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Laser Interstitial Thermal Therapy Induces Robust Local Immune Response for Newly Diagnosed Glioblastoma with Long-term Survival and Disease Control

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Abstract

Laser interstitial thermal therapy (LITT) is a minimally invasive neurosurgical technique used to ablate intra-axial brain tumors. The impact of LITT on the tumor microenvironment is scarcely reported. Nonablative LITT-induced hyperthermia (33-43˚C) increases intra-tumoral mutational burden and neoantigen production, promoting immunogenic cell death. To understand the local immune response post-LITT, we performed longitudinal molecular profiling in a newly diagnosed glioblastoma and conducted a systematic review of anti-tumoral immune responses after LITT. A 51-year-old male presented after a fall with progressive dizziness, ataxia, and worsening headaches with a small, frontal ring-enhancing lesion. After clinical and radiographic progression, the patient underwent stereotactic needle biopsy, confirming an IDH-WT World Health Organization Grade IV Glioblastoma, followed by LITT. The patient was subsequently started on adjuvant temozolomide, and 60 Gy fractionated radiotherapy to the post-LITT tumor volume. After 3 months, surgical debulking was conducted due to perilesional vasogenic edema and cognitive decline, with H&E staining demonstrating perivascular lymphocytic infiltration. Postoperative serial imaging over 3 years showed no evidence of tumor recurrence. The patient is currently alive 9 years after diagnosis. Multiplex immunofluorescence imaging of pre-LITT and post-LITT biopsies showed increased CD8 and activated macrophage infiltration and programmed death ligand 1 expression. This is the first depiction of the in-situ immune response to LITT and the first human clinical presentation of increased CD8 infiltration and programmed death ligand 1 expression in post-LITT tissue. Our findings point to LITT as a treatment approach with the potential for long-term delay of recurrence and improving response to immunotherapy.