

# A Rare Case of Acute Myeloid Leukemia with Translocation (3:3) Presenting with Features of Chronic Myelomonocytic Leukemia

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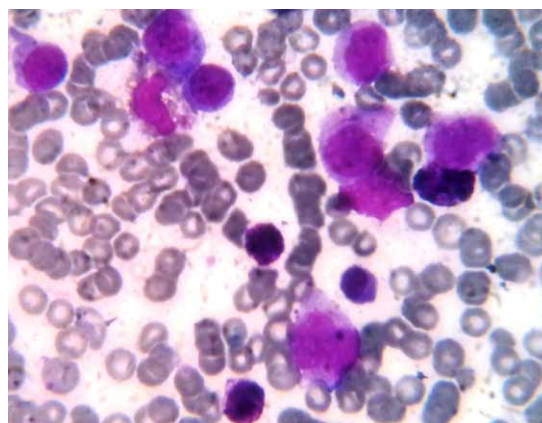
## Abstract

**Background:** Acute Myeloid Leukemia (AML) with translocation (3,3) is a form of AML that may present de novo or may arise from a previous myelodysplastic syndrome. It is often associated with normal or elevated peripheral blood platelet count and increased bone marrow megakaryocytes with associated multi lineage dysplasia. A subset of patients present with hepatosplenomegaly while a few cases have less than twenty percent blasts at the time of diagnosis, including cases with features of chronic myelomonocytic leukemia (CMML). Here we present a rare case presenting initially with features of CMML who eventually turned out to be a case of AML with translocation (3, 3).

**Key words:** Acute myeloid leukemia, translocation, malignancy.

## Introduction

Acute myeloid leukemia with inv(3)(q21;q26.2) or t(3;3)(q21;q26.2) has recently been included in the World Health Organization (WHO) classification as a distinct type of leukemia under the umbrella term "acute myeloid leukemia with recurrent cytogenetic abnormalities"<sup>1</sup>. Inv(3)(q21;q26.2) or t(3;3)(q21;q26.2) results in an inversion or homologous reciprocal translocation that leads to the juxtaposition of the ecotropic viral integration site-1 (EVI1) gene with the ribophorin 1(RPN1) gene. This rearrangement results in transcriptional activation of the EVI1 gene which is believed to have a critical role in the pathogenesis of myeloid neoplasms, by driving cellular proliferation and/or impairing differentiation<sup>2,3</sup>.



**Figure 1:** Basophilia observed in blood smear of the patient.

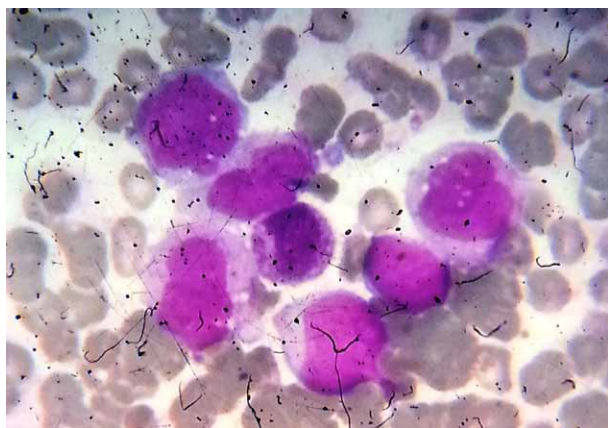
## Report of the Case

An elderly female of 65 years presented with the features of fatigue, hepatosplenomegaly and oral ulcers. Thorough hematological investigations were done, including complete blood count (CBC), Peripheral Blood film (PBF) examination, bone marrow aspiration and bone marrow biopsy. The CBC showed hemoglobin (Hb) of 11.2g/dl,

Total Leukocyte Count (TLC) of 47,750/mm<sup>3</sup> and platelets 180,000/mm<sup>3</sup>. The patient's differential leukocyte count revealed blast percentage of 05%, promyelocytes of 01%, myelocytes of 2%, metamyelocytes of 04%, neutrophils of 04%, lymphocytes of 40%, monocytes of 31%, basophils of 10% and eosinophils of 3%. Bone



**Figure 2:** Persistently high leukocyte count revealing blast percentage of 9%.



**Figure 3:** Persistent monocytosis in patient's blood smear.

marrow examination was advised, which revealed hyper cellular marrow with predominantly normoblastic erythroid maturation. There was myeloid hyperplasia with an increase in blast percentage (12%), basophilia (8%) (Figure 1), and monocyte count of 18%. A provisional diagnosis of chronic myeloproliferative disorder was made. However Real Time Polymerase Chain Reaction (RT-PCR) of the bone marrow aspirate revealed no gene-rearrangement for bcr-abl (Philadelphia chromosome negative). Based on negative profile of bcr-abl, possibility of CMML was considered and patient was put on treatment for CMML. However the patient's condition continued to deteriorate with a significant fall in hemoglobin

level and persistently high leukocyte count revealing blast percentage of 9% (Figure 2), and persistent monocytosis (Figure 3). Considering no improvement in the patient's condition, and her peripheral blood features, flow cytometry and cytogenetics of the patient's bone marrow aspirate was planned. The flow cytometric analysis revealed 10% cells positive for myeloid markers CD11b, CD13, CD15, CD33 and myeloperoxidase (MPO). These gated cells were also positive for monocytic markers CD14 and showed coexpression of CD36 and CD64. Markers for T and B lymphoid cells were negative.

Cytogenetic analysis of 20 metaphases revealed 17 metaphases showing 46XX with translocation involving q arm of chromosome 3 and q arm of chromosome 3 at band 3q 21 and 3q 26.2. Based on cytogenetic analysis, a diagnosis of AML with translocation (3:3) was made.

## Discussion

AML with translocation (3,3) represents 1 to 2 % of all myeloid leukemias. It occurs most commonly in adults with no sex predilection. AML with t(3,3) usually presents with anemia. Increased platelet count can also occur in 7- 22% of cases. Few cases can present with hepatosplenomegaly, while lymphadenopathy is an uncommon presentation.

The peripheral blood may show hypogranular neutrophils with Pseudo-Pelger-Huett anomaly. The blasts could be seen, although absence of blasts in the peripheral blood smear does not rule out the diagnosis. Giant platelets with hypogranular forms could also be observed. The blasts seen on the bone marrow can resemble any of the blast types of AML-NOS (Not Otherwise Specified), especially AML without maturation or Acute Myelomonocytic Leukemia or Acute Megakaryoblastic Leukemia. However a subset of cases may have blasts percentage less than 20% at the time of diagnosis especially in cases mimicking Chronic Myelomonocytic Leukemia. Dysplasia of megakaryocytes, erythroids and neutrophils is a common finding. The marrow eosinophils, basophils or mast cells may be increased. The blast cells generally express CD13, CD33, HLA-DR, CD34 and CD38. Some cases can show an aberrant expression of CD7. A subset of cases may express megakaryocytic markers such as CD41 and CD61. Patients with CML who may acquire inv(3)

(q21q26.2) or t(3;3)(q21;q26.2) are best considered as aggressive phases of chronic myelogenous leukemia, rather than AML with inv(3)(q21q26.2) or t(3;3)(q21;q26.2). AML with inv(3) or t(3;3) is an aggressive disease with short term survival.<sup>4,5,6</sup>

## Conclusion

The inv(3) or t(3;3) is found in ~1% of cytogenetically abnormal AMLs, with the inversion being twice as common as translocation. The prognosis of t(3;3)/inv(3) positive AML is universally poor, with minimal or no response to chemotherapy and very few long term survivors. AML with inv(3) or t(3;3) can present with a spectrum of presentations including that of CMML. Cases with inv(3) or t(3;3) and less than 20 % blasts must therefore be examined closely for the development of a more definite evidence of AML.

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