BI-02. DISRUPTION OF PERIVASCULAR ASTROCYTIC FOOT PROCESSES CHARACTERIZES MRI ENHANCEMENT IN PEDIATRIC BRAIN TUMORS

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Preservation of cross-talk between endothelial cells and astrocyte foot processes is vital to the integrity of the blood-brain barrier (BBB). The water channel protein, aquaporin-4 (AQ4), is polarizingly located at astrocytic foot processes surrounding vasculature. This study investigated whether disruption of the normal relationship between endothelial cells and astrocytic foot processes accounts for enhancement on magnetic resonance imaging (MRI) in three common pediatric brain tumors. Immunofluorescence was performed on surgically resected samples of pilocytic astrocytoma (n = 5), medulloblastoma (n = 5), and low-grade glioma (LGG; n = 1), utilizing antibodies against CD31 (an endothelial cell marker), GFAP, and AQ4. Additionally, clinical, radiographic, and histopathological parameters were collected. Radiographically, there was strong, moderate, and absent contrast enhancement of medulloblastomas, pilocytic astrocytomas, and LGG, respectively. Immunofluorescent staining demonstrated complete breakdown of the endothelial cell-astrocytic foot process relationship in medulloblastomas, characterized by scarce perivascular GFAP and AQ4 signals. In pilocytic astrocytomas, there was strikingly disorganized and disproportionately reduced AQ4 staining compared to the strong density of GFAP. In LGG, there was remarkably tight juxtaposition of AQ4 and GFAP signals, such that visualization of AQ4 alone could accurately delineate CD31-positive vasculature. BBB breakdown at the level of the relationship between endothelial cells and perivascular astrocytic foot processes reflected the extent of MRI enhancement in the studied tumors. In strongly-enhancing medulloblastoma, the predominant absence of GFAP- and AQ4-positive cells suggests complete perivascular denuding of astrocyte foot processes and reflects a likely non-glial cell of origin in this tumor. In pilocytic astrocytoma and LGG, GFAP abundance is consistent with the astrocytic nature of these tumors. However, unlike in LGG, AQ4 in pilocytic astrocytoma was disorganized around microvasculature, suggesting the tumor cells, despite being astrocyte-derived, cannot fulfill their physiological role of BBB support. Furthermore, AQ4 polarity around vasculature may better predict BBB integrity than perivascular GFAP in astrocytic tumors.