Concurrent Presence Of JAK2 and BCR ABL Mutation In A Patient With Thrombocytosis and Intermittent Leukocytosis

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Introduction

Chronic myeloproliferative neoplasms (MPN) are clonal disorders of hematopoietic stem cells, which fall into distinct categories based on a number of characteristics including the presence of the BCR-ABL1 gene fusion (chronic myelogenous leukemia) or the JAK2(V617F) mutation (polycythemia vera, primary myelofibrosis, and essential thrombocythemia). We describe an interesting case of a patient with simultaneous presence of both mutations.

Initial Presentation

Patient had gallbladder removal in 2013, and CBD stone removal in 2015. Between 2018 to 2020 the patient had multiple hospitalizations for gram-negative bacteremia of unclear etiology. Each time the patient was admitted to the hospital, he was noted to have critically elevated leukocytosis (>50 k) and thrombocytosis. Even after resolution of his acute symptoms, he was found to have lingering leukocytosis with absolute neutrophilia, basophilia, monocytosis and thrombocytosis. This prompted an oncology work-up. Patient's initial work-up revealed JAK2V617 F mutation as well as low-levels of BCR ABL by PCR study on the same date. Presence of BCR/ABL 1 transcript was highly concerning for concurrent cell clone that could lead to CML. Patient's bone marrow biopsy findings were consistent with chronic myeloproliferative neoplasm and revealed positive JAK2 mutation but was negative for BCR/ABL.

To Treat or Not To Treat

Patient's case was reviewed with a hematologist and it was decided that patient should be treated for essential thrombocytosis and his BCR ABL levels should be checked at regular intervals to ensure that the level is not rising. Clinical course was unsure at that time as it was possible that the BCR ABL level would decrease, but it was also possible that patient would develop chronic myelogenous leukemia, which has very high potential to convert to acute leukemia. Our patient was not fortunate enough to survive long enough for us to determine his clinical course as he passed away from pancreatic carcinoma months after this interesting finding.

References

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Summary

Myeloproliferative neoplasms are characterized by chronic myelogenous leukemia which is characterized by BCR/ABL fusion and production of tyrosine kinase and JAK2(V617 F) point mutations are associated with polycythemia vera, prjmary myelofibrosis and essential thrombocytosis. The underlying geneteic abnormality was one of the criteria on which the WHO has based the classification for myeloproliferative neoplasms. The WHO does not currently address the classification of myeloproliferative neoplasms that have more than one genetic abnormality. The coexistence of a JAK2(V617F) mutation and BCR-ABL1 is rare, and to our knowledge, less than 25 cases have been reported in the literature. Some patients were found to have pre-existing JAK 2 mutation, while others showed simultaneous identification of both clones. In all the cases it is unclear whether the same clone was carrying both mutations or they originated independently from different susceptible polyclonal stem cells. It has also been hypothesized that maybe JAK2 can happen after treatment with tyrosine kinase inhibitor therapy but coexistence has been noted in the absence of TKI therapy as well. In one of the reported cases patient was successfully treated with dasatanib and has good cytogenetic and hematologic response most likely due to multi kinase activity of dasatanib.