DOI: 10.7860/JCDR/2015/16407.6934

Letter to Editor

Pathology Section

The JAK2 V617F Mutation in Plasma Cell Neoplasms with Co-existing Erythrocytosis

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Keywords: Histological, Molecular, Myeloproliferative neoplasms, Persistent erythrocytosis

The acquired JAK2 V617F mutation, which results in constitutive activation of the intracellular JAK2 molecule required for normal haematopoietic cytokine signalling, is the most frequently observed mutation of the myeloproliferative neoplasms (MPN) and is present in 98% of polycythaemia vera cases and in 50-60% of patients with essential thrombocythaemia and primary myelofibrosis. Detection of this mutation is one of the major diagnostic criteria for these MPN according to the World Health Organization classification [1]. Identification of the JAK2 V617F is not only used to confirm the diagnosis of an MPN but is also used in the MPN elimination process when similar clinical and laboratory features, such as splenomegaly, splanchnic vein thrombosis, leucocytosis, erythrocytosis and thrombocytosis, are observed. A rare but recurrent feature of plasma cell neoplasms (PCN) is the presence of a co-existing, persistent erythrocytosis [2,3]. While concurrent plasma cell and myeloproliferative neoplasms have been reported, such cases inevitably display overt clinical, histological and molecular features of both myeloid and lymphoid malignancies [4].

In order to determine whether screening for the JAK2 V617F mutation is indicated in the investigation patients with PCN with co-existing erythrocytosis, a retrospective audit was performed on the number of such requests from a molecular diagnostic facility. From January 2006 to June 2015 inclusive, a total of 11,693 requests were received for JAK2 V617F testing at a central molecular diagnostic facility of which 15 (0.1%) were identified with clinical details supplied of a PCN with red cell indices suggestive of an MPN. The PCN was indicated as either myeloma (n=4) or monoclonal gammopathy of undetermined significance (MGUS, n=11) with features suggestive of an MPN given as polycythaemia (n=2), erythrocytosis (n=4) and raised haemoglobin and haematocrit (n=9). A JAK2 V617F screening assay (sensitivity 1% mutant allele burden) did not detect the mutation in any of the 15 patients.

While the impact on the overall laboratory workload is negligible, this observation in patients with a PCN and erythrocytosis without other clinical, histological or laboratory evidence of an MPN, suggests that investigation for the presence of the JAK2 V617F mutation is not warranted. The finding from this series is confirmatory of case reports of PCN in which the erythrocytosis was also found to be non-clonal and secondary in nature but its underlying cause remained pathologically undetermined [2,3]. The causes of erythrocytosis are many with renal impairment, often observed in PCN [5], worthy of consideration as the underlying cause in such cases.

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FINANCIAL OR OTHER COMPETING INTERESTS: The author declares no financial or other competing interests.

Date of Submission: **Aug 21, 2015**
Date of Peer Review: **Oct 07, 2015**
Date of Acceptance: **Oct 30, 2015**
Date of Publishing: **Dec 01, 2015**