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Secondary myelofibrosis in the natural history of JAK2, MPL and CALR mutated myeloproliferative neoplasms

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The WHO classification of the Myeloprolferative Neoplasms (MPN) distinguishes Essential Thrombocythemia (ET), Polycythemia Vera (PV) and Primary Myelofibrosis (PMF). Myelofibrosis (MF) is not a disease because reticulin and collagen fibrosis are produced by polyclonal fibroblasts in response to cytokines released from the clonal granulocytic and megakaryocytic progenitor cells in myeloproliferative disorders (MPD) in patients with ET and PV. The Hannover and Cologne Bone Marrow classification defined chronic or primary megakaryocytic granulocytic myeloproliferation (PMGM) as the third distinct prefibrotic MPN without features of PV. Vainchenker (2005) discovered the JAK2 V617F somatic mutation as the driver cause of ET, trilinear PV of erythrocytic, megakaryocytic and granulocytic myeloproliferation (EMGM) and myeloid neoplasia of the spleen with secondary MF. Prefibrotic JAK2 V617F mutated ET comprise three phenotypes: normocellular ET, ET with PV features in blood and bone marrow (prodromal PV) and hypercellular ET with predominant megakaryocytic granulocytic myeloproliferation (EMGM or masked PV) and moderate splenomegaly. JAK2 V617F mutated ET and PV are featured by medium sized to large (pleomorphic) megakaryocytes with only a few giant forms. JAK2 exon 12 mutated MPN usually present with idiopathic erythrocythemia or early PV. Bone marrow histology in MPL515 positive ET and MF show clustered small and giant megakaryocytes with hyperlobulated stag-horn like nuclei in a normocellular bone marrow with no features of PV already described in 1988 (Thiele). Bone marrow histology in prefibrotic CALR mutated ET and MF is associated with PMGM and dominated by dense clusters of large immature megakaryocytes with hypolobulated bulky (cloude-like) hyperchromatic nuclei, which are never seen in JAK2V617F, JAK2 exon 12 and MPL515 mutated MPN. Disease burden in JAK2, MPL and CALR mutated MPN is best reflected by the degree of anemia, splenomegaly, mutation allele burden, bone marrow cellularity and myelofibrosis.

Biography

J J Michiels is the founder of the Goodheart Institute & Foundation. He served as Assistant Professor to Professor of Nature Medicine at A. Kr. von dem Borne Department of Hematology, as a Consultant Scientist at Academic Medical Center Amsterdam during 1997-2000, as Consultant professor Hematology at Medical Diagnostic Center, Rijnmond Rotterdam 1998-2000. He is the Co-founder of Central European Vascular Forum: CEVF 2003 at University Hospital Antwerp, Belgium, Co-founder of European Society of Vascular Medicine: ESVM. He is also a founder of European Working Group on Myeloproliferatieve Disorders: EWG. MPD during 1999-2008 and European Working Group on Myeloproliferative Neoplasms: EWG.MPN. His research interests reflect in his wide range of publications in various national and international journals. He serves as a member of various associations apart from being Editorial board member of many reputed journals.

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