Editorial

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Advances in Bone Marrow Diagnostics of Patients with Cytopenia

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The World Health Organization (WHO) has recently revised the 4th Edition of the "Classification of Haematological Malignancies" (2016 WHO update, published 2017 [1]). The WHO Committee stressed the importance of integrated diagnostics of both myeloid and lymphoid malignancies where clinical data, cytology, morphology, immunophenotyping, cytogenetics, and molecular genetics data are combined before the final diagnosis is made. The integrated approach is now the "state-of-the-art" in bone marrow (BM) diagnostics with the results of the evaluation of the blood smears, BM smears, BM trephine biopsy with immunohistochemistry, flow cytometry of blood and/or BM cell suspension and genetic data either incorporated into one integrated report or discussed at the multidisciplinary conferences.

The 2016 WHO update was the topic of the XXIII European Bone Marrow Working Group (EBMWG) International Course and Workshop on Bone Marrow Pathology held on May 23–27, 2017, in Utrecht, The Netherlands. The Workshop invited cases of reactive cytopenia and dysplasia, clonal hematopoiesis of indeterminate potential, idiopathic cytopenia of undetermined significance, idiopathic dysplasia of undetermined significance, and overt myelodysplastic syndromes (MDS). In this issue of *Pathobiology*, the Workshop Panel summarizes the Workshop Cases illustrating diagnostic difficulties in these areas. Based on the lectures held during the Course, distinguished experts provide reviews of topics related to the Workshop Cases.

Diagnosis of MDS is one of the most challenging issues in BM diagnostics. Based on new data accumulated since 2008, the WHO classification has been substantially revised with the new nomenclature. R.P. Hasserjian gives a very practical review of the changes in the classification of MDS, focusing on which relevant information the hematopathologist needs to provide with an easy-to-follow algorithm for the final classification. Although classical karyotyping renders normal karyotype in 50% of patients, targeted sequencing finds mutations in more than 90% of MDS patients. Mutation of the *SF3B1* gene is already incorporated in the diagnostic criteria of MDS with ring sideroblasts [2]. It has also been recommended to investigate whether the *TP53* gene is mutated in patients with MDS with isolated del(5q). T. Haferlach reviews the role of molecular changes in diagnostics and prognostication of MDS patients. Advances in the understanding of the pathobiology of MDS also lead to the development of the new targeted therapies in this disease, which is exemplified by clinical trials with luspatercept active in MDS with ring sideroblasts [2]. However, several recent studies have

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shown that some mutations often found in MDS patients can also be detected (although usually at much lower variant frequency) in elderly individuals with no evidence of hematological malignancy [3]. Some, but not all, may develop MDS and some may have mildly abnormal blood values with no dysplasia or borderline dysplasia with blood values that do not reach WHO criteria for cytopenia. In some patients, mild cytopenia and/or borderline dysplasia are noted but no evidence for clonal hematopoiesis is found. These conditions have now been better defined as idiopathic cytopenia of unknown significance, clonal cytopenia of unknown significance, idiopathic dysplasia of unknown significance, and clonal hematopoiesis of indeterminate potential. P. Valent reviews the minimal criteria for MDS and the pre-MDS states giving also some practical recommendations for follow-up and management of these patients. Along with progress in molecular diagnostics, significant progress has been made in BM immunophenotyping of MDS patients [4]. C. Duetz, T.M. Westers, and A.A. van de Loosdrecht give an overview on how multiparameter flow cytometry can be applied for diagnosis, risk stratification, and therapy monitoring. Flow-cytometry diagnostic scores are reviewed, and a practical algorithm is proposed to be applied in cytopenic patients that would otherwise have inconclusive results. A lack of immunophenotypic aberrancies would help to exclude MDS, and the presence of significant immunophenotypic aberrancies would render MDS diagnosis or further follow-up.

WHO 2016 introduced a new provisional entity of "myeloid neoplasms with germline predisposition" [5]. J. Geyer focused in her review on the recently described entities and available data concerning BM histology. The reviewed entities include those with germline mutations of the genes such as *CEBPA*, *DDX41*, *RUNX1*, *ANKRD26*, *ETV6*, *GATA2*, and others. As these entities are currently underdiagnosed and underreported, it is important to increase our experience in both clinical and pathomorphological presentations of the patients. Another challenging diagnostic issue reviewed here by S. Wang is the work-up and diagnosis of hypereosinophilia. The review provides an excellent algorithm to be applied in differential diagnosis and highlights progress that has been made in genetic characterization of hematological malignancies that present with eosinophilia. Characteristic histological features of BM are described.

The review of Workshop Cases by K. Hebeda et al. focused on difficulties in separating true MDS from other causes of cytopenia. Seventeen cases were selected to illustrate issues such as clonal cytopenia that does not fulfill the minimal MDS criteria, familial predisposition, and MDS-diagnosed basis of recurrent cytogenetic abnormalities. Some of the cases of overt MDS illustrated important diagnostic difficulties.

In summary, we hope that this special issue of *Pathobiology* will be of interest to hematopathologists, clinical hematologists, and also to scientists who work in the field of MDS and other hematological malignancies.

References

1 Swerdlow SH, Campo E, Harris NL, Jaffe E, Pileri SA, Stein H, Thiele J, Arber DA, Hasserjian RP, LeBeau M, Orazi A, Siebert R (eds): WHO Classification of Tumours of Haematopoietic and Lymphoid Tissue. Lyon, IARC, 2017.

2 Arber DA, Hasserjian RP: Reclassifying myelodysplastic syndromes: what's where in the new WHO and why. Hematology Am Soc Hematol Educ Program 2015;2015:294–298.

3 Steensma DP, Bejar R, Jaiswal S, Lindsley RC, Sekeres MA, Hasserjian RP, Ebert BL: Clonal hematopoiesis of indeterminate potential and its distinction from myelodysplastic syndromes. Blood 2015;126:9–16.

4 Porwit A: Is there a role for flow cytometry in the evaluation of patients with myelodysplastic syndromes? Curr Hematol Malig Rep 2015;10:309–317.

5 Czuchlewski DR, Peterson LC: Myeloid neoplasms with germline predisposition: a new provisional entity within the world health organization classification. Surg Pathol Clin 2016;9:165–176.