Letter to the Editor

Incidental abnormal bone marrow signal on magnetic resonance imaging and reflexive testing for the *JAK2* V617F mutation

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With the increasing employment of imaging modalities in the diagnostic work up of patients comes an increase in the number of incidental cases with an abnormal bone marrow signal. Hematological malignancy can be visualized in the bone marrow by several imaging procedures but interpretation must also consider the variation in marrow appearances due to compositional changes associated with normal aging and hematological demand (1). While sporadic cases of acute leukemia, lymphoma, myeloma, metastatic carcinoma and myeloproliferative neoplasms (MPN) have been diagnosed from this initial finding by subsequent bone marrow biopsy and hematological work up (2,3), the utility of up-front reflexive screening for hematological malignancy-associated mutations in such incidental cases has not been assessed. The classical Philadelphia chromosome-negative MPN are clinically related, stem cell neoplasms characterised by hyper-expansion of mature hematopoietic cell lineages primarily in the bone marrow. The most common driver mutation of these MPN is the acquired *JAK2* V617F which results in constitutive activation of hematopoietic growth factor signalling and which is present in greater than 95% of patients with polycythemia vera and in 50–60% of patients with essential thrombocythemia and primary myelofibrosis (4). It is therefore of interest to note that from a cancer molecular diagnostics perspective, an isolated, atypical bone marrow magnetic resonance imaging (MRI) signal has become an infrequent but recurring trigger for requesting molecular analysis of the *JAK2* V617F.

In order to address the laboratory impact and clinical value of such requests, a retrospective audit was performed on all *JAK2* V617F requests received at a molecular diagnostics centre for hematological malignancies. From January 2006 to December 2017 inclusive, 15,562 diagnostic requests for *JAK2* V617F mutation analysis were received. Of these, 29 requests (0.2%) were received with the only clinical details provided on the request form of an abnormal BM signal upon MRI. The median age was 52 years and comprised 12 females and 17 males. Using a standardised allele-specific PCR screening assay capable of detecting a 2% mutant allele burden (5) and unchanged throughout the audit period, the *JAK2* V617F mutation was not detected in any of these 29 patients.

Diagnosis and classification of an MPN not only requires molecular detection of typical somatic events such as the *JAK2* V617F, *JAK2* exon 12, *CALR* exon 9 and *MPL* exon 10 mutations, but is also reliant on other clinical and hematological criteria (6). Selecting which patients to screen for the presence of the MPN driver mutations of *JAK2*, *CALR* and *MPL* requires careful consideration in order to optimize laboratory resources (7,8). While further hematological follow up in patients with an abnormal bone marrow signal on MRI is advocated and despite this molecular diagnostic analysis not appreciably impacting on the overall laboratory workload, reflexive testing for the *JAK2* V617F mutation in such cases without overt hematological evidence of an MPN appears inappropriate.

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Footnote

Conflicts of Interest: The author has no conflicts of interest to declare.

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