High frequency of MPL mutations among JAK2V617F-negative essential thrombocythemia and primary myelofibrosis selected by the presence of endogenous megakaryocytic colony

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Introduction and Aims:

- Spontaneous hematopoietic colony formation from bone marrow or peripheral blood is usually limited to the study of erythroid endogenous colony (EEC) in polycythemia vera according to the 2008 World Health Organization (WHO) classification.
- Endogenous megakaryocytic colony (EMC) growth, even if not included in WHO criteria, gives phenotypic argument for MPNs clonality especially in essential thrombocythemia (ET).
- This study aims to describe the current place of in vitro EMC in ET and primary myelofibrosis (PMF) in comparison to genetic abnormalities [JAK2V617F, mutations in the thrombopoietin receptor gene (MPL)].

A four-centre retrospective study:

- 190 Essential Thrombocythemia
- 15 Primary Myelofibrosis

Diagnosed between January 1st, 2007 and December 31st, 2010
According to 2008 WHO criteria or to British Committee for Standards in Haematology (BCSH)2 when bone marrow biopsy was not available

Clonogenic cultures (EEC and EMC) were assessed in peripheral blood and/or bone marrow using a standardized method.

JAK2V617F detected using ARMS-PCR (Amplification Refractory Mutation System).
MPL mutations detected using HRM (High Resolution Melt).

Materials and Methods:

Results:

In Primary Myelofibrosis

- JAK2V617F: 46.7%
- Culture (EEC and/or EMC): 40%
- Absence: 53.3%

No significant difference between JAK2V617F and culture results

In Essential Thrombocythemia

- JAK2V617F: 32.1%
- Culture (EEC and/or EMC): 67.9%
- Absence: 21.1%

Culture improves the diagnosis of ET
(Mac Nemar’s test, p<0.05)

In JAK2-negative PMF and ET

- Frequency of MPL mutations in selected population: 37.2%
- Usual frequencies of MPL mutations: 3% in ET and 10% in PMF

The association of EMC growth with the absence of JAK2 is interesting in selection of MPL mutant

Conclusions:

Endogenous megakaryocytic colony (EMC) growth, a useful parameter for the phenotypic and genotypic characterizations of MPNs:

- associated with EEC assays improved sensitivity of clonogenic cultures for the diagnosis of ET.
- serves as a predictive tool for the selection of MPL mutants among ET and PMF.

References: