DOI: 10.7860/JCDR/2017/25738.9522

Letter to Editor

Pathology Section

Molecular Investigation of a Suspected Myeloproliferative Neoplasm in Patients with Basophilia

STEPHEN E LANGABEER[1], KARL HASLAM[2]

Keywords: Basophils, Chronic myeloid leukaemia, Cytogenetic analyses

Dear Sir,

Peripheral blood basophilia, defined as basophils counts greater than 0.1 x10^9/l of blood, is a rare haematological finding with causes including hypersensitivity disorders, iron deficiency, chronic inflammation and infection. These reactive causes are uncommon and therefore marked basophilia should prompt the investigation of an underlying Myeloproliferative Neoplasm (MPN). The MPNs comprise of Chronic Myeloid Leukaemia (CML), Polycythaemia Vera (PV), Essential Thrombocythaemia (ET), Primary Myelofibrosis (PMF), and the less common chronic neutrophilic leukaemia, chronic eosinophilic leukaemia not otherwise specified, MPN unclassified, and mastocytosis [1]. The molecular genetic hallmark of CML is the *BCR-ABL1* fusion whereas in PV, ET and PMF, the most common mutations are the *JAK2* V617F and those within *CALR* exon 9 with a number of other myeloid neoplasm-associated mutations are present at lower frequencies. Basophilia can be a presenting feature of CML as well as of MPNs such as PV, ET and PMF [2]. Basophils may also be present in other rare myeloid malignancies such as acute basophilic leukaemia, acute myeloid leukaemia with the t(6;9) translocation and those harbouring fusions of *PDGFRA*, *PDGFRB* and *ETV6* [3,4]. While bone marrow morphology and cytogenetics are clearly important strands in the overall diagnosis to determine MPN phenotype, and characteristic translocations and rearrangements respectively, no guidelines exist of how to rationally approach the molecular aspects of the diagnostic process in patients with basophilia. In order to address this issue, a review was performed on those patients with basophilia referred for molecular investigation of an MPN.

A retrospective audit was performed on all patients with clinical details provided of basophilia, either alone or in conjunction with other haematological or clinical details, referred to a molecular diagnostic centre. Clinical details from *BCR-ABL1* and *JAK2* V617F requests were analysed from 1st January 2006 to the 30th June 2016 whereas *CALR* requests were audited from January 1st 2014 to 30th June 2016. During the audit period 7826, 13961 and 938 requests were received for *BCR-ABL1*, *JAK2* and *CALR* analysis respectively. A total of 211 requests were received with clinical details provided that included basophilia. Of 124 requests for the *BCR-ABL1*, the rearrangement was detected in 105 (84.7%); of 79 requests for *JAK2* V617F, the mutation was detected in 12 (15.2%); of eight requests for *CALR* mutation analysis, one (12.5%) was found to have a mutation.

While morphological and cytogenetic analyses are essential components of MPN diagnosis, molecular analysis is becoming an integral part of the process providing both diagnostic and prognostic information. Given the high percentage of *BCR-ABL1* identification in patients above with basophilia, it is recommended that a stepwise analysis of *BCR-ABL1*, then *JAK2* V617F, followed by *CALR* mutation analysis be implemented. It has been recently proposed that *BCR-ABL1* screening is limited to those patients presenting with a neutrophilia with left shift and a basophilia [5], however, in those patients in whom CML is excluded, further molecular investigation is clearly warranted. Whether additional scrutiny of other less common MPN-associated mutations is necessary may have to be balanced with the exclusion of reactive causes of basophilia.

REFERENCES

[1] Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, et al. The 2016 revision of the world health organization classification of myeloid neoplasms and acute leukemia. Blood. 2016;127:2391-405.
[2] Agis H, Krauth MT, Mosberger I, Müllauer L, Simonitsch-Klupp I, Schwartz LB, et al. Enumeration and immunohistochemical characterisation of bone marrow basophils in myeloproliferative disorders using the basophil specific monoclonal antibody 2D7. J Clin Pathol. 2006;59:396-402.
[3] Eveillard M, Desjonqueres A. Acute basophilic leukemia. Blood. 2014;123:3071.
[4] Chi Y, Lindgren V, Quigley S, Gaitonde S. Acute myelogenous leukemia with t(6;9)(p23;q34) and marrow basophilia: an overview. Arch Pathol Lab Med. 2008;132:1835-37.
[5] Ogunleye F, Ibrahim M, Allen E, Brennan N, Huang J, Yu Z, et al. BCR-ABL testing by polymerase chain reaction in patients with neutrophilia: the William Beaumont Hospital experience and the case for rational laboratory test requests. J Oncol Pract. 2016;12(12):e1001-e05.

PARTICULARS OF CONTRIBUTORS:
1. Clinical Scientist, Department of Cancer Molecular Diagnostics, St. James's Hospital, Dublin, Ireland.
2. Clinical Scientist, Department of Cancer Molecular Diagnostics, St. James's Hospital, Dublin, Ireland.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Mr. Stephen E Langabeer,
Cancer Molecular Diagnostics, St. James's Hospital, Dublin, Ireland.
E-mail: slangabeer@stjames.ie

FINANCIAL OR OTHER COMPETING INTERESTS: None.

Date of Submission: **Nov 30, 2016**
Date of Peer Review: **Dec 21, 2016**
Date of Acceptance: **Dec 23, 2016**
Date of Publishing: **Apr 01, 2017**