What are the common challenges in the diagnosis of MDS?

Welcome to Managing MDS. My name is Rami Komrokji and I am Professor of Oncologic Sciences and the Clinical Director at the Malignant Hematology Department at the Moffitt Cancer Center in Tampa, Florida. I am frequently asked, “What are the common challenges in the diagnosis of MDS?”

Typically, this is a very important step when we think of MDS patients. I think the art is really in making the diagnosis for MDS, and it could be one of the most challenging steps in managing MDS. In a paper published in Blood by the MD Anderson group, and in our experience, in 15-20% of cases, we changed the diagnosis of MDS, whether it is to a different grade, or cases of MDS that were missed. That is a big challenge. Obviously, commonly, the presentation for those patients are cytopenias. Then a bone marrow is done for those patients and there are certain findings which are diagnostic for MDS. Sometimes those findings are subtle and not easy to distinguish, so it requires an experienced hematopathologist, e.g. the dysplasia in MDS is not easy to distinguish. There are also some more objective findings, such as an increase in the blasts; however, one should be cautious about that, because an estimate of blasts on the bone marrow aspirate is still the gold standard. We often see blasts estimated based on flow cytometry, which could be obviously inaccurate. And in cases of, for example, CMML, blasts and promonocytes are considered added to the total percentage of the blasts in the bone marrow.

We see those cases where there are clear changes of MDS that were missed by inexperienced hematopathologists, but we also see cases where the dysplasia is really not quite there, and that is also a challenging situation. Nowadays, to add to the challenge, there is the incorporation of molecular data. In many of those patients, we incorporate molecular data testing for single gene mutations or somatic mutations using next-generation sequencing. Those, per se, are not diagnostic for MDS, but in the right setting, they could help to establish the diagnosis. So, another challenge now is how to incorporate those data. In reality, there is evidence of clonal hematopoesis in patients without cytopenia, called CHIP (clonal hematopoesis of indeterminate potential). There is what we call ICUS (idiopathic cytopenia of unknown significance), where patients have cytopenia but not enough dysplasia on the bone marrow. There is also the MDS and those somatic mutations can be seen in the spectrum of CHIP or ICUS, so the line to
diagnose MDS still remains pathological, in other words, showing the dysplasia on the bone marrow.

So, although those tests can be helpful in certain cases, in other cases they could be challenging, as well. For example, in the WHO new revision, in the past, we used to require more than 15% ring sideroblasts to make the diagnosis of a subtype of MDS called refractory anemia with ring sideroblasts. Now in the new classification, there is a suggestion that if patients have more than 5% ring sideroblasts but they have the mutation called SF3B1, which is a splicing mutation, then that calls for the presumptive diagnosis of refractory anemia with ring sideroblast. So again, it is challenging to make the diagnosis of MDS, recommendation of the dysplasia, estimate of the blasts, and incorporation of the molecular data, and it is definitely worthwhile spending some time establishing the diagnosis, and if in doubt, sending the pathology for an experienced hematopathologist to review.

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