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P996 UTILITY OF KIT P.D816 IN MYELOID NEOPLASM WITHOUT DOCUMENTED SYSTEMIC MASTOCYTOSIS TO DETECT HIDDEN MAST CELLS IN BONE MARROW

Topic: 15. Myeloproliferative neoplasms - Biology & Translational Research

Do Hwan Kim[1], Fuli Jia[1], Chi Young Ok[1]

[1] *Hematopathology, The University of Texas MD Anderson Cancer Center, Houston, United States*

Background: *KIT* p.D816 mutation is strongly associated with systemic mastocytosis (SM). Although it is not specific for SM, it is one of the diagnostic criteria for SM since its presence in the right morphologic context (i.e. presence of atypical mast cell clusters) is a strong support for neoplastic nature of mast cells. Next-generation sequencing (NGS) is now routinely performed in almost all bone marrow sample and KIT mutations are detected from patients who are not known or suspected to have SM.

Aims: Therefore, we wanted to assess if *KIT* mutations in this patient population are associated with unsuspected SM.

Methods: We searched NGS result in our institution between 1/1/2013 and 9/30/2021 with positive result for *KIT* mutation from patients with known/suspected myeloid neoplasms. Patients with previously documented history of systemic mastocytosis were excluded. Bone marrow biopsies from patients with *KIT* mutation were assessed with immunohistochemical stains for CD117 and mast cell tryptase (MST).

Results: A total of 49 patients who had *KIT* mutation and had available formalin-fixed paraffin embedded blocks were identified. Thirty-eight (77.6%) patients has acute myeloid leukemia (AML) and 6 patients had chronic myelomonocytic leukemia (CMML, 12.2%). The remaining patients had myelodysplastic syndrome (n=1), myelodysplastic/myeloproliferative neoplasm, unclassifiable (n=1), myeloproliferative neoplasm (MPN, n=1), AML in remission (n=1) and therapy-related myeloid neoplasm (n=1).

A total of 41 patients had a single *KIT* mutation and 8 patients had 2 or more *KIT* mutations. KIT p.D816V mutation was the most common mutation (n=38, 64.4%), followed by D816Y (n=8, 13.6%), D816H (n=5, 8.5%), Y418_D419insFF (n=2, 3.4%), R815_D816insVL (n=1, 1.7%), S197L (n=1, 1.7%), K558E (n=1, 1.7%), D419del (n=1, 1.7%), N822K (n=1, 1.7%) and R815_D816insIPP (n=1, 1.7%).

Immunohistochemical stains for CD117 and MST were performed in all 49 patients. The MST stain was more suitable since 10 patients (20%) had increased blasts with CD117 expression which obscured morphologic review. A total of 4 patient (8.2%) showed mast cell nodules where spindled shaped mast cells were present, meeting the criteria for SM. All four patients had *KIT* p.D816V mutation and had high mutant allelic frequency (~50%) except one patient (1%). These patients had MPN (n=1), AML (n=1), AML in remission (n=1) and CMML (n=1), respectively. One (2%) patient has increased (>10%) mast cells but scattered throughout the bone marrow space without nodules and mast cells were round-to-ovoid shape. Eleven patients (22.4%) showed rare scattered mast cells and 33 patients (67.3%) did not show mast cells at all.

Summary/Conclusion: We discovered approximately 8% of patients who had myeloid neoplasms with unexpected *KIT* mutations are met for systemic mastocytosis after additional immunohistochemical studies. Our data support that application of additional immunohistochemical studies are recommended to identify underrecognized SM when *KIT* mutations are unexpectedly found by molecular assays.