Coexistent *BCR-ABL1* and JAK2 V617F: converting CML dwarves to ET staghorns with imatinib therapy

A 67-year-old man was noted to have new-onset leukocytosis (white blood cell [WBC] count, $13.1 \times 10^3/\mu L$) and thrombocytosis (platelets [PLT], $670,000/\mu L$). The peripheral blood smear revealed granulocytes at all stages of maturation. A bone marrow (BM) biopsy revealed hypercellularity with an elevated M:E ratio. Megakaryocytes were predominantly small and hypolobated (panel A). Molecular studies revealed a *BCR-ABL1* (e14a2) fusion transcript and a JAK2 V617F mutation. BM cytogenetics demonstrated t(9;22) in 19 of 20 metaphase cells. Six months after initiation of imatinib, the patient’s WBC count decreased ($5.5 \times 10^3/\mu L$) with a normal differential, but PLT increased to $809,000/\mu L$. Quantitative reverse-transcriptase polymerase chain reaction revealed a 2.4-log decrease in *BCR-ABL1* levels. BM cytogenetics demonstrated t(9;22) in only 2 of 20 cells. A qualitative allelic discrimination assay was once again positive for JAK2 V617F, with an impression that the mutant allelic burden had increased from pretreatment levels. The BM was normocellular with a normal M:E ratio. The megakaryocytes showed a predominance of hyperlobated “staghorn” forms often present in clusters (panel B). In essence, imatinib therapy for chronic myelogenous leukemia had hematologically and morphologically unmasked essential thrombocythemia.

The cooccurrence of *BCR-ABL1* translocation and JAK2 V617F mutations are very rare, with fewer than 50 cases reported in the literature. Clinical and morphologic phenotypes may resemble one myeloproliferative neoplasm (MPN) rather than the other, and in some cases patients do not display features of a JAK2 V617F–positive MPN until after treatment with imatinib. It is unclear whether the JAK2 and *BCR-ABL1* alterations exist in the same clone or in competing clones, though a few studies support both possibilities. In the present case, there was a decrease (from 95% to 10%) in the quantity of cells harboring t(9;22) after treatment. Conversely, there was an impression of an increase in the relative percentage of the mutated JAK2 allele. These findings argue for the presence of 2 separate clones (one CML, the other ET) in this case, rather than a common clone harboring both genetic aberrations.
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