Methods: We screened a prospective database of 1892 patients (treated 2006-2017), identified 92 (5%) who lived > 3 years following BM diagnosis, and performed per patient analyses. Results: Median age at diagnosis of BM was 57 years (range 19-77), 77% were women. The most common tumors were lung (50%), breast (26%), thyroid (7%) and skin (5%). 42% had tumors with drug-targetable oncoproteins (e.g. EGFR mutant) and 15% expressed hormonal receptors. ECOG was <2 in 70%. 47% had stage IV disease at diagnosis (75% with brain as the first site). 55% had controlled extracranial disease at the time of BM diagnosis. Median BM diameter was 1.5 cm (range 0.2-7) and 62% had a single lesion. Treatment was with surgery, radiosurgery, whole brain radiation (WBRT), or systemic therapy alone in 38%, 62%, 52%, and 4%, respectively. 53% received targeted- or immuno-therapy. Median follow up was 63 months (range 36-113). 61% failed intracranially at a median 24 months (range 1-99). 5 and 10-year survival (from BM diagnosis) was 82%, and 34%, respectively. Neither upfront WBRT nor other variables tested correlated with improved survival. In patients who died, an MRI was available within 3 months from death in 57%; of those 55% had no active intracranial disease, suggesting that the majority of deaths were non-neurologic. Conclusion: In general, LTS of BM had a limited number of BM, inactive extracranial disease, and drug targetable mutations.

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Radiation induced meningioma in adult survivors of childhood leukemia or primary brain tumor treated with cranial radiotherapy: Incidence and screening recommendations

Maryam Dosani, Jordan Tran, Jessica L Conway, Karen Goddard.
Maryam.Dosani@bccancer.bc.ca

Purpose: Cranial radiotherapy (CRT) was commonly given for childhood leukemia and brain tumors. Survivors are at risk of late effects including radiation induced meningioma (RIM). Surveillance for RIM is not standardized . We aimed to determine the incidence, latency, and screening patterns for RIM. Materials and Methods: Retrospective chart review of all patients aged <18 years at the time of radiation (RT), treated with CRT for leukemia or a brain tumor in BC between 1981-2006. Patient, tumor, and treatment characteristics were collected. Actuarial statistics were calculated with Kaplan-Meier Curves. Patients were censored at the date of last normal cranial imaging, or development of a RIM. Results: 392 patients were identified. Median age (range) at CRT was 9.6 years. Median CRT dose was 28Gy. The original diagnosis was leukemia in 50%, glioma in 13%, medulloblastoma in 8%, ependymoma in 7%, neuroectodermal tumor in 7%, germ cell tumor in 5%, craniopharyngioma in 4%, and other pathologies in 6%. Median (range) of clinical follow-up (FU) was 13.2 (0-37.5) years. Median (range) of cranial imaging FU was 15.5 (0-21.2) years. There was no documented cranial imaging FU in 144 patients. Forty-eight patients developed a RIM. The median age (range) at RT for patients with RIM was 6.7 years. Only 8 of these cases presented with associated symptoms. The earliest RIM in our cohort occurred 10.2 years after CRT. On actuarial analysis, the median (95% CI) time to development of a meningioma was 29.8 (28.9-30.7) years. Incidence (95% CI) of meningioma at 10 years was 0%, 15 years was 5 (2-9)%, 20 years was 12 (6-18)%, 25 years was 33 (23-43)% and 30 years was 47 (37-68)%. Amongst patients with a RIM, the median dose of CRT was 45 Gy. The lowest dose of RT in a patient who developed RIM was 12 Gy. RT was delivered to the whole brain in 58% and partial brain in 42% of patients with a RIM. Conclusions: After CRT in pediatric patients, there is a significant risk of developing a RIM and a steady increase in this risk with ongoing follow-up. We recommend standardization of surveillance for these patients with screening beginning 10 years after completion of CRT.

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Characterization of the molecular consequences of CIC-knockout and neomorphic IDH1 R132H mutation on transcriptomic and epigenomic landscapes

Lee SD, Song J, Chan SY, Chittaranjan S, Marra MA
sdlee@bcgsc.ca

CIC, or Capicua, encodes a transcriptional repressor that is itself repressed by RAS/MAPK signalling. CIC is a recurrent target of somatic mutation in type 1 low grade gliomas (LGG), with at least half of the alterations predicted to be deleterious. Type 1 LGGs are a cohort of tumours that are molecularly defined by the loss of heterozygosity of chromosome arms 1p and 19q and the presence of neomorphic IDH1/2 mutations. Despite the high frequency of mutations in CIC within this tumour type, CIC‟s putative tumour suppressive role remains to be elucidated. It is also unclear how CIC may cooperate with neomorphic IDH1/2 to promote gliomagenesis. To comprehensively characterize the molecular consequences of CIC loss, we performed RNA-seq, Whole Genome Bisulfite Sequencing, and ChIP-seq on 6 different histone modifications on isogenic CIC-wildtype (WT) and CIC-knockout (KO) normal human astrocytes. To also investigate the collective effects of CIC deficiency and neomorphic IDH1 on the transcriptome and epigenome, we generated the same dataset in isogenic CIC-WT and CIC-KO astrocytes possessing the IDH1 R132H mutation. Analysis of differentially expressed genes illustrates the enrichment of oncogenic pathways in specifically the CIC-KO, IDH1-R132H cells, supporting a synergistic relationship between CIC loss and IDH1-R132H in driving tumour progression. Integrative analyses are ongoing to unveil the epigenetic mechanisms underpinning the regulatory changes in these isogenic cell line models.

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A systematic review in quality of life of patients with meningiomas: Effort towards developing a disease-specific questionnaire

A. Mansouri, V. Lam Shin Cheung, B. Karmur, J. Lam Shin Cheung, L. Hachem, S. Taslimi, F. Nassiri, S. Suppiah, K. Drummond, T. Walbert, R. Goldbrunner, Y. Santarius, M. D. Jenkinson, J. Snyder, I. Lee, K. Devine, C. Schichor, K. D. Aldape, G. Zadeh. brij.karmur@mail.utoronto.ca

BACKGROUND: Meningiomas are the most common primary benign brain tumors in adults. Given the extended life expectancy of most meningiomas, consideration of quality of life (QOL) is important when selecting the optimal management strategy. There