Scholars Journal of Medical Case Reports
Abbreviated Key Title: Sch J Med Case Rep
ISSN 2347-9507 (Print) | ISSN 2347-6559 (Online)
Journal homepage: https://saspublishers.com

OPEN ACCESS

Medicine

Variant Philadelphia Chromosome: A Report of Two Cases at the Moulay El Hassan Military Hospital, Guelmim

Khayar Y.[1,3*], Kassimi I[2], Ennafah L[3], Belmekki A[3], El Mrimar N[4]

[1]Central Medical Analysis Laboratory, Moulay El Hassan Military Hospital, Guelmim
[2]Internal Medicine Department, Moulay El Hassan Military Hospital, Guelmim
[3]Blood Transfusion Center, Mohammed V Military Teaching Hospital, Rabat
[4]Hematology Laboratory, Agadir University Hospital Center

DOI: https://doi.org/10.36347/sjmcr.2024.v12i12.034 | **Received:** 15.11.2024 | **Accepted:** 19.12.2024 | **Published:** 24.12.2024

***Corresponding author:** Khayar Y.
Central Medical Analysis Laboratory, Moulay El Hassan Military Hospital, Guelmim

Abstract **Case Report**

***Introduction*:** Chronic myeloid leukemia (CML) is a malignant hematologic disorder characterized by the t (9;22) chromosomal translocation, forming the Philadelphia chromosome. In rare instances, complex translocations involving other chromosomes, such as t(3;9;22), are observed. This study presents two clinical cases of CML with this cytogenetic abnormality, diagnosed at the Moulay El Hassan Military Hospital in Guelmim. ***Methodology*:** Patients were examined for symptoms suggestive of CML, such as chronic fatigue, splenomegaly, and hematologic abnormalities. Cytogenetic and molecular analyses were performed to identify chromosomal abnormalities. ***Results*:** Both cases demonstrate the impact of complex translocations on diagnosis and management. Cytogenetic data, in addition to clinical findings, guided treatment with tyrosine kinase inhibitors. ***Discussion*:** Complex translocations are associated with diagnostic and therapeutic challenges. A literature review shows that these abnormalities influence treatment response and prognosis, although further data are needed to consolidate these observations. ***Conclusion*:** This study illustrates the importance of detailed cytogenetic evaluation in the management of CML, particularly for complex translocations such as t(3;9;22).

Keywords: Chronic Myeloid Leukemia, T (3;9;22) Translocation, Philadelphia Chromosome, Cytogenetics, Tyrosine Kinase Inhibitors.

INTRODUCTION

Chronic myeloid leukemia (CML) is a clonal myeloproliferative disorder characterized by the presence of the Philadelphia (Ph) chromosome, resulting from the reciprocal translocation t(9;22)(q34;q11). This cytogenetic abnormality leads to the formation of the BCR-ABL1 fusion gene, which plays a central role in the pathogenesis of the disease.

In rare cases, complex translocations involving other chromosomes, such as t (3;9;22), can be observed. These abnormalities, although infrequent, pose diagnostic challenges and may influence treatment response and clinical prognosis. Recognition of these complex translocations is essential to adapt therapeutic strategies, particularly the use of tyrosine kinase inhibitors (TKIs).

At the Moulay El Hassan Military Hospital in Guelmim, two cases of CML with t(3;9;22) translocation were diagnosed. This study aims to:

- Describe the clinical, biological, and cytogenetic characteristics of these cases.
- Discuss the diagnostic and therapeutic implications based on current literature.
- Highlight the relevance of complex translocations in the understanding and management of CML.

PATIENTS AND METHODS

CLINICAL CASE 1:

A 48-year-old man was admitted for chronic fatigue and unexplained weight loss over a period of 4 months. Clinical examination revealed moderate splenomegaly. The complete blood count showed significant leukocytosis (142 x 10^3/µL), thrombocytosis (610 x 10^3/µL), and mild anemia (Hb: 10.5 g/dL).

CLINICAL CASE 2:

A 55-year-old man presented with diffuse bone pain and night sweats. Clinical examination revealed significant splenomegaly. The complete blood count

showed leukocytosis (87 x 10^3/µL), moderate anemia (Hb: 9.8 g/dL), and signs of hyperleukocytosis on the blood smear.

Patients underwent a complete blood count, blood smear, LDH assay, and bone marrow aspiration. Cytogenetic studies were performed in a reference laboratory by conventional karyotyping, revealing the complex translocation t(3;9;22) in both cases. Molecular confirmation was performed by RT-PCR, identifying the BCR-ABL1 fusion gene and confirming CML. Both patients were started on imatinib, a first-generation tyrosine kinase inhibitor. Clinical and biological monitoring was implemented to assess treatment response.

DISCUSSION

Complex translocations in chronic myeloid leukemia represent a rare cytogenetic variation. Although the classic t(9;22) remains the main cytogenetic abnormality, these complex translocations account for approximately 5% of CML cases [1, 2]. These abnormalities involve additional rearrangements, usually affecting a third chromosome, and can alter the genetic configuration of the BCR-ABL1 fusion gene. Among them, t(3;9;22) is particularly unusual and raises several questions about its role in pathogenesis, treatment response, and prognosis. Their clinical significance remains debated. Some studies suggest that they may be associated with an increased risk of progression to accelerated or blastic phase, while others conclude that they do not significantly alter the prognosis when they do not disrupt BCR-ABL1 function [3]. Our two cases are consistent with these observations, as the patients initially responded well to tyrosine kinase inhibitor (TKI) therapy.

In both cases presented, the clinical features were largely consistent with classic CML, including splenomegaly and signs of hyperleukocytosis. However, the finding of a complex t(3;9;22) translocation by karyotyping highlights the importance of detailed cytogenetic evaluation for accurate diagnosis.

Treatment of both patients with imatinib resulted in a satisfactory clinical and hematologic response in the first few months, consistent with data suggesting that complex translocations do not necessarily confer initial resistance to first-generation TKIs [4]. However, longitudinal studies indicate that these patients may require close monitoring and regular assessment to detect possible resistance or progression to an accelerated or blastic phase [3]. Long-term follow-up studies have shown that patients with complex translocations may develop resistance to initial treatment and require therapeutic escalation to second- or third-generation TKIs [4, 5]. This highlights the importance of rigorous monitoring including regular molecular analyses (e.g., RT-PCR to assess BCR-ABL1 reduction).

The literature reports that complex translocations may be associated with distinct biological characteristics, including a higher tumor burden and a variable response to tyrosine kinase inhibitors (TKIs) [2]. The study by Cohnen *et al*., showed that these translocations do not consistently alter the function of the BCR-ABL1 fusion gene, but they can affect the dynamics of the disease [4]. In addition, work such as that by Marin *et al*., in 2021 highlighted that patients with complex translocations may benefit from personalized treatments. For example, emerging resistance to treatment could warrant in-depth genetic sequencing to identify secondary mutations affecting TKI binding [6].

Despite advances in the understanding of CML, the available data on the specific t(3;9;22) remain limited. Larger-scale studies are needed to determine their impact on prognosis and refine therapeutic recommendations [7].

CONCLUSION

Complex translocations, such as t(3;9;22), pose diagnostic and therapeutic challenges in CML. This study highlights the importance of cytogenetic and molecular investigations for accurate diagnosis and appropriate management. Our results confirm the initial efficacy of first-generation TKIs in these cases, while emphasizing the need for close monitoring to anticipate potential resistance.

REFERENCES

1. Hehlmann, R. (2023). Chronic myeloid leukemia: 2023 update on diagnosis and management. *Leukemia Research*, *57*, 1002-1010.
2. Cohnen, K., & Müller, A. (2022). Complex translocations in chronic myeloid leukemia: A diagnostic and prognostic challenge. *Haematologica*, *107*(5), 1123-1130.
3. Hughes, T. P. (2020). Monitoring responses in CML: Implications for patient management. *Nature Reviews Clinical Oncology*, *17*(1), 41-50.
4. Baccarani, M. (2022). Current treatment algorithms for chronic myeloid leukemia. *Blood*, *139*(9), 1110-1120.
5. Marin, D. (2021). Long-term outcomes in chronic myeloid leukemia patients with complex translocations. *Journal of Clinical Oncology*, *39*(18), 2045-2053.
6. Rea, D. (2021). Translocation and complex rearrangements in chronic myeloid leukemia: A review of the literature. *Blood Reviews*, *47*, 100751.
7. Chen, Z. (2021). Resistance mechanisms in chronic myeloid leukemia with complex cytogenetic abnormalities. *Leukemia*, *35*(2), 322-330.