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CASE REPORT

Distinct role of *der(1;7)(q10;p10)* in myelodysplastic syndrome: diagnostic and treatment considerations; A case study.

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ABSTRACT

Background: Myelodysplastic syndrome (MDS) is a heterogeneous group of clonal hematopoietic disorders characterized by recurrent chromosomal abnormalities that guide diagnosis and prognosis. *Der(1;7)* is a relatively rare abnormality and was reported in 1%-3% of MDS patients and 1%-2% of acute myeloid leukemia patients. However, due to its rare occurrence, its prognostic evaluation remains under investigation.

Case Presentation: The present case was a 62-year-old male with a chromosomal abnormality of *der(1;7)(q10;p10)* along with a clonal evolution of deletion of chromosome 20q. A comprehensive assessment combining morphology, immunophenotyping, karyotyping, and fluorescence *in situ* hybridization provided valuable insights into the characterization and clonal behavior of this rare abnormality. The importance of the international prognostic scoring system-revised scoring in guiding treatment decisions, particularly highlighting the relevance of allo-grafting based on genetic findings in intermediate-risk cases was discussed.

Conclusion: The present study aligns with and supports ongoing efforts to refine the classification system by recognizing *der(1;7)* as an independent entity within the MDS classification, distinct from monosomy 7 or deletion 7q, with the ultimate goal of advancing personalized treatment approaches.

Keywords: MDS, der(1;7)(q10;p10), karyotyping, FISH, case report.

Introduction

Myelodysplastic syndrome (MDS), recently redefined by the World Health Organization (WHO) guidelines as "myelodysplastic neoplasms" with a 10% dysplasia threshold across all hematopoietic lineages, represents a heterogeneous group of clonal hematopoietic stem cell diseases characterized by cytopenia, dysplasia, ineffective hematopoiesis, recurrent genetic abnormalities, and an increased risk of progression to acute myeloid leukemia (AML) [1, 2].

Alongside blast percentage, cytogenetic abnormalities are crucial for diagnosis and are integral to both the international prognostic scoring system - revised (IPSS-R) and the WHO prognostic scoring system, guiding prognosis and therapeutic decisions [3].

In MDS, common cytogenetic abnormalities include deletions and monosomies affecting chromosomes 5 and 7 followed by Trisomy 8 and deletion 20q. MDS is associated with chromosomal abnormalities, with monosomy 7 and deletion of 20q being particularly poor prognostic and intermediate risk markers, respectively.

In addition to these recurrent abnormalities, unbalanced translocations are frequently observed, typically within complex karyotypes that are linked to disease transformation to AML [4, 5]. This is driven by multistep genetic clonal evolution with the sequential acquisition of mutations that are observed in 11.9%-39.0% of MDS cases [6].

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Complete or partial deletions of *chromosome 7 (-7/del7q)* are among the most frequent chromosomal abnormalities in myeloid neoplasms and are typically associated with poor prognosis. A rare variant of 7q deletion; *der(1;7)(q10;p10)* involves the formation of a derivative chromosome through an unbalanced whole-arm translocation between chromosomes 1 and 7. This results from an error in mitotic recombination within the centromeric regions, leading to copy number variations that include partial trisomy of 1q and partial monosomy of 7q.

Der(1;7) has been reported in 1%-3% of MDS patients and 1%-2% of AML patients. However, due to its rare occurrence, its prognostic evaluation is still under investigation [7, 8]. Allogeneic stem cell transplantation (allo-SCT) is the potentially curative treatment for high-risk MDS patients, including those with deletion 7/ monosomy 7.

The present case was the first documented case in Bahrain of a 62-year-old male with MDS associated with *der(1;7)* a variant form of deletion 7q with clonal evolution of chromosome 20q deletion who underwent successful allogeneic stem cell transplantation, resulting in remission and resolution of transfusion dependency. *Der(1;7)(q10;p10)* is illustrated along with clonal evolution by a combined karyotype and fluorescence *in situ* hybridization (FISH) analysis for diagnosis and monitoring. This study supported the ongoing efforts to consider *der(1;7)* as a distinct category within the MDS classification system.

Case Presentation

A 62-year-old male with a medical history significant for type 2 diabetes mellitus (diagnosed in the year 1996), hyperlipidemia, and benign essential hypertension (on treatment with Coversyl 10 mg daily, Relvar 100 mcg daily, and Ventolin 200 mcg as needed) was referred for evaluation of cytopenia in the year 2022. The patient, was asymptomatic but noted to have gradually worsening anemia, requiring frequent blood transfusions.

The patient was diagnosed with MDS in October 2022 following a bone marrow aspirate (BMA) and biopsy. The BMA showed trilineage hematopoiesis with erythroid dysplasia and a relative decrease in myelopoiesis. The cellularity of the marrow was mildly hypocellular at 35%. The patient's bone marrow biopsy revealed mildly hypocellular marrow with reduced myelopoiesis. Cytogenetic analysis revealed the presence of deletion 7q (64.4%) and deletion 20q (57.3%) by FISH, which are poor prognostic markers for MDS.

At the time of diagnosis, the patient was categorized as intermediate risk (IPSS-R score 4.23) due to the combination of clinical and genetic findings. The patient became transfusion-dependent, requiring regular blood transfusions (approximately weekly), and his clinical status deteriorated without transfusion support. Despite these challenges, the patient did not have blasts in his bone marrow, and no prior chemotherapy was administered.

Due to the progressive nature of the disease and the patient's transfusion dependence, he was referred for allo-SCT. A second bone marrow aspiration and biopsy, conducted in April 2024, revealed a hypocellular marrow (cellularity 20%-40%) with megaloblastic erythropoiesis, reduced myeloid cells, and small focal clusters of dysplastic megakaryocytes. Despite the erythroid predominance, there was no increase in reticulin fibrosis (WHO Grade MF 0).

MDS FISH analysis was positive for *derivative (1;7); deletion 7q and deletion 20q*, confirming the diagnosis of MDS MLD (MDS with multilineage dysplasia). Liver function tests were elevated, prompting a referral to gastroenterology, and a liver biopsy performed showed hepatic steatosis (Grade II) with steatohepatitis.

Due to the patient's poor prognostic markers and transfusion dependence, a multidisciplinary discussion at the tumor board led to the decision to proceed with allo-SCT. The patient underwent a pre-transplant conditioning regimen that included fludarabine, busulfan, total body irradiation, and post-transplant cyclophosphamide for graft-versus-host disease prophylaxis. Stem cells were infused from the patient's HLA-matched sibling donor, who was found to carry a thalassemia trait but no other significant genetic disorders. The patient had not received prior chemotherapy, and no blasts were present in his bone marrow at the time of the transplant.

The patient tolerated the transplantation well, and engraftment was confirmed shortly after the procedure. A bone marrow biopsy revealed a normocellular marrow with 60% cellularity. The bone marrow showed active trilineage hematopoiesis with normal megakaryopoiesis, erythropoiesis, and myelopoiesis. There was no evidence of dysplasia, malignant infiltration, or atypical cells, and the reticulin stain showed a normal pattern (WHO Grade 0-1 myelofibrosis). Additionally, MDS cytogenetic evaluation by karyotyping and FISH panel from the bone marrow was negative for *der(1;7)* as well as negative for deletion 7q/monosomy 7 and deletion 20q by FISH, confirming complete remission and successful engraftment.

Post-transplant, the patient was currently in remission, no longer requiring blood transfusions, and has regained normal hematopoietic function. The patient remained under close outpatient follow-up with regular monitoring of bone marrow function, liver enzymes, and other pertinent laboratory parameters. His performance status improved significantly, and he did not experience any major post-transplant complications to date.

Cytogenetic analysis was performed on unstimulated bone marrow specimens. Karyotype analysis unveiled an acquired abnormality that the apparent deletion 7q observed in FISH was due to partial monosomy for 7q resulting from an unbalanced translocation *der(1;7).*

The karyotype was designated as 46,XY,+1,der(1;7)(q10;p10)[7]/46,idem,del(20)(q13.1)[4]/46,XY[9] (ISCN-2020) [9] (Figure 1).

FISH analysis using Zytolight probes for chromosome 5q deletion/monosomy 5, 7q deletion/monosomy 7, Trisomy 8, and deletion 20q detection showed positive status for deletion 7q (64.4%) and 20q (57.3%) and negative status for 5q deletion/monosomy 5 and Trisomy 8.

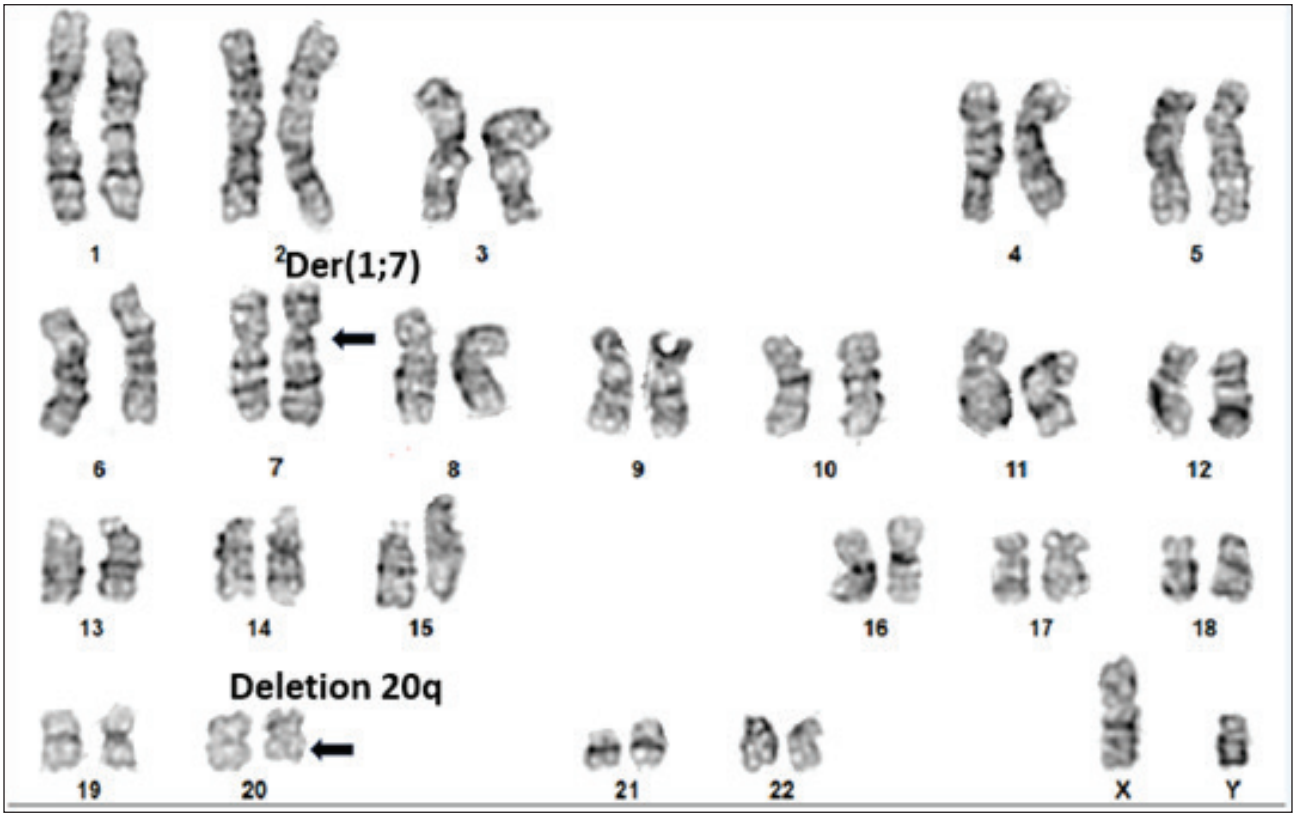

Figure 1. *G-banding Karyotype of Bone Marrow: Der(1;7)(q10;p10) and 20q12 Deletion at 525 Band Resolution.*

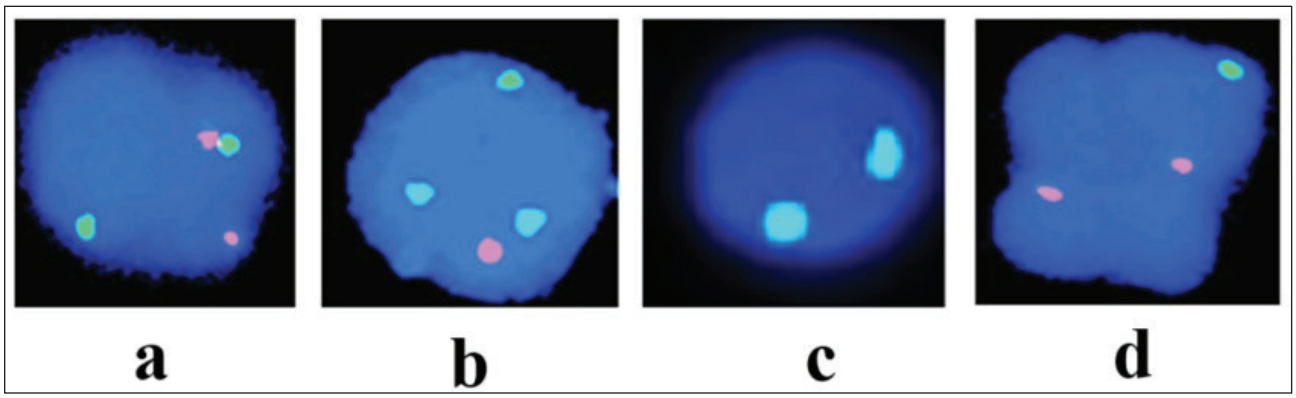

Figure 2a. *Interphase FISH with SPEC(5q31.2) EGR1/D5S23,D5S721 Probe: Negative for 5q Deletion. b: Interphase cell using SPEC 7q22.1/7q36.1/CEP7 FISH probe showing 2 aqua, 1 green, and 1 orange signal pattern indicating hemizygous loss in chromosome 7, particularly deletion 7q. c: Interphase FISH with centromeric probe for chromosome 8 showing two normal copies. d: Interphase cell using PTPRT/20q11 probe showing 2 orange, 1 green signal indicating deletion of the other homologue region of 20q11.*

Post-transplant FISH analysis showed a negative status for deletions 7q and 20q indicating a remission status (Figure 2).

Discussion

Formation of a derivative chromosome consisting of the short arm of chromosome 7 and the long arm of chromosome 1 is due to the whole arm translocation resulting in a net imbalance of loss of the long arm of chromosome 7, i.e., 7q and trisomy for the long arm of chromosome 1, i.e., 1q. Clonal evolution was presented by an additional 20q deletion. Post-transplant karyotype was normal suggesting a complete bone marrow engraftment.

The variable abnormal clone size between karyotyping and FISH results could be attributed to differential clone proliferation rates in cell culture, and hence, a combined approach using both karyotyping and FISH was required to gain a more comprehensive understanding of clonal percentages and to precisely characterize structural abnormalities. Together, these methods provide a more complete cytogenetic profile, which is essential for patient management and effective treatment selection and monitoring.

Derivative (1;7) is a rare, recurrent chromosomal abnormality associated primarily with AML M2, myeloid neoplasms, and MDS. Notably, it was occasionally observed in lymphoid disorders such as multiple myeloma, chronic lymphocytic leukemia, lymphomas, biphenotypic leukemia, and sarcomas [10, 11].

This broad multilineage association suggested a possible primary genetic event at the progenitor cell level, before lineage commitment.

Considering the prognostic perspective, *der(1;7)* has been classified within the poor prognosis group by the UK Medical Research Council trials for AML, where it is grouped alongside -7 and 7q deletions as a poor prognosis group, while the CALGB study assigned deletion 7q in an intermediate prognostic group, emphasizing the differing views in prognostic interpretations across studies [10, 11]. This discrepancy across studies highlighted the complexity in assessing prognosis for *Der(1;7),* a variant form of deletion 7q [12].

Some unique differences pointed out by a meta-analysis have shown that *der(1;7)* is associated with a longer time to AML progression and improved overall survival (OS) compared to monosomy 7, with an OS similar to that of *del(7q)* in MDS patients. The analysis also highlighted that *der(1;7)* differs from *−7/del(7q)* in several aspects: it is more prevalent in males, typically presents with lower blast and platelet counts than *del(7q),* and is associated with higher hemoglobin levels than monosomy 7. Additionally, *der(1;7)* is often accompanied by distinct co-occurring cytogenetic abnormalities and mutations. These findings suggested that *der(1;7)* might be considered a unique MDS subtype.

Based on the current study, integrating karyotyping and FISH at both diagnosis and follow-up provided comprehensive insights into the structural characterization of chromosomal abnormalities, as well as clonal evolution and expansion patterns. In this case, both the *derivative (1;7)* abnormality and a deletion on chromosome 20q were identified at diagnosis, signaling early clonal evolution with potential implications for overall survival.

The combination of *der(1;7)* with del(20q) could indicate a unique pathogenic behavior, especially as haploinsufficiency due to large deletions on the whole arm of chromosome 7 and specific gene deletions on 20q, such as ASXL1, that are linked to poorer outcomes and a greater risk of progression to AML [13].

There is an established distinction in MDS between the effects of chromosome 7q and 20q deletions, each of which drives disease progression through different mechanisms. The 7q deletion disrupts DNA repair, potentially leading to more aggressive MDS, particularly in therapy-related cases, while the 20q deletion affects cell differentiation, contributing to abnormal blood cell development. *Del(7q) or -7* in MDS is linked to poor prognosis, involving haploinsufficiency of genes in the 7q region, while isolated del(20q) occurs in early stage MDS and is associated with favorable outcomes but exists in complex karyotype with poor prognosis. However, no documented evidence exists to suggest an interplay or interaction between deletions of 7q and 20q [14].

While *del(20q)* is typically associated with a favorable prognosis when present as a sole abnormality in MDS, its appearance here as a secondary clone to *der(1;7)* adds complexity and prognostic variability, suggesting an evolving disease course.

These findings suggested that in MDS, *der(1;7)* and *del(20q)* support separate pathways of disease evolution, reflecting the complex genetic contributions to MDS progression. Given the patient's stable response to treatment so far, continued long-term follow-up would be crucial in assessing how this unique combination of abnormalities influences the disease's course over time.

The present case highlighted the complex interplay between genetic predisposition and regional influences in the predisposition of MDS. This is consistent with the findings, which suggested that environmental exposure to pesticides or therapeutics, combined with the nonrandom distribution of the *der(1;7)* chromosomal abnormality in Northwestern Europe, points to a potential founder effect linked to genetic susceptibility. Interestingly, *der(1;7)* was observed more frequently in Japanese populations compared to Caucasians, which might further reflect regional genetic variations and environmental influences [15].

This emphasizes the importance of regional case studies, such as the present case, in understanding rare chromosomal abnormalities like *der(1;7).* By examining the genetic landscape in specific populations, valuable insights were gained into how genetic susceptibility, coupled with environmental factors, contributes to the development and progression of diseases like MDS.

In the present case, the patient presented with transfusion dependency at diagnosis. The patient's need for regular blood transfusions and clinical decline in the absence of transfusion support are related to the severity of the disease. Despite these challenges, the lack of blast cells in the bone marrow suggested the absence of disease progression. In this context, the presence of *derivative (1;7)* could be viewed as an indicator of a more indolent, or slowly progressing, disease course.

Considering the presence of a *variant 7q deletion of Der(1;7)* prompted for consideration of an allogeneic stem cell transplantation (allo-SCT). Following transplantation, the patient experienced a restoration of normal hematopoietic function and showed a marked improvement in performance status, with no major complications during close outpatient follow-up.

Allo-SCT has thus provided a promising long-term treatment option, with the potential to enhance both prognosis and quality of life. This case aligns with findings from Lang W et al.'s meta-analysis, which associates *der(1;7)* with a relatively favorable prognosis, evidenced by a longer time to disease progression and improved overall survival compared to monosomy 7. The distinct mutation profile of *der(1;7)* characterized by higher frequencies of RUNX1, ETNK1, and EZH2 mutations and lower TP53 mutations by Lang W et al. further suggested that *der(1;7)* might represent a less aggressive MDS subtype [11].

These findings reinforced the view that *der(1;7)* might confer a more stable, manageable disease within the

distinct MDS disease spectrum, particularly when treated with allo-SCT. The patient's transfusion dependence and clinical decline in the absence of transfusion support emphasized the severity of the disease, underscoring the need for careful cytogenetic evaluation at diagnosis and follow-up. The identification of *der(1;7)* and 20q deletion through karyotyping and FISH provided key insights into the patient's clonal evolution and overall disease status, supporting the decision to proceed with allo-SCT.

The patient's positive response to allo-SCT and subsequent remission further reinforce the potential for improved therapeutic outcomes in cases with *der(1;7)*. This case highlighted the importance of integrated cytogenetic assessments in guiding effective treatment decisions and assessing disease evolution.

Conclusion

This study aimed to report this rare distinct genetic entity of *der(1;7)* in MDS along with treatment decisions to strengthen the incidence of this cytogenetic abnormality in MDS. This would help to build an evidence base that highlighted the unique and distinct genetic and clinical features associated with *der(1;7)*. As more cases with similar rare chromosomal findings are reported, it would become possible to prognosticate it strongly and formulate defined potential therapeutic targets. This accumulation of data could ultimately contribute to enhancing diagnosis, refining MDS classification, and improving patient management. The current findings aligned with existing literature advocates for recognizing variant of *deletion 7q; der(1;7)* as a distinct MDS subtype with a potentially less aggressive disease course compared to other genetic categories.

List of Abbreviations

AML	Acute myeloid leukemia
allo-SCT	Allogeneic stem cell transplantation
BMA	Bone marrow aspirate
FISH	Fluorescence *in situ* hybridization
IPSS-R	International Prognostic Scoring System - Revised
OS	Overall survival
WHO	World Health Organization

Conflict of interest

The authors of this article have no affiliations with or involvement in any organization or entity with any financial interest or non-financial interest in the subject matter or materials discussed in this manuscript.

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Consent for publication

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Author contributions

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