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Case Series

Two Chronic Myeloid Leukemia Patients Presenting with Isolated Thrombocytosis

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Abstract

Chronic myeloid leukemia (CML) usually present with high leukocyte counts and splenomegaly and isolated thrombocytosis is not a common condition in CML. We present two CML patients presenting with isolated thrombocytosis. ***Case 1:*** A 44-year-old male patient having isolated thrombocytosis with no additional features, was investigated with the suspicion of essential thrombocythemia (ET). However, he was found to be positive for BCR/ABL. Afterwords, imatinib with the dosage of 400 mg/day was started and a major molecular response was obtained. ***Case 2:*** A 74-year-old woman was referred to our outpatient clinic because of thrombocytosis. Her physical examination was normal without splenomegaly. Further investigations were planned with the doubt of ET, but the patient's BCR/ABL was positive. She was started imatinib and a major molecular response was obtained. In these cases, we explored the presence of BCR/ABL and found that they were positive. In conclusion, screening for BCR/ABL has a substantial significance in patients with isolated thrombocytosis and not exhibiting CML findings, to provide an effective therapeutic approach for these patients.

Keywords: ***CML, Ph Chromosome, BCR / ABL, Thrombocytosis, Imatinib***

Introduction

Chronic myeloid leukemia (CML), which is a clonal stem cell disease, usually presents with splenomegaly and high leukocyte counts caused by mature myeloid hyperplasia in the bone marrow. Philadelphia chromosome (Ph), generated by the t(9;22), is detected by cytogenetic examination in CML patients. This translocation leads to the fusion of the Abelson oncogene (ABL) from chromosome 9q34 with the breakpoint cluster region (BCR) on chromosome 22q11.2, t(9;22)(q34;q11.2) and actually produces BCR/ABL oncogene [1].

Essential thrombocythemia (ET) is also a clonal bone marrow disease in the group of BCR/ABL negative chronic myeloproliferative diseases (CMPDs). In about half of ET patients, the janus kinase (JAK) 2V617F mutation is detected and a minority of the patients have calreticulin (CALR), myeloproliferative leukemia virus oncogene (MPL) and other mutations. While thrombocytosis is the prominent feature of ET [2], it is not a common condition in CML.

Here, we present two CML patients presenting with isolated thrombocytosis.

Cases

Our first case was a 44-year-old male patient. During his routine control, his blood count was found to be as follows: White blood cell (WBC): 4.86 x 10^9/ L, neutrophil: 3.47 x10^9/ L, hemoglobin: 14 g/ dL, platelet: 1,189 x10^9/ L. His physical examination revealed no remarkable findings. Further investigations were planned with the suspicion of ET. However, he was found to be positive for Ph chromosome after the cytogenetic examination of the bone marrow. Afterwords, imatinib with the dosage of 400 mg/day was started and a major molecular response was obtained.

Our second case was a 74-year-old woman. She was referred to our outpatient clinic because of thrombocytosis. Her physical examination was normal without splenomegaly. The complete blood count was as follows; WBC: 9.18 10^9/ L, neutrophil: 5.47 10^9/ L, hemoglobin: 11.5 g/ dL and platelet: 1,822 x10^9/ L. Further investigations were planned with the doubt of ET. She was given hydroxyurea till the cytogenetic and molecular results were obtained. The patient's BCR/ABL was positive, thus hydroxyurea was ceased and imatinib was started with a dosage of 400 mg. Due to the cytopenia under imatinib 400 mg/day, the dosage of was declined to 300 mg and a major molecular response was obtained with imatinib 300 mg/day treatment.

Discussion

Chronic myeloproliferative diseases are conventionally categorized as BCR/ABL positive and BCR/ABL negative CMPDs [3]. While BCR/ABL negative CMPDs include polycythemia vera (PV), primary myelofibrosis (PMF) and ET, CML is the only member of

BCR/ABL positive CMPD [3]. Although ET is among the BCR/ABL negative CMPD group, Michielis et al. introduced a term called as Ph (+) ET which is characterized by increased small mononuclear megakaryocytes in the bone marrow smears and biopsies, in addition to thrombocytosis. Besides, there is no finding of CML regarding the peripheral blood smear and physical examination in Ph (+) positive ET patients. Moreover, microvascular or hemorrhagic complications are not observed in those patients different from both classical ET and CML [9,10]. Differently, the World Health Organization (WHO) assumes the BCR/ABL positive isolated thrombocytosis as CML, not ET [11]. This classification is concordant with Hannover Bone Marrow Classification who divided BCR/ABL positive CML into three separate groups as; CML- common type (CML-CT), CML-megakaryocyte-increased (CML-MI) and CML-megakaryocyte predominant (CML-MP) [11]. And BCR/ABL positive ET can be defined as a CML subtype as CML-MP. This classification seems to be more appropriate considering that the patients with isolated thrombosytosis and BCR/ABL positivity should be treated with tyrosine kinase inhibitors (TKIs). According to the WHO classification, exclusion of other myeloid neoplasms is mandatory for the diagnosis of ET [12]. Therefore, search for BCR/ABL is required in ET patients [12]. And our cases emphasize the significance of this criteria.

In these cases, we explored the presence of BCR/ABL and found that they were positive. Hence, they were treated with a TKI instead of hydroxyurea and major molecular reponse was obtained in two patients in the early period. Certainly, screening for BCR/ABL should not be omitted in patients with isolated thrombocytosis and not exhibiting CML findings such as splenomegaly and leukocytosis, to provide an effective therapeutic approach for these patients.

Abbreviations

CML: Chronic Myeloid Leukemia
ET: Essential Thrombocythemia
Ph: Philadelphia Chromosome
BCR: Breakpoint Cluster Region
ABL: Abelson Oncogene
CMPD: Chronic Myeloproliferative Diseases
JAK: Janus Kinase
MPL: Myeloproliferative Leukemia Virus Oncogene
CALR: Calreticulin
WBC: White Blood Cell
PV: Polycythemia Vera
PMF: Primary Myelofibrosis
CML-CT: CML- Common Type
CML-MI: CML-Megakaryocyte-Increased
CML-MP: CML-Megakaryocyte Predominant
TKI: Tyrosine Kinase Inhibitors

Declarations

Ethics Approval and Consent to Participate

Informed consents were obtained from our patients to publish the presentation.

Availability of Data and Material

Data are included in this published article and its additional file.

Competing Interests

The authors declare that they have no competing interests.

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Author Contributions

All authors contributed to the editing of the manuscript. IS wrote the manuscript and made the accompany-ing pictures.

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