Clinical and Medical Implications of Brain Tumors

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Brief Report

In neuro-oncology, gliomas and brain metastases remain formidable treatment obstacles. Despite decades of investigation, the exact pathophysiological mechanisms behind their unavoidable progression remain unknown. A strong association between the neurological system and cancer is critical for the beginning and progression of many brain tumours, as evidenced by a growing body of evidence from the study of "cancer neuroscience." In this vein, it was recently discovered that glioma cells themselves exploit neurodevelopmental pathways, which adds to brain tumour proliferation and resistance. Tumor micro tubes are long, thin membrane tubes that sprout from the cells of incurable gliomas and have characteristics similar to axonal and dendritic expansion in growing neurons. In a separate study, it was discovered that neural activity can promote glioma progression via paracrine processes, such as the production of neuroligin-3, which causes glioma cells to express a synaptic gene signature.

Neuronal communication pathways, such as glutamatergic, cholinergic, and adrenergic transmission, are used by tumours outside the brain to promote or inhibit tumour growth. All of these lines of inquiry eventually led to the recent finding of glutamatergic communication between neurons and brain tumour cells, which drives brain tumour development in high-grade paediatric and adult gliomas, as well as breast cancer brain metastases. On glioma cells, both direct synapses and indirect perisynaptic contacts resembling tripartite synapses were seen, but metastatic cells exclusively had perisynaptic contacts. Despite their fundamental differences, we propose that these two concepts be combined here since they both emphasise the delicate interplay between neurons and brain tumour cells. Therefore chose the term “Neuron-To Brain Tumor Synaptic Communication” (NBTSC), which covers both direct and indirect synaptic communication.

Given the difficulty and invasiveness of obtaining tissue samples for histopathological evaluations and genetic profiling, non-invasive in vivo biomarkers that predict tumour grades and molecular subtypes at the time of diagnosis and reflect biological changes over time would greatly benefit clinical assessment. Magnetic Resonance Imaging (MRI) has been extensively used in recent years to extract quantitative data indicating underlying pathophysiological properties of neoplastic tissue, an approach known as "radiomics." By using Three-Dimensional (3D) Volumes Of Interest (3D-VOIs) containing the entire tumour or Two-Dimensional (2D) in-plane Regions Of Interest (2D-ROIs) corresponding to “virtual samples” of the tumour, quantitative imaging-derived features for radiomic analyses can be extracted from either conventional MRI (cMRI) or advanced MRI (aMRI, including diffusion MRI (dMRI) and perfusion-weighted imaging (PWI)) maps. Shape features describe the tumor's geometric appearance, histogram-derived statistics ("first-order" features) describe the distribution of voxel intensities within the tumour (e.g., mean, median, percentiles, skewness), and textural features ("second-order" features) quantify the spatial patterns of voxel intensities among adjacent voxels.

Calcium imaging investigations were used to further establish the functional determinants of NBTSC. Short calcium transients were associated with tumour cell membrane depolarization’s using this approach, implying that synaptic input is translated into a calcium signal that is amplified in the tumour cell and then activates downstream pathways. The exact downstream pathways involved in the translation of synaptic stimulation to biological effects (e.g., proliferation and invasion) found in brain tumour cells will be elucidated in future research.

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