2007 Workshop of the Society for Hematopathology and European Association for Haematopathology

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The August and September issues of the Journal will include a series of proceedings from the Workshop of the Society for Hematopathology and European Association for Haematopathology, which was held in Indianapolis, IN, in November 2007. The Workshop focused on chronic myeloproliferative neoplasms (MPNs), myeloproliferative/myelodysplastic neoplasms, de novo and therapy-related myelodysplastic syndromes (MDS), extramedullary myeloid tumors, and mastocytosis. Cases of de novo acute myeloid leukemia were excluded. The goals of the Workshop were to correlate diagnostic hematopathology practice to the most recent discoveries in myeloid neoplasms and address diagnostic challenges through case discussions.

The Workshop and preparation of the proceedings coincided with the update of the World Health Organization (WHO) classification of hematopoietic and lymphoid neoplasms; thus, the articles discuss the individual diagnostic entities and submitted cases in light of this updated classification published in September 2008. The Workshop included plenary sessions and scientific lectures. The latter aimed to review recent advances in pathogenesis of myeloid neoplasms and developments in molecularly targeted therapies and to outline the role of molecular pathology and cytogenetics in determining the prognosis and monitoring of myeloid neoplasms. The plenary sessions included interesting cases selected to represent current issues in the diagnosis of myeloid neoplasms. The diagnostic approach was based on a careful integration of morphologic assessment with ancillary techniques such as immunophenotyping and cytogenetic and molecular studies, following the guidelines of the WHO classifications of tumors of hematopoietic and lymphoid tissues published in 2001 and updated in 2008.

Our increasing knowledge of the pathogenesis of myeloid neoplasms derives mostly from a better understanding of the molecular genetic abnormalities associated with these disorders. This trend was also clearly noticeable during the Workshop. Of the submitted cases, 97% included cytogenetic/genetic data, and in 61% of cases, the entity was defined or diagnosis supported by the presence of a specific genetic lesion. Nevertheless, the morphologic features and the assignment of lineage and maturation stage using flow cytometry or immunohistochemical analysis, all performed in the context of clinical history, retain their importance in the diagnostic workup. Thus, the high sample quality and the review of the original specimen, procured before any treatment is instituted, are prerequisites for the optimal diagnosis and subsequent patient management. In many cases, a thorough review of clinical, morphologic, and immunophenotypic features allows for the narrowing of the differential diagnosis and a selective (vs “shotgun”) application of ancillary genetic testing. Case discussions during workshop sessions emphasized the elements of this appropriate diagnostic process. The scientific panel did not issue a final consensus diagnosis in cases lacking adequate clinical data and in rare cases in which original diagnostic material, essential for optimal classification of the myeloid neoplasm, was not available. Those cases were rare because most of the submitted cases were comprehensively evaluated.

Workshop sessions included the all-encompassing diversity of myeloid neoplasms. Unusual cases and challenging diagnostic categories were presented in each session. Even in relatively well-understood entities such as chronic myelogenous leukemia, cases with atypical manifestations or rare variant translocations or developing unusual features during
disease progression may cause diagnostic challenges. The topic of disease follow-up, including the detection of BCR-ABL1 transcripts by polymerase chain reaction and molecular analysis of resistance to tyrosine kinase inhibitors, was discussed. These issues are presented by Vardiman2 in the article on chronic myelogenous leukemia.

The session on Philadelphia chromosome–negative MPNs included, in addition to the classic examples, rare entities such as chronic eosinophilic leukemia, chronic neutrophilic leukemia, difficult-to-classify cases of MPNs, and reactive mimickers of MPN. This session highlighted new MPN categories largely defined by genetic features and demonstrated caveats of molecular analysis. Thiele3 discusses the MPN session in the second article of the proceedings series.

MDS/MPNs proved to be among the most stimulating topics of the workshop. The challenge stemmed partially from the overlapping myeloproliferative and myelodysplastic features shared by these entities. In this context, a careful review of all relevant clinical and cytogenetic data to exclude other myeloproliferative or myelodysplastic neoplasms is of paramount importance. Nevertheless, there is a pressing need to develop more precise diagnostic criteria, ideally involving specific molecular genetic markers. This was particularly obvious in the category of atypical chronic myelogenous leukemia, BCR-ABL1 negative, and in the provisional entity of refractory anemia with ring sideroblasts and thrombocytosis. The Workshop cases included in the category of MDS/MPN are discussed by Foucar.4

De novo and therapy-related MDS were discussed in separate workshop sessions. Despite well-defined criteria for the diagnosis and subclassification of de novo MDS, several important issues were discussed during the session. This discussion included the respective roles of morphologic assessment and cytogenetics and their integration in cases in which morphologic features are at variance with cytogenetic/genetic data. The differential diagnoses of MDS with fibrosis and of hypoplastic variants of MDS can, at times, be challenging. These issues are discussed in detail by Orazi and Czader.5

The ever-expanding spectrum of therapy-related myeloid neoplasms was addressed in a separate session. Diverse clinical, morphologic, and cytogenetic/genetic manifestations were presented. The emphasis was placed on the current classification of these disorders based on the clinical outcome and genetic data. An updated approach for the diagnosis of therapy-related myeloid neoplasms is presented by Czader and Orazi in a separate article.6

The workshop also provided invaluable insight into the multifaceted manifestations of myeloid sarcoma. De novo cases and tumors arising in the course of previously diagnosed acute leukemia and myeloproliferative and myelodysplastic neoplasms were included. Diagnostic challenges and recommended approaches regarding how to resolve specific issues are expertly outlined by Campidelli et al.7

Last, but not least, the category of mast cell disease is discussed by Horny.8 For a long time, mast cell disease has been known for its diverse presentations. Despite increasing awareness of the prevalence of this disease and the availability of genetic testing, KITD816V mutation analysis, the diagnosis of mast cell disease is not always straightforward. Particularly challenging are cases of systemic mastocytosis with associated clonal hematologic non–mast cell lineage disorder, cases associated with eosinophilia, and cases of occult mastocytosis, when the mast cell proliferation is not apparent on initial morphologic review.

We hope that the following series of articles discussing diagnostic challenges and unusual disease manifestations in the context of the recently updated WHO classification of myeloid neoplasms will be useful for practicing pathologists. The complete set of lectures and workshop sessions including all cases of the workshop are freely available online at http://www.iupui.edu/~pathol/HematopathologyWorkshop/.

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References