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BACKGROUND: The efficacy of salvage resection (SR) of recurrent brain metastases (BrM) post-stereotactic radiosurgery (SRS) is not well described. We sought to characterize the impact of adjuvant post-salvage radiation therapy (PSRT) in this setting and identify tumor-specific variables that influence local control. METHODS: Retrospective analysis of post-SRS recurrent BrM that underwent SR between 2003–2020 at Memorial Sloan Kettering Cancer Center was performed. Cases with histologically-viable malignancy were included and stratified by receipt of adjuvant PSRT within 60 days of SR (PSRT cohort) vs. observation (observation cohort). Resection-site outcomes were described using cumulative incidences and univariate and multivariate competing risks regression accounting for clustering. RESULTS: One-hundred fifty-five recurrent BrM in 135 patients were included. Thirty-nine (25.2%) of the post-operative cavities were treated with adjuvant PSRT, and the remaining 116 (74.8%) cavities were initially observed. Gross- or near-total resection was associated with significantly improved local control compared to subtotal resection (p=0.007). Adjuvant PSRT was associated with a reduced rate of LR at 6 months [18.0% (95%CI: 9.8–33.1%) vs. 35.9% (95%CI: 27.9–46.2%) with initial observation] and 12 months [28.8% (95%CI: 17.0–48.8%) vs. 43.9% (95%CI: 36.2–53.4%)]. On multivariate analysis, adjuvant PSRT (p=0.095), low tumor-viability within the resected BrM (p=0.17), and first-time resection (p=0.035) all independently trended towards improved local control. BrM size at SR (≥3cm vs. <3cm, p=0.48), primary malignancy (p=0.35), and specific PSRT modality (whole or partial brain radiation vs. SRS, p=0.43) were not associated with differences in LR rate. Radiation necrosis (RN) was significantly increased in the PSRT cohort (HR 4.55, 95%CI: 1.26–16.39, p=0.02), though the total percentage with symptomatic RN remained low (PSRT cohort 5.1% vs observation cohort 0.9%). CONCLUSIONS: Local control after SR of a recurrent BrM may be optimized with gross- or near-total resection and adjuvant post-operative re-irradiation, with low symptomatic RN.

MLTI-06. SURGICAL RESECTION PLUS STEREOTACTIC RADIOSURGERY VERSUS SRS ALONE FOR LARGE BRAIN METASTASES: A COMPARATIVE STUDY

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PURPOSE: Large brain metastases (BRM) are challenging to manage. Therapeutic options include Stereotactic Radiosurgery (SRS) or surgery (S) with adjuvant SRS. We sought to compare overall survival (OS), radionecrosis (RN), local failure (LF), pachymeningeal (PMD) and leptomeningeal (LMD) disease in patients treated with SRS vs. S+SRS. METHODS: We reviewed a prospective registry database from 2009 to 2020 and identified all patients with BRM (≥4cc in volume) treated with SRS or S+SRS. WBRT or SRS re-targeting the index lesion were censoring events. Survival percentages were calculated using the Kaplan-Meier method. Differences between groups were tested using the Cox proportional hazards model. RESULTS: 383 patients were identified, 128 and 255 were treated with S+SRS and SRS, respectively. Median ages in the S+SRS and SRS groups were 62.2 (23.6–98.5) and 60.2 (20.2–97.4) (P 0.33). OS at 12 and 24 months was 69% and 41% vs 55% and 20% for the S+SRS and SRS groups, respectively hazard ratio (HR) 1.64 (1.23–2.18) (P<0.001). LF requiring salvage surgery at 12 and 24 months were 3% and 5% vs 8% and 10% for S+SRS and SRS groups, respectively (P 0.067). RN at 12 and 24 months were 9% and 17% vs 15% and 21% for S+SRS and SRS groups, respectively 1.32 HR (0.77–2.29) (P =0.32). PMD disease at 12 and 24 months were 16% and 21% vs 3% and 7% for S+SRS and SRS groups, respectively HR 0.26(0.12–0.56) (P < 0.001). LMD at 12 and 24 months were 4% and 6% vs 2% and 4% for S+SRS and SRS groups, respectively HR 0.73(0.25–2.17) (P 0.57). CONCLUSION: Surgical resection plus SRS correlated with improved OS and a trend towards a decreased incidence of LF compared to SRS alone. However, patients treated with S experienced an increased incidence of PMD.

OTHER

OTHR-01. UNMET CLINICAL NEEDS IN PATIENTS WITH BRAIN METASTASES IN THE CURRENT TREATMENT ERA

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INTRODUCTION: Brain metastases are associated with high morbidity and mortality. With the implementation of effective treatments, long-term survival is possible for some patients. However, most patients still die of their disease. The uncertain prognosis and potentially high symptom burden make managing these patients complex. We aimed to identify the unmet needs in the care of patients with brain metastases. METHOD: Consecutive patients with melanoma or NSCLC brain metastases completed questionnaires assessing distress (distress thermometer), quality-of-life (FACT-general), and information provided on potential symptoms, supportive care, and do-not-resuscitate code (study-specific questionnaire) between Nov'18-Nov'19. Separate focus groups were organized with patients with melanoma brain metastases, primary caregivers of deceased patients, and general practitioners. The results were discussed with hospital-based healthcare professionals to identify additional issues. RESULTS: Questionnaires were completed by 59 patients (25 melanoma, 34 NSCLC) at a median time after brain metastases diagnosis of 11.5 months (range: 0.7–88). Thirty-five patients (59%) experienced distress (distress thermometer ≥4), and 20 patients (34%) expressed interest in supportive care. Furthermore, 40 patients (68%) remembered being informed about potential brain metastases symptoms, and 18 patients (31%) would have liked more information on potential symptoms. Psychosocial support was offered to 31 patients (53%) and 17/51 primary caregivers (33%). Patients emphasized that, despite potential information overload, they preferred to be fully informed about potential symptoms, treatments including outcomes, and psychosocial support availability. Caregivers highlighted the caregiver burden and importance of advance care planning. General practitioners were keen for guidelines on brain metastases symptom management in the home setting. Hospital-based professionals advocated a structured approach, with early identification of palliative care needs and an overview of involved healthcare professionals. CONCLUSION: Our results highlight the need for structured, multidisciplinary management of patients with brain metastases with special attention to symptom and caregiver burden, information provision, and advance care planning.

OTHR-02. ENGINEERED "OF THE SHELF" ALLOGENEIC CELLULAR THERAPIES FOR METASTATIC BRAIN TUMORS

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Brain metastatic patients have multiple metastatic lesions or diagnostically challenging asymptomatic lesions, making surgery an inadequate therapeutic option. Given the challenges related to systemic delivery of a majority of therapeutic agents across the BBB, engineered cell based therapies offer an excellent platform to target metastatic tumors in the brain. We have established the use tumor cell surface receptor targeted allogeneic "off the shelf" gene engineered cellular therapies and developed two different approaches to treat brain metastases. In one approach, we have armed allogenic stem cells (SC) with oncolytic herpes virus (oHSV) variants and tested them in different mouse models of brain metastatic (BM) tumor derived from brain seeking metastatic melanoma tumor cells from patients. We show that intracarotid artery administration of SC-oHSV effectively tracks metastatic tumor lesions and significantly prolongs the survival of brain tumor bearing mice. We also show that a combination of SC-oHSV and PD-L1 blockade increases IFNγ-producing CD8+ tumor-infiltrating T lymphocytes and results in a profound extension of the median survival in syngeneic brain metastatic melanoma mouse models. In another approach, we have explored the versatility of cell mediated bi-functional EGFR and DR4/5-targeted treatment in basal like breast cancer (BLBC) mouse models featuring different patterns of brain metastasis. Most BLBC lines demonstrated a high sensitivity to EGFR and DR4/5 bi-targeting therapeutic protein, EVDRL [anti-EGFR VHH (EV) fused to DR ligand (DRL)]. Functional analyses using inhibitors and CRISPR-Cas9 knockouts revealed that the EV domain facilitated in augmenting DR4/5-DRL binding and enhancing DRL-induced apoptosis. EVDRL releasing allogeneic SCs alleviated tumor-burden and significantly increased survival in mouse models of residual-tumor after macrometastasis resection, perivascular niche micrometastasis, and leptomeningeal metastasis. These findings provide a clinically applicable therapeutic platform to target disseminated metastatic lesions in the brain and define a new paradigm for treatment of brain metastases.

OTHR-03. BRAIN METASTASIS AMONG OVARIAN CANCER PATIENTS

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BACKGROUND: Brain metastasis (BM) are uncommon among ovarian cancer (OC) patients. Their frequency, risk factors and clinical repercussions are not well described. We assessed OC patients who developed BM, the role of BRCA status and survival implications. METHODS: Study cohort included OC patients treated at our center, from 2002–2020. We retrospectively evaluated clinical parameters, risk for BM development and association with survival data. RESULTS: Among 972 OC patients, 28 (2.9%) were diagnosed with BM. Comparing the BM to non-BM group, median age of 60 across both groups, stage III-IV at diagnosis was more common among BM group (96.4% vs. 84.8%, p=0.0065) while platinum sensitivity was similar

(92.3% in BM vs. 80.8% in non-BM, p=0.2193). Out of 658 patients tested for BRCA, 33.6% (n=221) were BRCA mutation carriers (BRCA+). Of the patients with BM, 22 tested for BRCA, 13 were carriers. BRCA+ was significantly higher in the BM group compared to the non-BM group (59.1% vs. 32.9%, p=0.0123). Among BRCA+ the rate of BM was higher than among BRCA- (5.8% vs. 2.1%, p=0.0123, HR=3.029; 95%CI: 1.4–6.5). Median time from OC diagnosis to BM and from disease recurrence to BM, was longer for BRCA+ compared to BRCA- (44.3mo vs. 32.3mo and 11.8mo vs. 0.7mo, respectively). Median survival (mOS) was not significantly different among patients with BM compared to those without BM (59.4mo vs. 71.2mo, p=0.36). Following diagnosis of BM, mOS was 20.6mo among BRCA+ and 12.3mo among BRCA- (p=0.4266). No correlation was demonstrated with PARP inhibitors or bevacizumab treatment and subsequent development of BM. CONCLUSION: BM are an infrequent event among OC patients. However, the risk is three-folds higher among BRCA+. Interestingly, BM do not significantly alter survival among OC patients. Our work suggests that the higher rate of BM in BRCA+ may be related to longer survival. Another hypothesis requiring further evaluation, is possible higher brain tropism among this population.

OTHR-04. GYNECOLOGICAL MALIGNANCIES WITH METASTASIS TO THE CENTRAL NERVOUS SYSTEM: A CASE SERIES AND SYSTEMATIC REVIEW OF THE LITERATURE

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INTRODUCTION: Gynecologic malignancies are an increasingly common proportion of central nervous system metastatic disease. As genetic sequencing technology improves and becomes more accessible, mutations associated with CNS metastasis are easier to elucidate. The aims of this case series and systematic literature review are to describe the patient population with CNS metastatic disease from a gynecologic primary, and to investigate why the proportion of CNS metastasis from gynecologic malignancies is increasing. Ultimately, we hope to improve understanding of this subset of metastatic CNS malignancies and improve management strategies. METHODS: A literature review of articles describing patients from 1990–2020 who were diagnosed with CNS metastasis from a known gynecologic primary malignancy was performed. Demographics, cancer type, mutation characteristics, management for metastatic disease, progression free survival, number of CNS metastases, and location of metastatic disease were assessed. Inclusion criteria were age>18 years, diagnosis of primary ovarian, uterine, or cervical cancer with confirmed metastatic disease to the CNS, including brain parenchyma, leptomeninges, or intradural spinal cord or dural metastases. Exclusion criteria included pediatric population and bony metastases (e.g., bony spine metastases without evidence of meningeal/parenchymal invasion). RESULTS: Our review showed that patients with gynecological metastasis to the CNS generally have worse outcomes regarding overall survival, progression free survival, and quality of life than patients without CNS metastasis. DISCUSSION: Our results infer that the reported increase in incidence of CNS metastasis from gynecologic malignancies is a reflection of improvement of detection given advances in technology, improved patient follow up, and increased overall survival of patients with gynecologic malignancies. Further characterization of mutations from gynecologic malignancies associated with brain metastasis could result in development of more treatment options for patients in the future and help determine factors that contribute to developing metastasis to the CNS of various degrees, thus, potentially inform treatment strategies.

OTHR-05. DIAGNOSIS AND TREATMENT OF SOLITARY PITUITARY METASTATIC CANCER: A CASE SERIES

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OBJECTIVE: Metastatic pituitary carcinoma accounted for only 1% of pituitary lesions. METHODS: Patients with isolated pituitary metastatic carcinoma admitted to our hospital from 2014 to 2018 were retrospectively collected, clinical features and prognosis were analyzed. RESULTS: A total of 5 patients (4 males and 1 female) with a median age of 48 years (21 to 66 years) were included, all with single intracranial pituitary nodules as the initial clinical presentation. The related symptoms were visual impairment (5/5 cases), hypopituitarism (5/5 cases), visual field defect (5/5 cases), headache (4/5 cases), hypothyroidism (4/5 cases), diabetes insipidus (2/5 cases). All the 5 patients received surgical resection (total or partial resection) of tumors in the sellar region via nasal sphenoidal approach. Postoperative pathology confirmed that 4 cases were metastatic adenocarcinoma and 1 case was metastatic squamous carcinoma. Further imaging examinations, such as CT or whole-body PET/CT, confirmed that the primary lesions of all the 5 patients were from the lung. Gene testing indicated that 3 of the 4 adenocarcinoma patients were EGFR mutation positive and 1 of the 4 adenocarcinoma patients was ROS1 mutation positive. Patients received radiotherapy (5/5 cases), targeted therapy (4/5 cases), or chemotherapy (1/5 cases) after surgery. Survival follow-up to May 2019 showed that 4 patients had died, with a survival of 2, August, 28, and 30 months, respectively, and 1 patient was still alive with a survival of 4 months. CONCLUSION: The first clinical manifestation of isolated pituitary metastatic carcinoma is nervous system related symptoms, which is easily misdiagnosed. The most of the primary lesions are from lung, especially lung adenocarcinoma with positive driver gene. Surgery, radiotherapy combined with targeted therapy or chemotherapy can provide survival benefits for patients with pituitary metastatic carcinoma.

OTHR-06. PACS LESION TRACKING TOOL PROVIDES REAL TIME AUTOMATIC INFORMATION ON BRAIN TUMOR METASTASIS GROWTH CURVES AND RECIST CRITERIA

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OBJECTIVE: Communicating metastatic brain treatment response can be complicated. A widely used method to assess clinical response is called response evaluation criteria in solid tumors or RECIST. In our study, we use a PACS Lesion Tracking Tool (TT) to assess intracranial metastasis using RECIST criteria. We predict that the TT will be superior to the standard radiology reports. METHODS: Nuance ® mPowerTM was used to identify 30 patients with brain metastasis who received brain MRI from 4/2020–4/2021. Patient's first brain MRI with metastasis was set as baseline and subsequent 3 brain MRI studies were examined. All lesions were measured on post-gadolinium sequence and defined as target lesions or new lesions. The TT was used to measure lesion size over time with creation of growth curves and RECIST outcomes, which include stable disease, progressive disease, partial response, or complete response. Subsequently, RECIST evaluations were compared with radiologic impressions for discrepancy, and further evaluations were made to see if it made a clinical difference in patient management and/or provide additional useful information. These evaluations were given a rating of agree/yes, equivocal, or disagree/no. They were assessed by 3 neuroradiologists. RESULTS: Number of lesions ranged from 1–27. The assessments from 3 neuroradiologists were averaged. Comparing impression versus RECIST evaluation, the results demonstrated the following: 8/30 disagreement, 4/30 equivocal, and 18/30 agreement. Using more stringent criteria, assessing whether the TT would result in either change in patient management or provide additional useful information, the results were the following: 6/30 yes, 4/30 equivocal, and 20/30 no. DISCUSSION: In addition to providing real time RECIST criteria evaluations and visually descriptive lesion growth tables, the TT was easy to use. Interpretation of these additional data provided more clarity and was found to be superior to standard radiology report.

OTHR-07. SYSTEMATIC REVIEW AND META-ANALYSIS OF LUNG CANCER BRAIN METASTASIS AND PRIMARY TUMOR PD-L1 EXPRESSION DISCORDANCE

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BACKGROUND: Novel immunotherapeutic strategies, such as those targeting the PD-1/PD-L1 axis, are promising in patients with metastatic lung cancer and are often administered when tumors show PD-L1 positivity. The objective of this study was to analyze PD-L1 receptor discordance in tumor cell between the primary tumor and lung cancer brain metastasis (LCBM). METHODS: A systematic review of series published prior to April 2021 obtained from the Medline database of biopsied or resected LCBM evaluating PD-L1 discordance was performed using PRISMA guidelines. Weighted random effects models were used to calculate pooled estimates. RESULTS: Six full-text articles (n=247 patients) with a median of 32 patients in each study (range: 24–73 patients) reported PD-L1 receptor expression analyses of both primary lung tumors and brain metastases. The majority of patients (81%) were smokers, with 67% non-small cell lung cancer and 33% small cell lung cancer. The pooled estimate for overall PD-LI receptor concordance between primary and LCBM was 76% (95% CI: 52%-90). The positivity rate varied when analyzed by various cutoff levels of PD-L1 expression; for <1% ex-