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Serum ferritin as a biomarker of polycythemia vera?

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LETTER TO THE EDITOR

The measurement of serum ferritin and transferrin saturation are the most commonly used tests for evaluating iron deficiency with low ferritin concentrations reflecting iron depletion (1). One cause of iron deficiency is the over-production of red blood cells, as evident in most patients with the myeloproliferative neoplasm of polycythemia vera (PV) (2), a malignancy in which there is constitutive activation of erythropoietin receptor signalling pathway due the acquisition of the *JAK2* p.V617F mutation.

The current World Health Organization (WHO) criteria for PV diagnosis are gender-specific raised hemoglobin or hematocrit levels, tri-lineage bone marrow hypercellularity, the presence of the *JAK2* p.V61F (acquired in more than 95% of cases) or exon 12 mutations, and a low serum erythropoietin concentration (3).

Additionally, these guidelines also detail the entity of masked PV, in which an iron deficiency due to the enhanced red blood cell proliferation results in an apparently normal presenting hemoglobin concentration, the diagnostic principles of which have subsequently been validated (4).

Despite subnormal serum ferritin not being a diagnostic requirement for PV, a low ferritin level in the absence of other features of PV has become a sporadic trigger for requesting *JAK2* p.V617F molecular analysis. In order to address the clinical value and laboratory impact of such requests, a retrospective audit was performed on all *JAK2* p.V617F requests received at a molecular diagnostics centre for hematological malignancies.

From January 2006 to December 2017 inclusive, 15562 diagnostic requests for *JAK2* p.V617F mutation analysis were received. Of these, 64 requests (0.4%) were received with the only clinical details provided on the request form of a subnormal serum ferritin (normal range 23–393 ng/mL). The median age was 58 years and comprised 42 males and 22 females. Using a standardised allele-specific PCR screening assay (5) capable of detecting a 2% mutant allele burden and unchanged throughout the audit period, the *JAK2* p.V617F mutation was not detected in any of these 64 patients.

Which patients to screen for the myeloproliferative neoplasm associated mutations of *JAK2*, *CALR* and *MPL* requires careful consideration in order to optimise laboratory resources (6,7). While the number of requests for *JAK2* p.V617F mutation in patients with low serum ferritin does not appreciably impact on overall laboratory workload, reflexive screening for the *JAK2* p.V617F mutation in patients with isolated subnormal ferritin levels and no further evidence of PV or masked PV appears inappropriate.

REFERENCES

1. Daru J, Colman K, Stanworth SJ, De La Salle B, Wood EM, Pasricha SR. Serum ferritin as an indicator of iron status: what do we need to know? Am J Clin Nutr 2017;106(Suppl 6):1634S-1639S.

2. Verstovsek S, Harrison CN, Kiladjian JJ, Miller C, Naim AB, Paranagama DC, Habr D, Vannucchi AM. Markers of iron deficiency in patients with polycythemia vera receiving ruxolitinib or best available therapy. Leuk Res 2017;56:52-59.

3. Arber DA, Orazi A, Hasserjian R, Thiele J, Borowitz MJ, Le Beau MM, Bloomfield CD, Cazzola M, Vardiman JW. The 2016 revision to the World Health Organization classification of myeloid neoplasms and acute leukemia. Blood 2016;20:2391-2405.

4. Misawa K, Yasuda H, Araki M, Ochiai T, Morishita S, Nudejima M, Hironaka Y, Shirane S, Edahiro Y, Gotoh A, Ohsaka A, Komatsu N. The 2016 WHO diagnostic criteria for polycythemia vera renders an accurate diagnosis to a broader range of patients including masked polycythemia vera: comparison with the 2008 WHO diagnostic criteria. Am J Hematol 2017;92:E128-E130.

5. Bench AJ, White HE, Foroni L, Godfrey AL, Gerrard G, Akiki S, Awan A, Carter I, Goday-Fernandez A, Langabeer SE, Clench T, Clark J, Evans PA, Grimwade D, Schuh A, McMullin MF, Green AR, Harrison CN, Cross NC. Molecular diagnosis of the myeloproliferative neoplasms: UK guidelines for the detection of JAK2 V617F and other relevant mutations. Br J Haematol 2013;160:25-34.

6. Tefferi A, Noel P, Hanson CA. Uses and abuses of JAK2 and MPL mutation tests in myeloproliferative neoplasms. J Mol Diagn 2011;13:461-466.

7. Haslam K, Langabeer SE. Who to screen for calreticulin mutations? An audit of real-life practice and review of current evidence. Eur J Intern Med 2017;40:e22-e23.