

論 文 概 要

○ 論文題目

Prominence of nestin-expressing Schwann-like cells in the bone marrow of myelodysplastic syndromes with severe fibrosis

(線維化を伴う骨髄異形成症候群患者の骨髄ではネスチン陽性シュワン細胞様構造が異常増殖している)

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目 的:

Nestin-expressing stromal cells (NECs) and Schwann cells in the bone marrow (BM) play crucial roles as a niche for normal hematopoietic stem cells in mice. Both of these types of cells were reportedly decreased in myeloproliferative neoplasms (MPN) patients and also in a mouse model. Conversely, an increase in NECs was reported in acute myeloid leukemia. Accordingly, it is of interest whether and how these BM stromal cells are structured in myelodysplastic syndromes (MDS). In this study, we focused on NECs and glial fibrillary acidic protein (GFAP)-expressing stromal cells in the BM of MDS patients.

対象と方法:

Forty-five patients with MDS, and 16 patients with MPN divided into two groups as MPN-associated MF (12 cases) and chronic myelogenous leukemia (CML) (4 cases) were enrolled in the study. Samples from 17 patients with non-Hodgkin lymphoma (NHL) without BM involvement were analyzed as the control. We used archived formalin-fixed paraffin-embedded (FFPE) BM biopsy samples from these patients for silver staining and immunostaining, and mononuclear frozen cells BM aspirate samples for genetic analysis. Immunostaining were performed with antibodies against nestin, CD34, α -smooth muscle actin (α -SMA), GFAP, neurofilament heavy chain (NFH), and others.

結 果:

We identified 19 (42.2%) MDS with fibrosis (MDS-F) cases, 7 (15.5%) had fibrosis grade 3 (MF3) and 12 (26.7%) had MF2, and 26 (57.8%) remaining patients identified as MDS without fibrosis (MDS w/o F), 11 (24.5%) were MF1, and 15 (33.3%), as MF0. The 12 MPN-associated MF cases were evaluated as MF2 or MF3. We found a marked increase of NECs in MDS-F patients at a high frequency (9/19; 47.4%), but not in MDS w/o F (0/26; 0%) and MPN (0/12; 0%) patients, including both MPN-associated MF and CML. In 8 of the 9 MDS-F cases (88.9%) with the NEC increase, a majority of NECs also expressed GFAP, with an additional increase in GFAP single-positive cells. Furthermore, in 7 of them, we found a prominent structure characterized by NFH staining surrounded by NECs with GFAP expression or GFAP single-positive cells.

考 察:

Our findings suggest that increase of NECs in BM of MDS-F patients may have an important role in promotion of BM myelofibrosis. According to immunostaining results, NECs expressing the GFAP may represent the rejuvenated Schwann cells that start to proliferate with some stimulation in MDS-F, but not in MPN-associated MF. Therefore, nestin may have a potential marker to distinguish MDS-F and MPN-associated MF. In

addition, it is reasonable to hypothesize that the abnormally enhanced Schwann cell proliferation induces axonal extension. Consequently, the increase in nestin-expressing Schwann-like cells in the BM is likely to have a significance in the pathophysiology of myelofibrosis in patients with MDS.

結 論:

We have identified a unique subgroup of MDS-F characterized by the abnormal proliferation of a structure comprising terminal nerve axons and the surrounding Schwann-like cells, typically accompanying severe fibrosis and hypercellular BM. This structure could have a relevance to the pathophysiology of MDS-F.