Unbalanced rearrangement der(9;18)(p10;q10) in a patient with polycythemia vera

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Clinics

Age and sex
69 years old female patient.

Previous history
No preleukemia; no previous malignancy; no inborn condition of note.

Organomegaly
no hepatomegaly, splenomegaly, no enlarged lymph nodes, no central nervous system involvement (there was no apparent central nervous system involvement at diagnosis).

Blood

WBC: 15.2X 10^9/l
HB: 11.7g/dl
Platelets: 894X 10^9/l
Blasts: 0% peripheral
Bone marrow: 2% blasts

Immunophenotype
NA
Rearranged Ig Tcr
NA
Diagnosis
Polycythemia vera

Survival

Date of diagnosis: 03-2005
Treatment: Phlebotomy
Complete remission: NA
Treatment related death: no
Relapse: NA
Status: Alive. Last follow up: 03-2010
Survival: 62 months

Karyotype

Sample: Bone marrow biopsy Sep 17th 2009.
Culture time: analysis was performed on overnight colcemid and 24-hour cultures.
Banding: 400 band level.
Results:
46,XX,+9,der(9;18)(p10;q10)[11]/46,XX[9]
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Karyotype of a metaphase from the follow up specimen from September 2009 (four years after the initial diagnosis), 24-hour culture.

FISH confirmation for an extra copy of 9p.

Comments

We describe a new case of der(9;18)(p10;q10) detected in a patient with polycythemia vera (PV). This rare rearrangement has been reported in five cases of PV and one case of therapy associated acute myeloid leukemia (t-AML) after essential thrombocythemia (ET). Two of the five cases of PV showed progression from PV to post-polycythemic fibrosis, suggesting an association between this cytogenetic abnormality and disease progression.

The patient presented in this report was diagnosed with PV in 2005. Fluorescence In Situ Hybridization (FISH) testing for the BCR/ABL translocation was performed at diagnosis and was negative. Subsequent molecular analysis detected the presence of the JAK2 V617F mutation. The patient had a bone marrow biopsy in September of 2009, due to worsening anemia which was at that time attributed to excessive phlebotomy. Cytogenetic analysis showed the presence of the der(9;18)(p10;q10) in eleven out of twenty analyzed cells. At the later follow-up visit in February 2010, progression to the spent phase of PV was suspected, based on the worsening of the patient's clinical presentation. However, the next bone marrow biopsy from March 2010 only revealed mildly increased reticulin fibrosis. In summary, although the patient currently does not have pathohistological signs of progression, clinically she is exhibiting worsening of the disease.

Gain of function of the JAK2 gene at 9p24 has a crucial role in the pathogenesis of myeloproliferative neoplasms. It has been proposed that the der(9;18)(p10;q10) contributes to the pathogenesis of PV through the gain of 9p, leading to an extra copy of the JAK2 gene. For the patient presented in this report the clinical significance of the der(9;18)(p10;q10) cannot be fully interpreted due to the absence of the cytogenetic results at diagnosis. However, concurrence between the detection of this cytogenetic abnormality and worsening of the patient's symptoms suggests that the der(9;18)(p10;q10) may have been an early marker of the disease evolution.

Gain of 9p resulting from +i(9)(p10) has been reported in two cases of PV, further indicating this gain as a recurrent finding in PV. Our patient is known to carry the activating JAK2 V617F mutation. One can hypothesize that in combination with this mutation, gain of an extra copy of either the mutated or the normal JAK2 allele through formation of the der(9;18)(p10;q10) contributed to the progression of the patient's disease. Our report therefore further suggests the association between the unbalanced rearrangement der(9;18)(p10;q10) and an advanced stage of polycythemia vera.

References


This article should be referenced as such: