A Case of Chronic Myelogenous Leukemia Occurring in a Patient CALR positive Essential Thrombocythemia

Ahmad Khalil [1,2], Dany Abi Gerges [1], Jessy Al Chidaic [1,2], Kamal Al Zahran [1], Ahmad Ibrahim [1,2]

1 Middle East Institute of Health - University Hospital, Bsalim, Lebanon
2 Lebanese University, Faculty of Medicine, Beirut, Lebanon

On September the 11th 2019, the Middle East Institute of Health - University Hospital -Lebanon, presented a case of Chronic Myelogenous Leukemia occurring in a patient CALR Positive Essential Thrombocytopenia. This is the seventh reported case in the world and was presented by our expert doctors from Lebanon at the Society Of Hematology Oncology, SOHO 2019 Houston - USA.

Introduction

Chronic myeloproliferative disorders (MPDs) include polycythemia Vera (PV), primary myelofibrosis (PMF), and Essential Thrombocythemia (ET) [1]. Chronic myeloid leukemia (CML) is a myeloproliferative neoplasm with an incidence of 1–2 cases per 100 000 adults and it is characterized by a balanced genetic translocation, t (9; 22) (q34; q11.2), involving a fusion of the Abelson gene (ABL1) from chromosome 9q34 with the breakpoint cluster region (BCR) gene on chromosome 22q11.2 [2].

In Essential Thrombocythemia (ET), 50% to 65% of the patients carry the JAK2 V617F mutation, whereas only 5% of patients carry MPL exon 10 mutations. More recently, CALR exon 9 mutations were identified in 20% to 25% of ET patients [3], and it affects relatively young individuals and is characterized by markedly elevated platelet count but relatively low thrombotic risk and no progression to polycythemia Vera [4].

Case Presentation

• A 53 year-old woman presented in April 7, 2017 for generalized fatigue and weakness, the general workup showed high WBC 360.000/µl, neutrophil 40%, hemoglobin 9.1g//dl with MCV 87 fl and platelets count 1.565.000/µl, Karyotype 46, XX, t (9; 22)(q23;q11), PCR BCR-ABL positive with b3a2 transcription (p210), jak-2 mutation negative and echo abdomen showed homogenous splenomegaly 17 to 18 cm, bone marrow biopsy showed bone marrow infiltration by atypical elements relevant to CML.

• She's diagnosed with Ph. Positive CML high risk EUTOS score (201), and she started treatment with Nilotinib 300 mg twice daily, one month after treatment, the WBC and platelet count decreased to normal value (figure 1) and 3 months after treatment, PCR BCR-ABL decreased to less than 1 %, but after this, the platelet count increased to more than 1.000.000/µl (figure 1). In review of old file we found one complete blood and platelet count done in November 2013 that showed WBC 9290/µl with neutrophil 58%, hemoglobin 12.5g/dl and platelet Count 1.967.000/µl but this blood test neglected and no follow up was done.

Figure1. Platelet count after starting Nilotinib

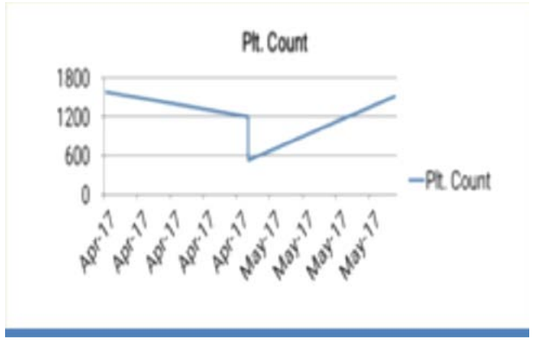

Table1. Previously reported cases of ET with transformation CML [1]

No.	Age/ sex	JAK-2 V617F	Initial Treatment For the CMPD	Transformation To CML (years)	Response To CML treatment
1	58/F	ND	HU	18	CCyR
2	65/F	ND	HU	6	PCyR
3	73/M	ND	HU	12	PCyR
4	38/F	ND	Aspirin	13	CCyR
5	82/M	ND	HU	9	CCyR
6	49/F	ND	Aspirin	7	CCyR

• We continue in workup for ET, MPL mutation was negative, CALR mutation was positive.

• The treatment continued with Nilotinib and Hydroxyurea with decreased of platelet count to less than 1.000.0000/

Discussion

This case report describes a case of ET and BCR-ABL positive CML and high probability of ET with transformation into CML. Patients with ET commonly transform into PMF and AML, but the emergence of CML is rare. To our knowledge, only six previous cases of this association have been reported in the literature [1] (Table1). The patient described in the present case report continues to have ET, while CML is in remission, indicating a persistence of an ET clone. In this case, we can't know if ET transformed to CML because the diagnoses of ET was retrospectively.
On the emergence of CML, previously reported cases used treatment with imatinib mesylate (in four cases) and interferon-alpha (in one case). Although patient in fifth and six case started therapy with a second-generation tyrosine kinase inhibitor (TKI), Nilotinib, the adverse events resulted in her being switched to Imatinib in contrast to our case that stayed on Nilotinib.

Conclusion

• A case of the rare association between Essential Thrombocythemia (ET) and the progression to chronic myelogenous leukemia (CML) has been reported with the expression of the BCR-ABL gene.
• Only six previous cases have been identified in the literature and this rare case highlights the importance of cytogenetic testing in cases of chronic myeloproliferative disorders (MPDs) that transform to CML, not only to confirm the diagnosis but to plan treatment, as Philadelphia chromosome-positive and -negative cases differ in their management.

References

1. A case of Chronic Myelogenous Leukemia occurring in patient treated for Essential Thrombocythemia; American journal of cases report 2019.
2. Chronic myeloid leukemia: 2018 update on diagnosis, therapy and monitoring; ASH 2017.
3. CALR-positive myeloproliferative disorder in a patient with Ph-positive chronic myeloid leukemia in durable treatment-free remission: a case report; Stem Cell investigation 2018.
4. JAK2 or CALR mutation status defines subtypes of essential thrombocythemia with substantially different clinical course and outcomes; Blood 2014