P21. MYELODYSPLASIC / MYELOPROLIFERTIVE NEOPLASIA – A DIAGNOSTIC CHALLANGE FOR THE CLINICIAN.

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Introduction: Myelodysplastic/ myeloproliferative neoplasia display combined dysplastic and proliferative features. The 2008 WHO classification of myeloid neoplasia included four entities in this category: chronic myelomonocytic leukemia, juvenile myelomonocytic leukemia, BCR/ABL1 negative atypical chronic myeloid leukemia, myelodysplastic/ myeloproliferative neoplasia – unclassified, and a provisional entity, refractory anemia with ringed sideroblast associated with marked thrombocytosis (RARS-T).

Materials and methods: We present three cases of patients diagnosed with RARS-T in our clinic between 2012-2014.

Results: The first patient, a female 77 years old, presented with anemia, erythroid dysplasia and ringed sideroblasts at morphologic evaluation of bone marrow (BM). The BM cytogenetics revealed del(11p) and t(3;6) and the first diagnosis was RARS. After 4 months of evolution she presented with myeloproliferative features, including hepatosplenomegaly, leukocytosis and left shift to myeloblast, thrombocytosis. This picture led to JAK2 V617F testing which resulted positive; the triphine bone marrow biopsy showed large atypical megakaryocytes proliferation. Based on these new elements the final diagnosis was RARS-T.

The second case, a 89 years old male patient, presented with anemia and marked thrombocytosis; BM morphology showed erythroid dysplasia and the presence of ringed sideroblast; BM cytogenetics revealed a normal karyotype, JAK2 mutation was positive and triphine BM biopsy revealed large atypical megakaryocytes proliferation and erythroid hypoplasia, which was a particular feature. The diagnosis in this case was also RARS-T.

The third case, a male of 75 years old, presented with mild hepatosplenomegaly, anemia, marked leukocytosis and left shift to myeloblast, erythroid and magakaryocytic dysplasia and the presence of ringed sideroblasts at BM morphology. The testing for BCR/ABL1 fusion gene resulted negative and BM cytogenetics failed because of absence of metaphases. The diagnosis at this point was MDS/MPN – unclassified. Later on progresive increasing thrombocytosis apeared and, consecutively, JAK2 mutation was tested, yealding a negative result this time. Yet, the diagnosis was also RARS-T.

Conclusions: We want to highlight the clinical, morphological, genetical and molecular diversity of this MDS/MPN entity, which could be explained by different molecular pathogenic mechanisms. The testing of different markers could be helpfull, one example being SF3B1 mutations that were demonstrated to play a pathogenic role in the apearance of ringed sideroblasts. The therapeutic means in this disease are quite limited. Hydroxyurea is a good cytoreductive agent, but with deleterious effects on anemia, Lenalidomide proved beneficial in some cases, but it is inaccessible to patients from our country. The identification of new molecular markers could be the source of new targeted therapies.