They are often hypervascular and locally adherent, which increases hemorrhage risk and limits surgical resection, leading to increased risk of recurrence. We report a case of SCO treated at our institution and provide a review of the current literature. METHODS: A 75-year-old male with a history of hypertension, left thalamic stroke, Parkinson's disease, and normal pressure hypertension presented to neurosurgery clinic with bitemporal hemianopsia, hyponatremia, and abnormal gait and mobility. Imaging showed an enhancing intra- and suprasellar, hyperdense tumor mass measuring 3.0 cm in diameter. We performed a systemic literature search in the PubMed database to identify previous reports of spindle cell oncocytoma. After exclusion of studies that did not meet criteria, 32 publications were selected for critical reading. RESULTS: The patient underwent an endoscopic transsphenoidal resection of the tumor via a multi-disciplinary team. The tumor was fibrous and adherent to the intrasellar dura, with gross invasion of the diaphragm sella, necessitating partial resection of the diaphragm. The defect was repaired, and the patient made an uncomplicated recovery. Post-operatively, the patient experienced improved vision. Upon literature review, SCO present in older adults with an average age of 56.2 ± 14.7 with visual deficits (67.9%), headache (33.3%), hypopituitarism (24.7%), and nausea (11.1%). Full resection was achieved in 38.6% of cases leading to recurrence rate of 23.5% with an average time until recurrence of 32.5 months (range 1-120 months). CONCLUSION: Careful surgical technique is needed due to SCO hypervascularity and strong adherence to minimize risk of injury to surrounding neurovascular structures. Long-term follow up is recommended due risk of recurrence.

TUMOR MICROENVIRONMENT/ANGIOGENESIS/ METABOLISM/INVASION

TAMI-01. BRAIN METASTASES: CURRENT LITERATURE REVIEW

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PURPOSE: As more information is gathered about brain metastases, it still remains that the current prognosis of brain metastases is very poor. Due to this, it is imperative that physicians are aware of the most important components regarding brain metastases. This literature review will encompass the most current literature in order to highlight the most crucial information. METHODS: All mentioned studies and literature reviews cited in the paper were obtained through various sites, and were published between 1996 and 2017. The main components that were required from the papers reviewed included where in the body the brain metastases originated from, where in the brain they tended to spread to, what the signs and symptoms typical of patients with brain metastases are, and what the options are in terms of treatment. RESULTS: Using the results from a variety of studies performed within the past three decades, it is apparent that brain metastases most commonly originate from, in order of increasing frequency, lung cancer, breast cancer, melanoma, and colorectal cancer. In addition, it is reaffirmed that the magnetic resonance imaging (MRI) is the best diagnostic tool to be used when dealing with brain metastases. The most frequent signs and symptoms of a brain metastases include cognitive changes, headaches, weakness, and seizures. Finally, supportive treatment includes use of corticosteroids, antiepileptic drugs (AEDs), and anticoagulation therapy. Definitive treatment for brain metastases varies based on size, location, and prevalence in the brain, but the most effective options include chemotherapy, radiation therapy, and surgery. CONCLUSIONS: The study's results confirm the need for more research to be done regarding brain metastases, and better options to increase the survival of patients.

TAMI-02. DEPLETION OF INTRATUMORAL TUMOR-ASSOCIATED MACROPHAGES AND MICROGLIA (TAM/M) IMPROVES CHECKPOINT-INHIBITION THERAPY FOR BRAIN METASTASIS FROM LUNG CANCER

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BACKGROUND: Brain metastases dramatically limit prognosis of lung cancer patients. Unlike systemic disease, brain metastases from lung cancer poorly respond to checkpoint-inhibition therapy. Targeting the immunosuppressive tumor-associated macrophages and microglia (TAM/M) and their receptor CSF1R may increase efficacy of checkpoint-inhibitors. METHODS: Cranial windows were prepared in fully immunocompetent, transgenic CX3CR1$^{GFP/wt}$-mice with green-fluorescent TAM/M. Intracranial injection of red-fluorescent Lewis Lung Carcinoma-cells was performed, and mice received one of the following three treatments: PD1-inhibition only (n = 8); PD1-inhibition combined with an anti-CSF1R-antibody (exhibiting limited blood-brain-barrier permeability under physiologic conditions, n = 8); or PD1-inhibition combined with a small molecular CSF1R-inhibitor (exhibiting high blood-brain-barrier permeability, n = 7). Tumor growth and TAM/M were followed by repetitive two-photon laser-scanning-microscopy over weeks. RESULTS: Following intracranial injection, metastases were detected in all three treatment groups within eight days. In mice receiving PD1-inhibition only, metastases showed exponential growth which was paralleled by intra- and peritumoral accumulation of TAM/M. Treatment with an anti-CSF1R-antibody resulted in significantly lower numbers of intratumoral TAM/M given increased tumoral blood-brain-barrier permeability, but did not substantially affect peritumoral TAM/M or TAM/M localized in the healthy contralateral hemisphere. In contrast, treatment with a small molecular CSF1R-inhibitor not only reduced the number of intratumoral TAM/M, but also of peritumoral and contralateral TAM/M. Compared to PD1-inhibition only, the addition of either an anti-CSF1R-antibody or a small molecular CSF1R-inhibitor resulted in decreased tumor growth (tumor size on day 12: 8.3 mm^2 (PD1-inhibition only) versus 0.9 mm^2 (PD1-inhibition + anti-CSF1R-antibody) versus 2.5 mm^2 (PD1-inhibition + small molecular CSF1R-inhibitor)) (p = 0.01). The beneficial effects of the small molecular CSF1R-inhibitor in reducing tumor growth were similar to those of the anti-CSF1R-antibody. CONCLUSION: Targeting intratumoral TAM/M using CSF1-inhibition may increase the efficacy of checkpoint-inhibition therapy for cerebral lung cancer metastases. This approach warrants further evaluation in preclinical and clinical studies.

TAMI-03. PROGNOSTIC SIGNIFICANCE OF NEUTROPHIL-TO-LYMPHOCYTE RATIO (NLR) IN PATIENTS WITH BRAIN METASTASES FROM DIFFERENT TUMOR ORIGINS

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PURPOSE: Brain metastases (BMs) represent the most common adult intracranial malignancy. The prognosis of BMs is subject to many factors, *i.e.*, the number, size and locations of the metastatic sites, tumor origins, pathologic types, gene mutation status, metastatic sites, and KPS *etc*. This study aimed to evaluate the prognostic value of neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and lymphocyte-to-monocyte ratio (LMR) in brain metastases. METHODS: A total of 480 patients diagnosed with brain metastases from a wide range of tumor origins, *i.e.*, NSCLC, SCLC, breast cancer, melanoma, prostate, kidney, gastrointestinal cancer, cervical carcinoma, ovarian cancer, choriocarcinoma of uterus were retrospectively analyzed. Pre-radiotherapy NLR, PLR, and LMR were calculated as total neutrophil/lymphocyte, platelet/Lymphocyte, lymphocyte/monocyte, respectively. Survival rates were estimated using the Kaplan-Meier survival analysis. Cox regression models were used to identify independent prognostic factors. RESULTS: The median overall survival (OS) was 14.4 months [95%CI: 13.4-15.5]. The median overall survival after radiotherapy was significantly different between patients with NLR< 4 and those with NLR≥4 (OS 16.3 mo. vs. 12.2 mo., P< 0.0001). No significant difference was observed between PLR vs. OS, and LMR vs. OS (PLR< 180: HR=1.221, P=0.240; LMR< 4: HR=0.753, P=0.141). The Cox regression model for the continuous metric values revealed that the NLR increased every 1.0 was associated with additional 5.9% of fatal risk (HR: 1.059; 95%CI = 1.033–1.087, P< 0.0001). NLR was validated as an independent prognostic factor for risk of death after adjusting for sex, age, and KPS. CONCLUSIONS: We revealed pre-treatment NLR is an independent prognostic factor in patients with brain metastases for poor OS, independent of different tumor origins. The NLR warrants further studies using sub-group analysis and validation in external cohorts. Future studies in this parameter have a potential to facilitate more precise risk-stratifications to guide personalized treatment for BM.

TAMI-04. OLFACTORY RECEPTOR 5B21 DRIVES BREAST CANCER BRAIN METASTASIS THROUGH STAT3/NFKB/CEBPB PATHWAY

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Olfactory receptors (ORs), responsible for the sense of smell, play an essential role in various physiological processes outside the nasal epithelium, including cancer. In breast cancer, however, the expression and function of ORs remain understudied. We established a breast cancer metastasis model by intracardiac injection of MDA-MB-231 (231P) in immunocompromised mice and produced a series of derivative cell lines from developed metastatic sites, including the brain-seeking clone (231Br). We examined the significance of ORs transcript abundance in primary and metastatic breast cancer to dif-

ferent tissues, including the brain, bone, and lung. While 20 OR transcripts were differentially expressed in distant metastases, OR5B21 displayed high expression in all three metastatic sites with respect to the primary tumor, especially in brain metastasis with 13 fold higher than the primary site. Metastatic clones showed distinguishing higher invasion biological characteristics compared to parental cells in vivo and in vitro. Knockdown of OR5B21 significantly decreased the invasion and migration of MDA-MB-231 Brain-seeking metastatic cell as well as metastasis to different organs, including the brain, while overexpression of OR5B21 had the opposite effect. Mechanistically, OR5B21 expression was associated with epithelial to mesenchymal transition through the STAT3/NFkB/CEBPβ signaling pathway. We propose OR5B21 (and potentially other ORs) as a novel oncogene contributing to breast cancer brain metastasis and a potential target for adjuvant therapy.

TAMI-05. FATTY ACID SYNTHESIS IS REQUIRED FOR HER2+ BREAST CANCER BRAIN METASTASIS

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Brain metastases are refractory to therapies that control systemic disease in patients with human epidermal growth factor receptor 2-positive breast cancer and the brain microenvironment contributes to this therapy resistance. Nutrient availability can vary across tissues, therefore metabolic adaptations required for brain metastatic breast cancer growth may introduce liabilities that can be exploited for therapy. Here we assessed how metabolism differs between breast tumors in brain versus extracranial sites and found that fatty acid synthesis is elevated in breast tumors growing in the brain. We determine that this phenotype is an adaptation to decreased lipid availability in the brain relative to other tissues, resulting in site-specific dependency on fatty acid synthesis for breast tumors growing at this site. Genetic or pharmacological inhibition of fatty acid synthase reduces human epidermal growth factor receptor 2-positive breast tumor growth in the brain, demonstrating that differences in nutrient availability across metastatic sites can result in targetable metabolic dependencies.

TAMI-06. TUMOR CELL-DERIVED CYTOKINE EXPRESSION CHANGES ASSOCIATED WITH BRAIN METASTASIS IN A SYNGENEIC MOUSE MODEL OF BREAST CANCER

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Breast cancer is the most common malignancy in women in the United States, and brain metastases occur in almost a third of patients with metastatic dissemination. Immunoediting is a critical component of metastatic tumor cell elimination, and tumor clones that develop immune-escape mechanisms are associated with progression and metastatic dissemination. We hypothesized that breast cancer brain metastatic cells harbor immunomodulatory cytokine expression changes that promote an immunosuppressive environment to avoid immune cell-mediated elimination. To study this, a syngeneic mouse model of metastatic breast cancer was used. A brain metastatic line derived from the 4T1 breast cancer parental cell line was created by serially selecting brain metastatic populations of cells after intracardiac injection (4T1 BrM). A gene-expression analysis using an 800-gene cancer immunology-specific microarray panel was performed comparing the 4T1 parental and 4T1 BrM lines. 4T1 BrM cells demonstrate gene expression changes promoting immunosuppression including significant upregulation of IL18 and Lgals9 (Galectin-9) and downregulation of CD40, IL2rg, CCL2, and EOMES. When compared to 4T1 parental lines, the 4T1 BrM line demonstrated decreased expression of CCL2 and increased expression of GM-CSF on a cytokine array, corresponding to results obtained from gene expression analysis. These results suggest tumor-intrinsic cytokine expression changes that may mediate an immunosuppressive environment.

TAMI-07. TUMOR-EDUCATED PLATELETS GUIDE BREAST CANCER BRAIN METASTASIS AND PROMOTE THERAPEUTIC RESISTANCE

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BACKGROUND: Platelets have been shown to play an important role in systemic and local tumor modulation. Once encountered by tumor cells, platelets are educated to collect and release pro-tumor factors in the tumor/microenvironment, serving as a guiding partner for metastasis. This educational program, however, is not well understood. METHODS: Wild-type platelets (WTPs) were isolated from blood of healthy humans or mice, whereas tumor-educated platelets (TEPs) were isolated from blood of breast cancer patients or from tumor-bearing donor mice. The tumorigenic and modulatory effect of these two types of platelets on breast cancer was examined *in-vitro* and *in-vivo*. RESULTS: Here, we show that TEPs acquire tumor promoting functions and drive breast cancer progression, metastasis to distal sites specifically the brain, as well as therapeutic resistance. Importantly, TEPs promoted an increased pro-tumorigenic effect on metastatic breast cancer, compared to their wild-type counterpart, promoting epithelial to mesenchymal transition through NF-κB/STAT3 signaling axis via C/EBPβ transcription factor. CONCLUSION: Our findings point to the important role of TEPs in breast cancer brain metastasis and therapeutic resistance, which could have a major implication in other tumor types, endorsing TEPs as a potential therapeutic target.

TAMI-08. THE CCL2-CCR2 ASTROCYTE-CANCER CELL AXIS IN TUMOR EXTRAVASATION AT THE BRAIN

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Although brain metastases are common in cancer patients, little is known about the mechanisms of extravasation across the blood-brain barrier (BBB), a key step in the metastatic cascade that regulates the entry of cancer cells into the brain parenchyma through its selective endothelial barrier. Progress in this area has been impeded by challenges in conducting high spatio-temporal resolution imaging in vivo and isolating factors and cellular interactions directly contributing to extravasation rather than cancer survival and proliferation in the brain tissue. To address these limitations, we engineered a three-dimensional in vitro BBB microvascular model with endothelial cells derived from induced pluripotent stem cells, brain pericytes, and astrocytes, into which we perfused cancer cells to recapitulate their circulation and extravasation at the BBB. With this platform, we revealed that astrocytes play a major role in promoting cancer cell transmigration via their secretion of C-C motif chemokine ligand 2 (CCL2). We found that this chemokine promoted the chemotaxis and chemokinesis of cancer cells via their C-C chemokine receptor type 2 (CCR2), with no significant changes in vascular permeability. These findings were validated in vivo, where CCR2-deficient cancer cells exhibited significantly reduced cancer cell arrest and transmigration in mouse brain capillaries. Our results attest to the translational value of our BBB-on-a-chip model and reveal that the CCL2-CCR2 astrocyte-cancer cell axis plays a fundamental role in extravasation and consequently metastasis to the brain.

TAMI-09. INTRAOPERATIVE MICRODIALYSIS AS A FEASIBLE PLATFORM FOR METABOLIC AND PHARMACODYNAMIC BIOMARKER DISCOVERY

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BACKGROUND: Progress for gliomas is slowed in part by the paucity of mechanistic feedback during treatment with experimental therapies. Access to extracellular tumor pharmacodynamic biomarkers could provide an avenue to accelerate progress. We have initiated a program of intra-operative microdialysis to accelerate biomarker discovery and to identify candidate outcome measures for translational therapies. METHODS: Intraoperative microdialysis was performed with M-dialysis 100kDA catheters and 107 variable rate pumps under an IDE. Four IDH-mutant and two IDH-WT lesions were studied intraoperatively with 3 divergently placed catheters. Microperfusate (artifical CSF+ 3% dextran) was perfused at 2uL/min and collected in 20 min increments. Paired CSF was also obtained when accessible. A parallel cohort of nude mice bearing human IDH-mutant, IDH-WT, or sham intracranial xenografts (n=6-12) underwent intratumoral microdialysis. A pilot murine study of intracranial drug delivery was performed via concurrent microdialysis during convection-enhanced delivery (CED) of saline or the IDH-inhibitor AG120. RESULTS: Microdialysate from IDH-mutant intracranial xenografts revealed >100 differentially abundant metabolites compared to sham or IDH-WT tumors, including D2-HG (21x) and MTA(18x), p< 10^-5. The most significantly abundant metabolite was DMA (4x, p< 10^-10). 15-1000uM D2HG was recovered from intra-operative human IDH-mutant tumors and 1-2uM from normal brain adjacent to IDH-WT gliomas and < 1uM in all IDH-WT samples. Forty metabolites differentiated enhancing tumor from adjacent brain in 3/3 paired human samples including upregulated Aminoacyl-tRNA biosynthesis and downregulated purine metabolism. Serial aliquots of microdialysate during saline CED yielded steady D2-HG levels whereas CED with AG120 yielded undetectable D2-HG within 6 hours. CONCLUSION: The extracellular metabolic landscape of glioma is diverse, dynamic and reflects tumor