The First Case of Decitabine Successfully in Treatment of Atypical Chronic Myeloid Leukemia with CEBPA Double Mutation

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Abstract

**Background:** Atypical chronic myeloid leukemia (aCML) treated with decitabine is never reported.

**Methods:** We admitted a 69-year-old man with splenomegaly, hyperleucocytosis, thrombocytopenia and anemia, then morphology, immunology, cytogenetics and molecular biology analysis of bone marrow were performed and the diagnosis of aCML was made. The patient was initially treated with decitabine chemotherapy (20 mg/m²×5 days). The patient achieved complete hematology and morphologic remission after three cycle’s treatment.

**Results:** The data demonstrated that the diagnosis was aCML, which may be misdiagnosed easily. The patient responded very well to decitabine.

**Conclusion:** This case provides evidence that decitabine is effective for therapy in aCML, and demonstrated a new safety and efficacy strategy in the management of other myeloproliferative diseases.

Introduction

Atypical chronic myelogenous leukemia, aCML is a subtype of myelodysplastic/myeloproliferative diseases (myelodysplastic/chronic myeloproliferative syndromes, MDS/MPN), it occurs in the elderly, the incidence rate about 1/100,000, or less [1]. In brief, aCML is characterized by peripheral leukocytosis, circulating immature granulocytes, obvious abnormalities, and abnormal clone cells without Ph chromosome and bcr/abl fusion gene [2]. Overall, aCML is generally associated with poor outcome, and no special drug has so far proved to be effective in this disorder. In this report we summarize our experience with decitabine (5-aza-2-deoxycytidine) in a patient diagnosed with aCML.

Case Report

We admitted a 69-year-old man for anorexia, fatigue and shortness of breath for three months and dizzy ten days. Physical examination revealed pallor and mild splenomegaly and needle-like shortness of breath for three months and dizzy ten days. Physical examination revealed pallor and mild splenomegaly and needle-like shortness of breath for three months and dizzy ten days. Blood count returned to normal level, bone marrow showed no blast and dysplasia cells after three cycles of therapy (Figure 1).

Discussion

An aCML is a syndrome of abnormal chromatin clumping. Peripheral blood smears showing leukocytosis, immature granulocytes, and neutrophils with abnormal condensation of the nuclear chromatin. The 2008 WHO diagnostic criteria for aCML [3] is basically a neutrophilic leukocytosis with dysgranulopoiesis and circulating immature granulocytes, and its diagnosis relies on: 1) Peripheral blood leukocytosis (WBC ≥ 13×10⁹/L) due to increased number of neutrophils and their precursors, with prominent dysgranulopoiesis. 2) No Philadelphia chromosome or BCR-ABL fusion gene. 3) No rearrangement of PDGFRα or PDGFRβ. 4) Neutrophil precursors promyelocytes, myelocytes, metamyelocytes are 10% of WBCs. 5) Minimal absolute basophilia; basophils usually 2% of the WBCs. 6) No or minimal absolute monocytes; monocytes are 10% of WBCs. 7) Hypercellular BM with granulocytic proliferation and granulocytic dysplasia, with or without dysplasia in the erythroid and megakaryocytic lineages. 8) 20% blasts in blood and/or BM. This patient meets the aCML diagnostic criteria. He has mild splenomegaly and normal chromosomes, negative BCR-ABL fusion gene, peripheral blood monocytes <1.0×10⁹/L, immature neutrophils in the bone marrow is 44.5%, therefore, it can be excluded the diagnosis of Chronic Myelogenous Leukemia (CML), Chronic Myelogenous Leukemia (CML) and chronic neutrophilic leukemia (CNL). So the diagnosis of aCML was correct.

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Received June 27, 2013; Accepted July 07, 2013; Published July 11, 2013


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Until recently, the most common karyotypic changes reported in aCML include trisomy 8 and del (20q), abnormalities involving other chromosomes such as 12, 13, 14, 17, 19 and 21 have also been described [4,5] but no specific chromosomal changes correlations with disease features were found in aCML patients. Many gene mutations have been found in aCML, such as, NRAS /KRAS (33% patients), TET2 (33% patients) CBL (10% patients), E2H2 (13% patients) and SETBP1 (25% patients) and so on [6-9], some of which are associated with poor prognosis, but CEBPA double mutations has not been reported in aCML. In this case, the patient has normal chromosome and CEBPA double mutations, and may suggest that the CEBPA double mutations also is one molecular biology feature and associated with

![Figure 1: The level of leukocyte hemoglobin and Platelet after decitabine treatment.](image-url)
good prognosis in aCML as some as in acute myeloid leukemia patients [10,11].

aCML patients showed poor prognosis when treated with conventional chemotherapy, the median survival is only 24 to 25 months [12,13]. A retrospective study in MD Anderson Cancer Center [12] found that: Age (>65 years), anemia (hemoglobin<10 g/dl), white blood cell count (WBC>50×10^9/L) are three independent factors in aCML. Kolhoff [14] confirmed that allogeneic hematopoietic stem cell transplantation (HSCT) evaluated the outcome of aCML, but most aCML patients are not suitable for HSCT for their media age >60 years [13].

Decitabine is a hypomethylating agent that can reverse the DNA methylation process and induce tumor cells differentiation or apoptosis of tumor cells to normal cells [15]. In recent years, decitabine is widely used in MDS patients, and achieved good results. A phase II study demonstrates that the response rate in the 177 patients evaluated (median age 70 years) was 49% [16]. Patients with high-risk cytogenetic abnormalities according to the IPSS risk criteria showed better overall survival than those with intermediate-risk abnormalities and a rather low toxicity profile in elderly patient group. In our case, the patient were 69 years old and not suitable for bone marrow transplantation, and then accepted chemotherapy with decitabine (20 mg/m^2× 5 days). He obtained complete hematology and morphologic remission after three cycles of decitabine. An aCML has both myeloproliferative and myelodysplastic disorders characters, which maybe result in the effective treatment with decitabine.

In conclusion, aCML is difficult to distinguish from CML, CNL and CMML, which is easy to misdiagnosis clinically. Our study suggests that the CEBPA double mutations may be associated with good prognosis in aCML. Decitabine shows obvious clinical efficacy in treatment of aCML, especially for those elder people without the chance of bone marrow transplantation, and demonstrated a new safety and efficacy strategy in the management of other myeloproliferative diseases.

Acknowledgments

This work was supported by Science Research Foundation of Health department of zhejiang province (Grant #2011KYA0540 and Grant #2013KYA083), National Natural Science Foundation of China (Grant # 81101792), Science Research Foundation of Chinese traditional medicine of Zhejiang Province (Grant #2011ZB064 and 2013ZA074) and Research Fund for the Doctoral Program of Higher Education of China (Grant #201101120105).

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