Targeted eliminating myeloid-derived suppressor cells with doxorubicin by regulating STAT pathway to alleviate tumor immunosuppression in neuroblastoma

Weili Xu[1], Suolin Li[1], Zhigang Hu[1], Hui Zhou[1], Shaojian Xie[1], and Guixin Li[1]

[1]Second Hospital of Hebei Medical University

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Abstract

Background High agglomeration of myeloid-derived suppressor cell (MDSC) in tumor microenvironment resulted in immune escape and affected therapeutic effects. Doxorubicin (DOX) or dopamine (DA) is found the specific drug to selectively remove or maturate MDSC. How to effectively eliminate MDSC in neuroblastoma (NB) and its mechanism need to be clarified. Procedure In the present study, BALB/c tumor-bearing mice model were established by NB cells injection, then grouped into DOX2.5 mg/kg group, DOX5 mg/kg group, DA50 mg/kg group and control group. DOX or DA were injected intravenously in advance, then quantity and distribution of MDSC, proliferation and infiltration of T cell, Treg level and TAM polarization, MDSC related functional molecules in vivo and expression of proteins in signal transducer and activator of transcription (STAT) pathway in MDSC were detected and compared respectively at 14 d, 17 d and 23 d after inoculation. The tumor growth were compared between the groups. Results After DOX or DA administration, in each experimental group, MDSC ratio all decreased. STAT1, p-STAT1 and activated caspase-3 decreased, but STAT3, p-STAT3, STAT5, p-STAT5, STAT6, p-STAT6, Arg-1 and IDO increased. Simutaneously, compared with the control group, T cell proliferation in tumor first increased and then inhibited, infiltration of T cells increased, TAM polarization and Treg level reduced, the tumor growth was inhibited. Changes in above indicators were most significant in DOX2.5mg/kg group. Conclusions Low-dose DOX administration can eliminate MDSC in NB by regulating STAT signaling pathway in MDSC, thus remove immunosuppression and improve immune efficacy of NB.

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