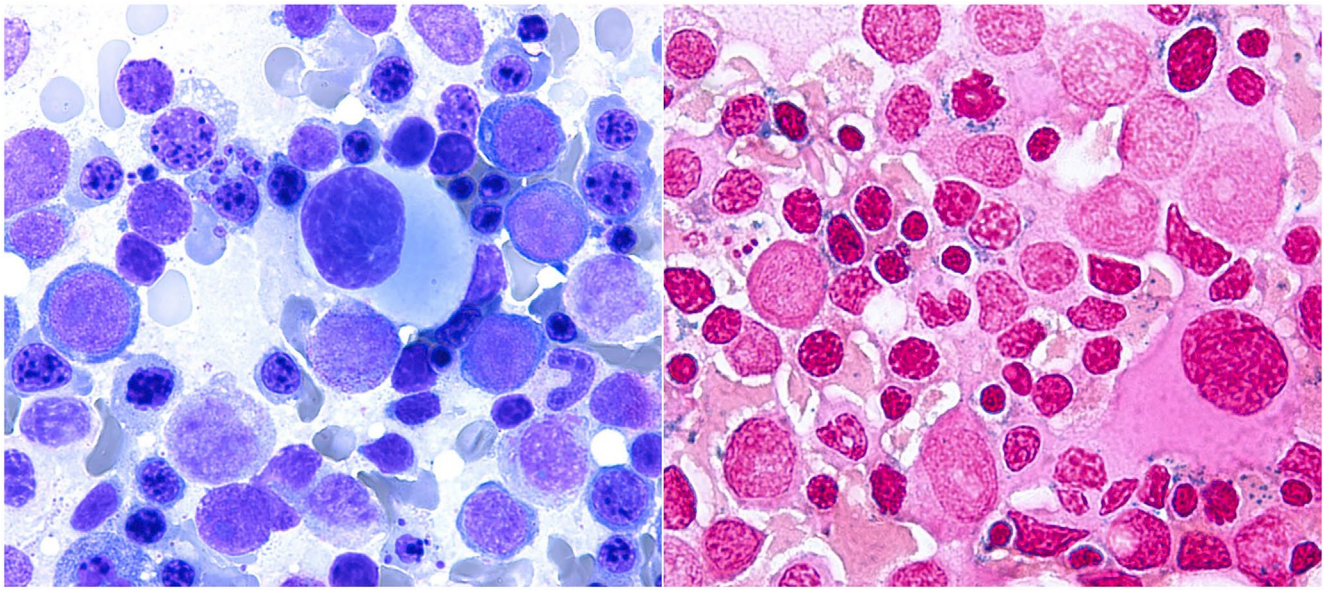
IMAGES IN HAEMATOLOGY

Monolobated megakaryocytes and ring sideroblasts: A morphological prelude to multihit *TP53* and complex karyotype



A 76-year-old male with a history of localised pelvic radiotherapy for prostate cancer 6 years earlier presented with fatigue and severe pancytopenia (haemoglobin 80 g/L, normocytic; platelets 50×10^9/L; leucocytes 1.5×10^9/L; neutrophils 0.3×10^9/L; no peripheral blasts). Bone marrow aspiration was hypercellular for age with erythroid hyperplasia and striking trilineage dysplasia. Erythroid precursors displayed nuclear irregularities, megaloblastoid changes and multinuclearity. Numerous small, monolobated megakaryocytes were present. Myeloblasts accounted for 4% of nucleated cells (left image, May–Grünwald stain, 100× lens objective). Iron staining revealed 43% ring sideroblasts (right image, Perls' staining, 100× lens objective). Cytogenetic analysis revealed a complex karyotype in which del(5q) and del(17p) were present across all metaphases: 47,XY,del(5)(q15q33),del(17)(p11.2),-18,-20,+21,+22,+mar[20]. Targeted next-generation sequencing (NGS) identified a likely pathogenic *TP53* mutation (c.711G>A, p.Met237Ile) with a variant allele frequency (VAF) of 43%, in the absence of other myeloid-associated mutations, including *SF3B1* and other spliceosome genes.

According to recent classifications, the final diagnosis was myelodysplastic syndrome (MDS) with biallelic *TP53* inactivation (WHO 2022)[1]/MDS with mutated *TP53* (ICC 2022),[2] corresponding to very high-risk disease by Molecular International Prognostic Scoring System (IPSS-M). Given the patient's prior exposure to pelvic radiotherapy for prostate cancer, the possibility of a post-cytotoxic therapy MDS (WHO 2022) or an MDS with the therapy-related qualifier (ICC 2022) cannot be excluded.

This case underscores the value of integrated diagnostics. Initial morphology—monolobated megakaryocytes and ring sideroblasts—raised the possibility of MDS-del(5q) or MDS-*SF3B1*, but marked erythroid dysplasia and hyperplasia, atypical for isolated del(5q), indicated more aggressive biology. The detection of a complex karyotype and biallelic *TP53* alterations ultimately reclassified this case.

While del(5q) occurs in 10%–20% of MDS, only ~5% fit strict criteria for MDS with low blasts and isolated del(5q).[1–3] Most are excluded due to excess blasts or additional cytogenetic changes, requiring reclassification. *TP53* mutations occur in ~18% of del(5q) MDS, yet only biallelic alterations (4%–6%) associate with genomic instability, lenalidomide resistance and poor prognosis.[4,5] In such cases, *TP53* status overrides other features in guiding disease behaviour and therapy. This case illustrates that, although cytomorphology offers useful clues, reliance solely on del(5q)-like features or ring sideroblasts risks misclassification, underscoring the importance of an integrated diagnostic approach.

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PATIENT CONSENT STATEMENT
The patient provided written informed consent prior to participation.

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