Received: 17 May 2019 | Revised: 2 June 2019 | Accepted: 3 June 2019

DOI: 10.1002/jcla.22961

CASE REPORT

WILEY

Chronic myeloid leukemia blast crisis presented with AML of t(9;22) and t(3;14) mimicking acute lymphocytic leukemia

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Abstract

Background: Clinically, 90%-95% of cases of CML have the characteristic t(9;22)(q34.1;q11.2) translocation that leads to the Philadelphia (Ph) chromosome. Rarely, patients with CML can present directly in a blast crisis (BC). While most blast crises are of myeloid origin, myeloid BC with ALL-like morphologic features and Ph-positive acute myeloid leukemia (AML) is rare, especially at the time of CML diagnosis.

Case presentation: A 20-year-old man presented with Ph chromosome-positive AML mimicking acute lymphocytic leukemia (ALL). Bone marrow (BM) aspiration revealed AML with ALL-like morphologic features. The results of the immunophenotypic analysis suggested AML. Cytogenetic analysis of the BM cells revealed a 46,XY,t(3;14)(q21;q32),t(9;22)(q34;q11.2)[20] karyotype. Thus, we called the condition AML mimicking ALL. The patient was diagnosed with myeloid BC based on the combination of clinical, cytologic, and cytogenetic studies.

Conclusion: To date, no case reports of a patient diagnosed with CML BC presented with Ph chromosome-positive AML mimicking ALL have been reported. We present the case given its rarity, easy misdiagnosis, and poor prognosis. It is important to combine clinical, cytologic, and cytogenetic analyses in distinguishing CML BC from de novo AML with the t(9;22), and further cases should be accumulated to explore how to improve the prognosis of the patients.

KEYWORDS

blast crisis, chronic myeloid leukemia, cytogenetic analysis, cytologic analysis

1 | BACKGROUND

Tumor biology and molecular genetic techniques have broadened our knowledge of genetic variation in cancers[1,2] such as CML—for example, Ph translocation t(9;22)(q34;q11), which is considered to be a diagnostic and prognostic biomarker in CML. Clinically, 90%-95% of cases of CML have the characteristic t(9;22) (q34.1; q11.2) translocation that leads to the Ph chromosome. In addition, 20% and 2% of adult patients with ALL and AML have the exactly same cytogenetic marker, respectively.[3] AML is a heterogeneous disorder resulted from clonal multiplication of malignant myeloid precursors which were blocked differentiation in these cells, and it is the most common AL in adults, which is heterogeneous in the aspects of morphological, clinical, and cytogenetic features. Certain cytogenetic aberrations can be conducive to estimate AML subtypes and judge their reaction to treatment.[4] Roughly, 10%-12% of CML patients show additional chromosomal aberrations (ACAs) in chronic phase and blast crisis. ACAs, especially when complex, present to be a biomarker of CML evolution, and ACAs can be a important clue

in treatment strategies.[5] Rarely, patients with CML can present directly in a blast crisis. While most blast crises are of myeloid origin, myeloid blast crisis with ALL-like morphologic features and Ph-positive AML is rare, especially at the time of CML diagnosis.[6,7] This is the first case of CML blast crisis presented with AML of t(9;22) and t(3;14) double translocation mimicking ALL. Clinical features were more suggestive of CML in myeloid blast crisis than de novo AML with the t(9;22). Further careful observation is required for clinical, cytologic, and cytogenetic changes during disease development.

2 | CASE PRESENTATION

A 20-year-old man sought medical attention on March 26, 2019, with a 4-month history of fever and abdominal distension. Obvious splenomegaly was detected by palpation and computed tomography. Laboratory findings were as follows: White blood cell count was 175.87 × 10^9/L, red blood cell count was 1.76 × 10^{12}/L, hemoglobin was 98 g/L, platelet count was 107 × 10^9/L, serum lactate dehydrogenase was 545 U/L (normal value 15-220 U/L), and human immunodeficiency virus was negative. Peripheral blood smear revealed approximately 92% blast cells (Figure 1A). Subsequently, BM aspirate revealed the blasts accounted for 97% of all nucleated cells (Figure 1B). The blasts were negative for myeloperoxidase (MPO; Figure 1C). The blasts were supported with ALL-like morphologic and primary cytochemical staining features. Flow cytometry immunophenotyping revealed the abnormal cell population with 92.91% of nucleated cells. The cell population was positive for HLA-DR, CD13, CD33, CD34, and CD38; a few cells expressed CD10 and CD117; and a very few cells expressed CD36. The results of the immunophenotypic analysis suggested AML. The diagnose according to the FAB criteria was AML-M0.[8] A cytogenetic study revealed that bone marrow cells were 46,XY,t(3;14)(q21;q32),t(9;22)(q34;q11.2)[20] karyotype in all twenty examined cells (Figure 2), and BCR/ABL p210 fusion gene was positive using fluorescence PCR method. Clinical features of the patient were more suggestive of CML in myeloid blast crisis than de novo AML with the t(9;22). We started treatment with cytarabine, homoharringtonine, and imatinib mesylate after the diagnosis was established. The splenomegaly obviously shrank, peripheral blood smears showed blasts decreased to 10%, and eosinophilia and basophilia were easy to be seen after 26 days of combination chemotherapy. (Figure 1D) Unfortunately, we had to stop imatinib mesylate due to agranulocytosis and infection. After anti-infection treatment, although white blood cells gradually increased, the spleen enlarged simultaneously. Unfortunately, the patient refused combination chemotherapy again and was discharged on request due to his family's financial status. He was administered orally imatinib (400 mg/d) at home. However, the patient came back again due to uncontrollable fever one month after discharge, peripheral blood smears of the patient indicated 90% blast cells, and the disease gradually became difficult to control.

3 | DISCUSSION

Tumor biology and molecular genetic techniques have broaden our knowledge of genetic variation in cancers such as CML—for example, Ph translocation t(9;22)(q34;q11), which is considered to be a diagnostic and prognostic biomarker in CML. Patients should be evaluated for Ph and BCR/ABL p210 fusion gene before chemotherapy, and it is precious to trace these mutations in the therapeutic process. BCR-ABL fusion protein in CML activates tyrosine kinase, which leads to maintenance of the malignant phenotype. Imatinib, which is a selective inhibitor of BCR-ABL, induces major cytogenetic remission (MCR) or complete cytogenetic remission (CCR) in the most CML patients during first chronic phase (CP). CML develops from a CP, which is characterized by the Ph as the only cytogenetic abnormality, is always related to ACAs.[9]

Most patients with BC show multiple mutations, and more than 80% show ACAs in addition to the Ph chromosome in a form of nonrandom. Tyrosine kinase inhibitors have proved to improve survival of BC patient. The most frequent abnormalities are trisomy 8, 19, extra copy of Ph chromosome and isochromosome 17q. Less common aberrations are monosomy 7, 17, deletion of Y chromosome; trisomy 17 and 21, and t(3;21)(q26;q22) translocation.[9] The appearance of ACAs during blast crisis has been reported by several authors. Patel B B et al[10] described two patients presented with myeloid blast crisis (MBC) with clonal evolution affecting 16q22 (t(16;16)(p13;q22) and inv(16)(p13;q22), usually found in de novo AML, and both patients showed obvious extramedullary disease and had poor prognosis. Yafei Yin et al[11] reported a case of CML presenting with MBC with trisomy 8 and t(10;12;11)(q24;p13;q13), and he failed to achieve the second remission. However, the influence of t(3;14)(q21;q32) on prognosis of CML-MBC is unclear, due to rarity of ACAs reported in CML patients. Based on the poor prognosis of our patient, it seems that ACAs may not carry favorable outcome to CML BC patients.

At present, BC is still a challenge in the treatment of CML. Conventional chemotherapy does not work well to the majority of BC patients, and long-term survival has not been achieved by treatment with tyrosine kinase inhibitor alone. The treatment goal of CML BC is the return to CP or the induction of a remission. Mainstays are TKIs giving consideration to the type of mutation and allo-SCT as quickly as possible. If TKIs alone are not adequate, AL-type induction therapy should be tried, cytosine arabinoside and anthracyclines in myeloid BC, vincristine and prednisone for lymphoid BC, or TKI in combination with AL-type induction chemotherapy, and therapy decisions should take the individual patients' situations into account.[12]

Of course no single clinical or hematologic feature differentiates CML blast crisis from Ph-positive AML in an individual patient. However, we herein describe a young man presented with Ph chromosome-positive AML mimicking ALL. Regarding the disease, our patients showed obvious splenomegaly at the first visit to our hospital, Ph chromosome and BCR/ABL 210 fusion gene positive revealed by cytogenetic and gene expression analysis. Furthermore, certain clinical, cytomorphological features of CML were observed

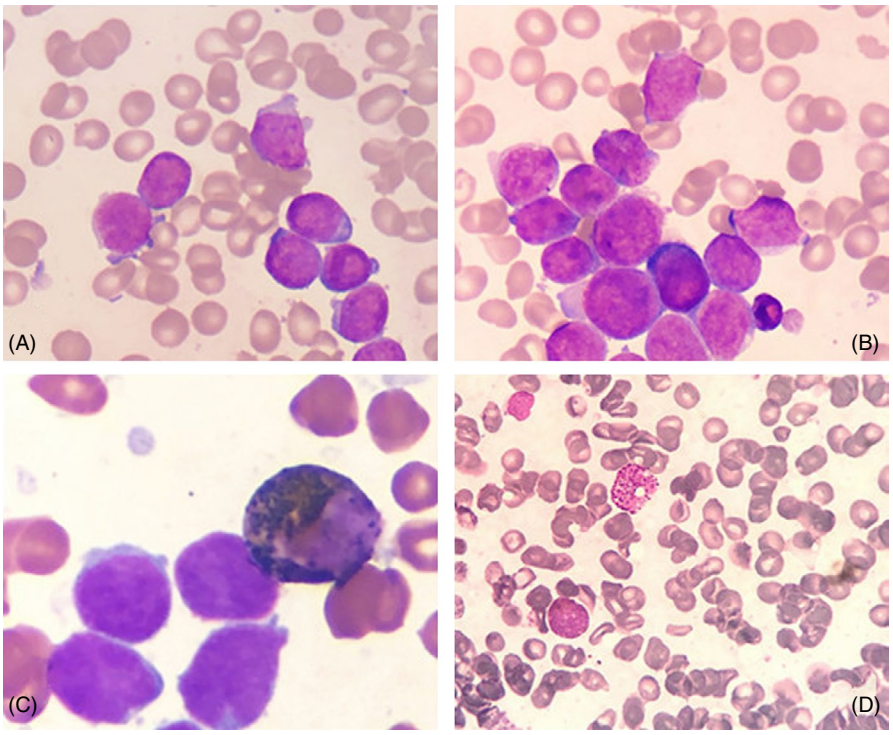

FIGURE 1 A, Peripheral blood smear revealed approximately 92% blast cells. (Wright-Giemsa,×1000). B, BM aspirate revealed the blasts accounted for 97% of all nucleated cells. (Wright-Giemsa,×1000). C, The blasts were negative for myeloperoxidase. (MPO, ×1000). D, Peripheral blood smears showed eosinophilia and basophilia were easy to be seen when the patient responded to induction therapy. (Wright-Giemsa, ×1000)

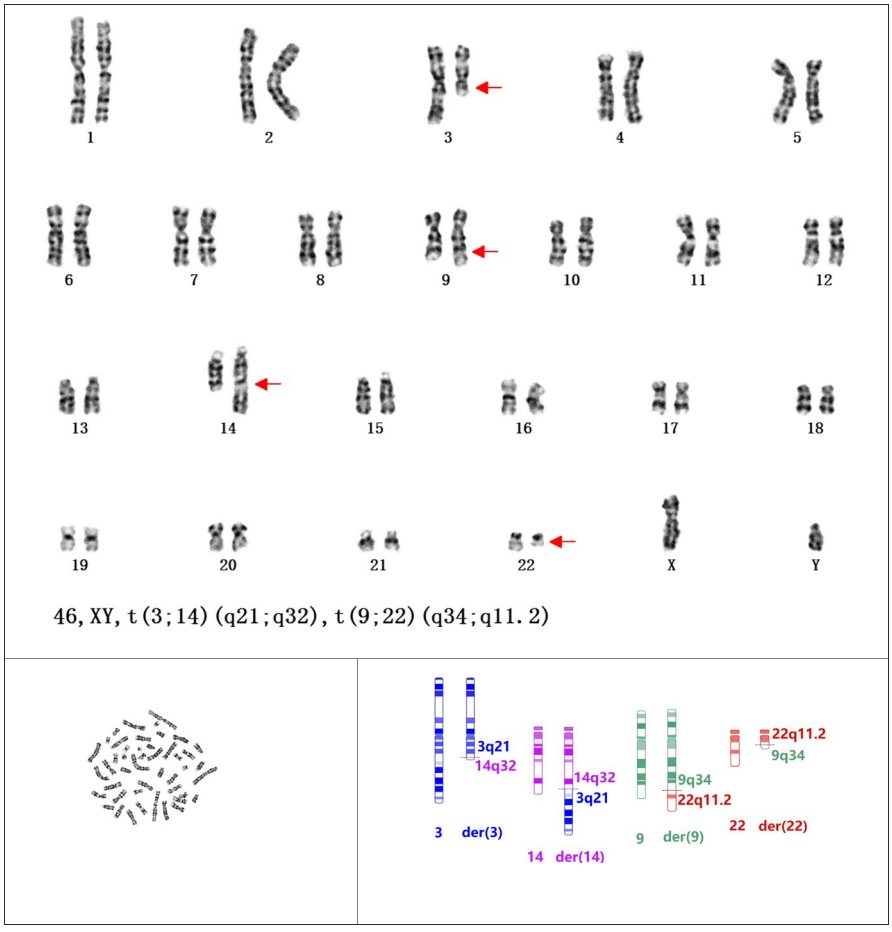

FIGURE 2 A cytogenetic study revealed that bone marrow cells were 46,XY,t(3;14)(q21;q32),t(9;22)(q34;q11.2)[20] karyotype in all twenty examined cells

in the patient when he responded to induction therapy. The splenomegaly obviously shrank, blasts decreased markedly, and eosinophilia and basophilia of peripheral blood smear were easy to be seen after combination chemotherapy; The spleen of the patient enlarged again after stopping imatinib mesylate. In addition, ACAs commonly observed in CML-MBC at the cytogenetic level, and the patient in

our study presented with AML of t(9;22) and t(3;14). These findings confirmed that these myeloid primitive cells originated from chronic myeloid leukemia clone. We presumed that our patients suffered from undetected chronic phase CML.

4 | CONCLUSION

In conclusion, this is the first case of CML BC presented with AML of t(9;22) and t(3;14) mimicking ALL. The case shows it is vital to combine clinical, cytologic, and cytogenetic analysis in distinguishing CML BC from de novo AML with the t(9;22).

CONFLICT OF INTEREST

The authors declare that there are no conflicts of interest.

AUTHORS CONTRIBUTIONS

Keyu liu wrote the article. Jintian hu, Xueqing wang, and Lili contributed to patient's diagnosis. Keyu liu and Li li contributed to revision of the initial manuscript and final approval.

ETHICAL APPROVAL

Informed consent has been obtained by the authors.

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How to cite this article: Liu K, Hu J, Wang X, Li L. Chronic myeloid leukemia blast crisis presented with AML of t(9;22) and t(3;14) mimicking acute lymphocytic leukemia. *J Clin Lab Anal*. 2019;33:e22961. https://doi.org/10.1002/jcla.22961