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LETTER TO THE EDITOR

Possibility of transformation of primary myelofibrosis to ALL without JAK2V617F mutation

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To the editor,

In this letter, we wish to point out the possibility of transformation of myelofibrosis in acute lymphocytic leukemia without the presence of JAK2V617F mutation.

Myeloproliferative neoplasms (MPN) are hematologic malignant diseases characterized by a clonal proliferation of one or several lineages [1]. They represent a phenotypically diverse group of chronic myeloid malignancies that are characterized by the presence of clonal hematopoiesis and an excessive production of terminally differentiated myeloid blood cells. Typically, they include four main clinical entities: polycythemia vera (PV), essential thrombocythemia (ET), primary myelofibrosis (PMF), and chronic myeloid leukemia (CML). PV, ET, and PMF are usually subcategorized as bcr-abl-negative MPN. However, sporadic cases of bcr-abl-positive patients with transformation of primary myelofibrosis were reported but without JAK2V617F mutation [2].

The prevalence of JAK2V617F mutation [3] differs between various variants of MF with the higher detection rate for patients with post-PV MF (91 %) if compared to PMF (45 %) and post-ET MF (39 %). Some works emphasize the importance of the predictive role of JAK2V617F mutation for this transformation. JAK2V617F mutation is also discussed in myeloproliferative disease and primary myelofibrosis as well, in respect to clinical prognosis and transformation [4, 5]. The JAK2V617F mutation was reported to found positive in 7 out of 17 (64 %) analyzed patients with PMF and with transformation to leukemia. The risk of transformation to acute leukemia in investigated patients was around 31 % in JAK-2 positive, but several studies also indicated possibility of transformation in JAK-2-negative PMF. However, majority of patients were transformed to acute myeloid leukemia. We previously reported possibility of transformation of PMF to acute lymphocytic leukemia (ALL) [2] and only an additional case in literature reported transformation of refractory anemia with ring sideroblasts (RARS) to ALL [4] with 20q- cytogenetic. Patients with PV had also possibility to transform to PMF, frequently regarding to JAK-2 mutation. However, no difference in the frequency of transformation PV patients to acute myeloid leukemia was observed between the JAK2 positive and JAK2 negative [4].

Here, we want to emphasize the possibility thatPMF can transform into ALL, probably regarding molecular disturbance in immature hematopoietic precursor cell. Briefly, we previously reported that patient with 20q- cytogenetic anomaly, which is usually a favorable cytogenetic prognostic factor, can transform to ALL with Philadelphia-positive finding, but without JAK2V617F mutation, and with fatal outcome after 10 months [2] pointing out the other factors that can lead to transformation of PMF into ALL.

Since leukemogenesis is a complex process caused by one or multiple gene alterations, which perturbs the regulation of development and maturation of the multipotent hemopoietic progenitor cells gradually leading to acute leukemia, here we want to point out that they may have other molecular and cytogenetic changes except JAK2V617F mutation, which can be important during transformation. We suggested the

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