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617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

Relationship between Sarcopenia and the Heterogeneity and Microenvironment of Acute Myeloid Leukemia Based on Single-Cell Transcriptome Sequencing

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Background: High intratumoral heterogeneity heterogeneity (ITH) and changes in bone marrow microenvironment (BMM) components are important for drug resistance and recurrence in patients with acute myeloid leukemia (AML), and may also influence the phenotype of sarcopenia. This study aims to determine the relationship between sarcopenia and the heterogeneity and microenvironment of AML.
Method: Body composition was assessed by bioelectrical impedance analysis before treatment. Sarcopenia was diagnosed by low muscle quantity according to European Working Group on Sarcopenia in Older People 2 (EWGSOP2). Bone marrow samples from 9 patients with relapsed or refractory AML were used to perform single-cell transcriptome sequencing (scRNA-seq) to analyze the differences in tumor cell subsets and microenvironmental components between AML patients with or without sarcopenia. The samples of 19 newly diagnosed AML patients were further collected for bulk RNA-seq, and deconvolution was done. Bioinformatics methods were used to verify the differences in cell subsets of microenvironmental components in patients with and without sarcopenia, as well as the genes and signaling pathways of tumor cells with differential expression.
Results: Nine leukemia-like cell subsets were identified in AML patients by scRNA-seq. In AML patients with sarcopenia, hematopoietic stem cell (HSC) subsets accounted for a significantly higher proportion of malignant cells, while progenitor cells and monocytes showed a higher proportion in patients without sarcopenia. In sarcopenic group, there were significantly fewer neutrophils, megakaryocytes, and $CD8^+$ Tcm cells in the microenvironment component, while significantly more immunosuppressed Treg cells. After deconvolution of bulk RNA-seq data from 19 newly diagnosed AML patients, it was confirmed that Treg cells were more distributed in sarcopenic patients. Among them, 167 genes were significantly up-regulated, and the most significantly up-regulated 5 genes were ME3, UBE2E3, PCSK5, LAMC1 and PTPRF. A total of 224 significantly down-regulated genes were identified, including RNF18B, TNFAIP3, GALNT2, ORM2 and IL1R2. Pathway enrichment of differentially expressed genes was found, including signaling pathways regulating pluripotency of stem cells, Hippo signaling pathway, protein digestion and absorption pathway, etc.
Conclusion: Sarcopenia may be related to immunosuppressive microenvironment and affect the prognosis of AML patients.

Disclosures No relevant conflicts of interest to declare.

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