Morphological classification of the myelodysplastic syndromes: how much more education of diagnosticians is necessary?

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Within the past decade the World Health Organization (WHO) has published two extensive and well-regarded syllabi on the classification and definitions of the myelodysplastic syndromes (MDS).[1,2] Although predominantly based on the French-American-British (FAB) morphological approach to the five well-described subtypes,[3] additional features were included such as multilineage dysplasia of two or more cell lines to separate such cases from pure refractory anemia (RA) or refractory anemia with ring sideroblasts (RARS) in patients with <5% blasts and to separate refractory anemia with excess blasts (RAEB) into two types; furthermore, RAEB in transformation (RAEB-T) (now considered to be acute myeloid leukemia) was eliminated. Validation of the revised proposals followed rather quickly from Institutions in which investigators had considerable experience and large numbers of cases.[4,5]

However some have questioned the reliance on the minimal threshold of 10% dysplasia in any one of the three major cell lines (erythroid, granulocytic and megakaryocytic) to confirm a diagnosis of MDS in the absence of certain cytogenetic/molecular abnormalities in patients with less than 5% blasts. For example, Parmentier and co-workers[6] studied peripheral blood and bone marrow films from bone marrow donors and had difficulty obtaining a high degree of concordance among four 'experienced morphologists" using the 10% cutoff. The agreement was much better when the threshold was raised to 20%.

One can always question the definition of an "experienced morphologist" based on certain arbitrary criteria (board certification, academic institution, worldwide recognition as an authority based on publications, workshops, chapters in books, atlases, etc.). Nonetheless criteria for assessment of the percentage of blasts or dysplasia should be so well described that the vast majority of "readers" will be able to agree. At least for the percentage of blasts and ring sideroblasts, Mufti and co-workers achieved this goal.[7]

In this current issue of Haematologica, Senet and associates from the Spanish MDS Cooperative group (GESMD) report their findings, having looked at 50 patients with MDS and assessed the degree of agreement among, again, "four experienced cytologists".[8] This must be a magic number! Table 3 in their article shows the statistical analyses of the interobserver degree of agreement. There are some very interesting results, including a high degree of concordance on bone marrow blasts, including <2% blasts and number of ring sideroblasts, validating Mufti's findings as well as those of Greenberg *et al.* in the revised International Prognostic Scoring System,[9] but a less good concordance for peripheral blood blasts (for which the standard error can be quite wide with very low blood counts).

Of great interest was the excellent agreement in the granulocytic and megakaryocytic lineages but not the erythroid line, even when the "10% threshold" was raised to as high as 40%. Distinguishing mild megaloblastic change from dysplastic erythroid precursors continues to be a challenge.

What remains to be achieved is better quantification of granulocytic dysplastic features, such as hypogranularity, nuclear projections and degrees of nuclear condensation, as well as reconsideration of raising the 10% threshold, when contemplating a new diagnosis of presumed low-grade MDS. Uniformity of diagnostic features and concordance are major goals of the European Hematology Association's Morphology Database.

The European LeukemiaNet's Morphology Database is managed by a Diagnostic Platform focusing on flow cytometric and morphological panels and is chaired by G Zini and MC Benè, respectively.[10]

For the present and the foreseeable future morphology remains the gold standard for the diagnosis of MDS, but let the "buyer beware". MDS centers of excellence have been established worldwide by the MDS Foundation (*www.mds-foundation.org*) where patients and physicians can be assured of, at least, a confirmatory assessment of their diagnosis.

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