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A comprehensive single-cell analysis reveals the impact of laser interstitial thermal therapy on the tumor microenvironment in glioblastoma

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Abstract

Glioblastoma (GBM) remains the most lethal intracranial malignancy in the central nervous system with limited therapeutic options. Laser interstitial thermal therapy (LITT) has emerged as a novel minimally invasive treatment for GBM. Around the core ablation zone of LITT, there exists a sublethal ablation zone caused by sublethal hyperthermia (below 46 °C), which is located in the peripheral region of the tumor containing highly invasive GBM cells. The effects of LITT on the tumor cells and microenvironment within this region have been rarely reported. Here, we used an in vivo intracranial rat model of GBM to investigate the effects of LITT-induced sublethal hyperthermia on GBM through single-cell RNA sequencing and immunofluorescence assay. We show that sublethal hyperthermia promotes cytotoxic T cell infiltration, drives the maturation of conventional type 2 dendritic cell, enhances germinal center B cell recruitment, and reduces M2 macrophage infiltration. Additionally, we observe a marked decrease in GBM malignancy and DNA repair capacity. Through cell-cell communication analysis, we identified key changes characterized by enhanced interactions between extracellular matrix-related cells and GBM. By further integrating spatial transcriptomic and survival analyses, we uncovered that sublethal hyperthermia suppresses the tumor by weakening interactions between collagen-related genes and Cd44. On the other hand, it promotes tumor angiogenesis and proliferation by enhancing the interaction between Ptn and Ncl. Our study highlights the complex and opposing effects of LITT-induced sublethal hyperthermia on GBM, offering new mechanistic insights and potential therapeutic targets to optimize its clinical application.

Keywords: glioblastoma; laser interstitial thermal therapy; single-cell analysis; tumor microenvironment.