High Frequency of the JAK2 V617F Mutation
in Patients with Trisomy of Chromosome 9

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INTRODUCTION

The previous studies assessing the relationship of cytogenetic abnormalities to JAK2 status have not shown any significant associations, although numbers have generally been too small to make a definitive comment. We therefore assessed the JAK2 V617F mutation status of 337 patients from 39 centers (175 males, 161 females; median age at time of study 71 years old, range 32-98).

The JAK2 V617F mutation was found in 109/337 pts (32 %):
- typical MPD-Ph- (47 %) cases,
- MDS-Ph (4.5 %),
- 8q-syndrome (60 %),
- AML-Ph- (64 %),
- CMML (42 %),
- MDS/MPD (36 %)

Tab 1

A clonal cytogenetic abnormality was detected by R-banding in 159/337 cases (47 %).

The JAK2 mutation was associated with a chromosomal abnormality in 81/159 cases (51 %) Tab 2

RESULTS

The most common chromosome abnormality associated with JAK2 mutation was the gain of chromosome 9 (n=22, Associated with JAK2 mutation: 19/22 cases 86%)

Tab 2.

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The JAK2 V617F mutation was not found in the case of de novo AML, and 2 typical MDS cases Tab 4.

CONCLUSION

In this study the gain of chromosome 9 associated with JAK2 V617F mutation was the most frequent chromosome abnormality (100%) observed in typical MPDs and atypical syndrome such as AML/MPD.

In summary, previous studies assessing the relationship of cytogenetic abnormalities to JAK2 status did not show any significant association. The del(20q), del(13q), trisomy 8 and del(5q) are associated with JAK2 mutation.

The JAK2 mutation was associated with MDS/MPD-u (n=3, JAK2 mutated), secondary AML post MDS, n=1 (JAK2 mutated), atypical MPD, n=6 (100% JAK2 mutated), CMML, n=1(JAK2 mutated). The V617F mutation was not found in the case of de novo AML, and 2 typical MDS cases Tab 4.

9 males, 10 females, the median age: 68 years old, range 40-98 years old, median white cell count (WCC) 11 G/l, range 2.4-50.7 G/l (13/19 pts> 10G/l), median hemoglobin 13.5 g/dl, range 9-20.2 g/dl (5/19 pts> 17g/dl), median platelet count 667G/l range 9-1769 G/l (9/19 pts> 500 G/l). The BCR/ABL transcript (multiplex PCR) was not detected in all of these cases Tab 5.

The most common chromosome abnormality associated with JAK2 mutation was the gain of chromosome 9 (n=22, associated with JAK2 mutation: 19/22 cases 86%) Tab 2. The second most common abnormality was partial deletion of 20q (n=30, Associated with JAK2 mutation: 19/30 cases 63%), the partial or complete loss of chromosome 7 (n=16, Associated with JAK2 mutation: 6/11), deletion of 5q- (n=10, Associated with JAK2 mutation: 6/10), gain of chromosome 8 (n=11, Associated with JAK2 mutation: 7/11), partial deletion of 11q (n=8, Associated with JAK2 mutation: 5/8), partial deletion of 12p (n=6, Associated with JAK2 mutation 4/6), partial deletion of 13q (n=5, Associated with JAK2: 4/5) Tab 2.

Patients with trisomy 9 and JAK2 mutation were classified as follows: polycythemia vera (PV) n=4 (100% JAK2 mutated), essential thrombocythemia (ET) n=3 (100% JAK2 mutated), idiopathic myelofibrosis (IMF), n=2 (100% JAK2 mutated)

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In summary, previous studies assessing the relationship of cytogenetic abnormalities to JAK2 status did not show any significant association. The del(20q), del(13q), trisomy 8 and del(5q) are known to be recurring non-specific cytogenetic abnormalities, and some of them are also detectable in patients with JAK2 mutation positive or negative. We describe here a significant association between the JAK2 V617F mutation and trisomy of chromosome 9 that was detected in a cohort of patients with gain of chromosome 9. Clearly, in addition to JAK2, the JAK2 mutation was found in other disease entities, high frequency in the case of atypical MPDs particularly in the case of aCML. Previously, Campbell et al. reported 10 patients with a trisomy 9, in typical MPDs, all of them were V617F+. A longer follow-up and morphological diagnosis is however necessary to determine the prognostic significance of JAK2 mutation and +9 in the cases of classic myeloproliferative syndromes and atypical syndrome such as MDS/MPD overlap syndrome.

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