61. EXPRESSION OF ANDROGEN RECEPTOR IN BREAST CANCER BRAIN METASTASIS

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INTRODUCTION: Treatment options for women with breast cancer brain metastases (BrM) are generally limited to surgery and/or radiotherapy because most systemic therapies do not cross the blood-brain barrier. Androgen receptors (ARs) are frequently expressed in breast cancer and anti-androgenic therapies have been shown to penetrate the central nervous system. In this study, we analyzed the expression of AR in breast cancer BrM to identify patients who may benefit from anti-androgenic therapies.

METHODS: Consecutive BrM resected in our institution (July 1999 - June 2013) were identified from the Anatomic Pathology departmental database. Cases that were signed out as breast origin given the available immunohistochemical profile and clinical history were included. A tissue microarray was constructed using 1 mm cores in triplicates and stained by immunohistochemistry for AR, ER, PR and HER2 (SP170, SP1, IE2385; Ventana Medical Systems, Tucson AZ, USA). HER2 gene amplification was determined by INFORM HER2 DNA and Chromosome 17 (both by Ventana Medical Systems, Tucson AZ, USA). Immunohistochemistry was used to determine intensity of staining using 3+ (strong nuclear staining), 2+ (moderate nuclear staining), and 1+ (weak nuclear staining) for AR, ER, PR and HER2. 61 breast cancer BrM with available tissue blocks, AR was expressed in 38 (62%) cases. Among BrMs of luminal A subtype (ER+, PR+, HER2-), Ki67<16%), 50% expressed AR (n=12). Within the luminal B subtype (ER+, PR+/-, HER2+), 75% expressed AR (100%), whereas in HER2+ breast cancer BrM 66% expressed AR (n=8/12). Among 14 BrM of HER2+ subtype (ER-, PR-, HER2+), 71% expressed AR (n=10/14). Only 30% of triple negative BrM (ER-, PR-, HER2-) were AR+ (n=4/14); CONCLUSION: Almost two-thirds of breast cancer BrM expressed AR. HER2+ luminal B and HER2+ subtypes were most likely to be AR+, while only 30% of triple negative BrM were AR+. Our data suggests that certain subtypes of breast cancer BrM are more likely to be AR+ and could serve as a potential therapeutic target.

62. PRESENCE OF EXTRACRANIAL TUMORS INFLUENCES RESPONSE TO IMMUNE CHECKPOINT INHIBITORS IN A PRE-CLINICAL MODEL OF MELANOMA BRAIN METASTASIS

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Up to 75% of patients with melanoma develop brain metastases. While immune checkpoint inhibitors (ICI) targeting PD-1 and CTLA4 have revolutionized the treatment of metastatic melanoma, responses within the immune-specialized microenvironment of the brain are not well understood and there is a paucity of animal models to investigate the effect of ICI intracranially. We characterized responses to checkpoint inhibitors in a syngeneic mouse model of melanoma brain metastasis with concurrent intracranial and extracranial melanoma. D204V3 melanoma (obtained from David Fisher laboratory) were derived using UVB irradiation from D4M.3A melanoma cell line and implanted into the striatum using stereotactic injection or subcutaneously injected into the flank of C57BL/6 mice. Mice were then treated with anti-PD-1 antibody, anti-CTLA4 antibody, a combination of anti-PD-1 and anti-CTLA4, or isotube controls. While mice with intracranial melanoma alone had no response to monotherapy with anti-PD-1 or anti-CTLA4 antibody (p>1 and 0.1, respectively), and only a slight response to combination with concurrent subcutaneous tumors had significantly improved responses to anti-PD-1, anti-CTLA4 and combination treatment (p=0.002, 0.01 and 0.01 respectively compared to mice with intracranial tumors alone with equivalent treatment). These results demonstrate that the presence of extracranial tumor can augment response to ICI in pre-clinical mouse models of melanoma brain metastasis. We have therefore established a pre-clinical model with concurrent intracranial and extracranial tumors to better recapitulate the clinically observed context of melanoma brain metastases and lead to a better understanding of the setting in which ICI are effective for patients with this devastating complication.
important prognostic factor that should be considered by clinicians treating BrM patients. We identify CIRBP as a functional mediator of this process.

66. CLINICAL CHARACTERISTICS AND RESULTS OF PEDIATRIC SOLID TUMORS WITH BRAIN METASTASES: EXPERIENCE FROM A SINGLE REFERRAL CANCER CENTER

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BACKGROUND: 80% of childhood cancer are located in low- and middle-income countries (LMIC). The most common form of presentation is disseminated or metastatic disease. The rate of survival has not been equitable across the world, since in these countries only 1 of 5 children are cured. OBJECTIVE: To evaluate the clinical and pathohistological features of patients with metastatic pediatric solid tumors, in a single referral cancer center in Honduras. METHODS: We conducted a retrospective review of patients diagnosed with pediatric solid tumors from January 2010 to April 2020. Among the 260 patients through a collection form, we obtained: sociodemographic characteristics, clinical presentation at diagnosis, common histological subtypes, sites of metastasis, treatment and outcome at the time of follow-up. RESULTS: During the last 10 years, 260 cases of childhood cancer were referred to our center for treatment. 127 patients (48.8%), have a solid tumor, patients ranged in age from 1 to 18 years and distribution for sex was 38% for male and 62% females. At the time of initial diagnosis 40/127 (31%) have advanced disease (stages III and IV). We found brain metastases in 22/40 cases (55%), the primary cancer was localized at CNS in 13/22 (59%) and the most common extracranial tumors causing brain metastases were neuroblastoma (4/22), rhabdomyosarcoma (3/22), retinoblastoma (2/22). Currently in the follow-up there were 18/22 (82%) died and 4/22 (18%) are in treatment with palliative intent. CONCLUSION: There is a lack of information about the epidemiology of brain metastases among children with solid tumors in the low/middle income countries (LMIC) where the prognosis of metastatic disease is very poor, despite efforts, multimodal therapy and multidisciplinary management, in absence of other options like bone marrow transplantation, and reliable access to high-quality medicines. For our countries, timely diagnosis is still the main determining factor for cure.

67. INCREASED RISK OF BREAST CANCER BRAIN METASTASIS WITH EGFR AND KI-67 EXPRESSION: A SYSTEMATIC REVIEW AND META-ANALYSIS

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PURPOSE: This study aims to conduct a systematic review of the literature to identify biomarkers associated with breast cancer brain metastasis (BrM) and BCBM. A systematic review was conducted in PubMed, Embase, Web of Science, and Cochrane for relevant literature up until October 1, 2018. Case reports, conference abstracts, and expert opinions/letters were excluded. Studies were included if they investigated risk factors for BCBM in a cohort of patients with locoregional or metastatic breast cancer of any subtype. RESULTS: Of 364 studies that were screened, 117 were selected for inclusion and review. Twenty-eight unique biomarkers were investigated, of which three (EGFR, Ki-67, and p33) were assessed by more than two authors. In a pooled analysis of 3 studies, EGFR expression was associated with an increased risk of BM (RR 3.48, 95% CI 2.27–5.32, P=0.0%, p-interaction = 0.39, n= 571 patients). In a pooled analysis of 5 studies, increased Ki-67 expression was associated with an increased risk of BM (RR 2.91, 95% CI 1.96–4.32, P=59%, p-interaction = 0.05, n= 1,178). In a pooled analysis of 4 studies, p33 expression was not associated with a statistically significant increased risk of BCBM with p33 was not found to be statistically significant. Future studies are needed to develop more robust prediction models, as well as evaluate the other biomarkers identified in this study, which could help clinicians identify patients at high risk of breast cancer brain metastasis.

68. FRAMELESS, VAULT-FREE RADIOSURGERY: INITIAL CLINICAL EXPERIENCE WITH THE ZAP-X STEREOTACTIC SYSTEM

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The Zap-X is a novel self-contained and self-shielded dedicated radiosurgery system developed and manufactured by ZAP Surgical Systems, Inc. of San Carlos, California. Intended for the stereotactic radiosurgery (SRS) treatment of benign and malignant intracranial and cervical spine lesions, this gyroscopically stabilized 3 megavolt (MV) linear accelerator (LINAC) provides a unique radiosurgical alternative for selected patients. Beginning in January 2019, a total of 38 metastatic lesions in 24 patients were treated in our facility. Radiation prescription doses ranged from 1500–1900 Gy (single fraction) to 2300 Gy (five fractions), with treatment volumes ranging from .04 to 15.3 cc. Dose times averaged 45 minutes or less. Target coverage, dose homogeneity, and conformity were comparable to the existing Gamma Knife, CyberKnife and LINAC-based radiosurgery treatment systems in daily use at our facility. As with other frameless radiosurgery platforms, the Zap-X proved particularly useful in situations where either surgery or single-fraction radiosurgery was considered a less desirable treatment option; or when fractionated radiosurgery was thought to be radiobiologically advantageous. All treatments were completed without complication. At two months post-treatment, all lesions showed complete or partial response to therapy based on MRI scan. None of our patients experienced treatment-related skin reaction, cognitive deficits, fatigue or steroid dependency. Among patients who had previously undergone Gamma Knife treatment, there was a clear preference for frameless radiosurgery. In our experience, the Zap-X delivery system offers a high-precision, patient-friendly and cost-effective alternative to traditional dedicated radiosurgical platforms.

69. PERMANENT INTRACAVITARY CS131 BRACHYTHERAPY FOR PREVIOUSLY-IRRADIATED RECURRENT BRAIN METASTASES: INITIAL CLINICAL AND RADIATION SAFETY EXPERIENCE

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OBJECTIVE: Recurrence of previously-irradiated brain metastases (BrM) presents a significant challenge. We describe our initial experience using salvage resection with Cs131 brachytherapy in previously-irradiated BrM. METHODS: Between September 2019 and April 2020, 9 patients with recurrent BrM underwent maximally-safe metastasectomy. Following pathological confirmation of viable recurrence, cavities were implanted with permanent Cs131 brachytherapy (GammaTile, GT Medical Technologies). Prescribed dose was 60Gy at 5mm from the cavity. Postimplant dosimetry (V100) was calculated on postoperative day 1 fused CT/MRI. Intraoperative team exposure was recorded using intraoperative ring dosimetry, and patient dose-rates measured postoperatively informed patient, family and medical-staff exposure modeling. RESULTS: Nine patients (55% female, median age 54) underwent 10 implantations (6 supratentorial, 4 infratentorial). Median preoperative maximum diameter was 3.5cm (2.3–6.3) and histologies included breast, gastrointestinal, lung, kidney and oral cavity squamous cell carcinomas. Five had undergone prior resection or laser ablation. All lesions received ≤81 Gy in 3 fractions. Median V100 dose coverage of the cavities and uniform 5mm expansion of the cavities were 99% (79–100%) and 79% (51–95%), respectively. Median measured exposure rates were 90mR/hr (28–152) on contact, 9.13mR/hr (2.7–13.9) at 30cm and 1.4mR/hr (0.6–2.3) at 1 meter from the patient. Mean ring dose was 6.83mrem (0–18) for the radiation oncologist and 19.7mrem (0–15) for the neurosurgeon. Modeled lifetime family-member and visitor exposure was 116mrem (52-193mrem) and healthcare worker exposure was 39mrem (17-64mrem), all well below regulatory limits. There were no immediate wound complications or unanticipated neurologic injuries. CONCLUSION: In our early experience, salvage interstitial Cs131 implantation was safely employed for recurrent brain metastases.

70. A PHASE 1–2 CLINICAL TRIAL OF EO1001, A NOVEL IRREVERSIBLE PAN-ERBB INHIBITOR WITH PROMISING BRAIN PENETRATION

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CNS metastasis has become a prominent driver of morbidity and mortality in recent years as new targeted therapies have improved systemic outcomes. Mutations in the ErbB family of kinases are known oncdrivers in many of these tumors. ErbB family member “crosstalk” is associated with rapid development acquired resistance to ErbB TKIs. The development of agents targeting