CD271+ mesenchymal stromal cells in myeloproliferative neoplasms Philadelphia-negative

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Introduction: Myeloproliferative neoplasms Philadelphia-negative (MPN Ph-) are heterogenous group of malignancies, characterized by presence of *JAK2* or *CALR* or *MPL* mutation in most of the cases. Their clinical picture and prognosis differ significantly, thus they require a different management, however in initial phases of these MPN development, the diagnosis may not be straightforward. These neoplasms differ significantly on histological grounds, not only in hematopoietic cells morphology and architecture, but also their microenvironmental features. Mesenchymal stromal cells (MSCs) CD271-positive play a major role in hematopoietic stem cells renewal, and have been analyzed previously in context of solid tumor propagation and some hematological cancers development. Aim of this study is to analyze the quantity and architecture of CD271-positive MSCs in three main Philadelphia-negative myeloproliferative neoplasms with the main focus on primary myelofibrosis.

Methods: Formalin-fixed paraffin-embedded bone marrow (BM) trephine biopsies from 30 patients, diagnosed with primary myelofibrosis (MF), polycythemia vera (PV) or essential thrombocytemia (ET), were sliced into 4 µm-thick slides and stained immunohistochemically using anti-CD271 monoclonal antibody (Abcam). Staining area was measured digitally - slides were scanned using NanoZoomer 2.0 slide scanner. Next, a representative slide area of at least 0.3 mm² was analyzed using ImageJ software, to measure the extent of anti-CD271 staining. Area occupied by adipocytes was subtracted in calculations. Additionally, stained cells histotopography and architecture was assessed by two pathologists using conventional light microscopy. Histological examination was blinded to final diagnosis and any clinical data or laboratory parameters.

Results: In cases of ET and PV CD271+ MSCs processes were forming a loose meshwork, mostly with perivascular and periadipocytic distribution. In cases of PMF, CD271+ cells were arranged in dense meshwork entwining hematopoietic cells. They were forming numerous thick bundles.

The stained area percentage was similar in cases of PV and ET, and had a mean value of 12,2% and 9,5% respectively. In contrast, most cases of PMF showed intense staining with a mean value of 24,1%. Interestingly, there was not a significant difference between PMF in fibrotic stage and prefibrotic PMF – 26,5% and 23,6% respectively.

Conclusion: These are preliminary results. Although we have analyzed a very small group of patients, a strong relationship between MF and high CD271+ cells density in bone marrow is visible. Similar level of density in cases of PMF in early phase and overt fibrosis shows, that anti-CD271 staining might be useful in differentiating prePMF from other MPNs on histopathological examination. Our study suggests, that microenvironmental niche created by CD271+ MSCs may be an important factor in development of high-grade myeloproliferative neoplasms.