A Hematogenous Route for Medulloblastoma Leptomeningeal Metastases.


While the preponderance of morbidity and mortality in medulloblastoma patients are due to metastatic disease, most research focuses on the primary tumor due to a dearth of metastatic tissue samples and model systems. Medulloblastoma metastases are found almost exclusively on the leptomeningeal surface of the brain and spinal cord; dissemination is therefore thought to occur through shedding of primary tumor cells into the cerebrospinal fluid followed by distal re-implantation on the leptomeninges. We present evidence for medulloblastoma circulating tumor cells (CTCs) in therapy-naive patients and demonstrate in vivo, through flank xenografting and parabiosis, that medulloblastoma CTCs can spread through the blood to the leptomeningeal space to form leptomeningeal metastases. Medulloblastoma leptomeningeal metastases express high levels of the chemokine CCL2, and expression of CCL2 in medulloblastoma in vivo is sufficient to drive leptomeningeal dissemination. Hematogenous dissemination of medulloblastoma offers a new opportunity to diagnose and treat lethal disseminated medulloblastoma.

KEYWORDS: brain tumors; circulating tumor cells; medulloblastoma; metastases; pediatric cancer

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