Title

NCMP-13. ID8 OVARIAN CANCER MOUSE MODEL MIMICS NEUROLOGICAL SEQUELAE OF OVARIAN CANCER IN WOMEN

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tution with left eye vision changes, and focal neurological deficits. A brain MRI showed an enhancing lesion within his left medulla extending to the cerebellum. Cerebrospinal fluid (CSF) analysis was positive for EBV and negative for malignancy. He was diagnosed with VZV vasculopathy and discharged home on IV Acyclovir for 14 days and a 5-day course of oral prednisone 60 mg. Three months later, a repeat brain MRI showed multiple new enhancing lesions bilaterally along the periventricular white matter with involvement of the corpus callosum with several lesions in peripheral locations of the cerebrum, cerebellum, and brainstem. He presented to local ER with intermittent encephalopathy, acute left eye vision blurriness and was started on steroids. He was transferred to our institution and had CSF analysis which was positive for EBV and negative for malignancy. Due to rapid progression of his symptoms, he underwent gross total resection of the left frontal lesion which showed EBV-induced diffuse large B-cell lymphoma (DLBCL). His Mycophenolate Mofetil was discontinued and he had a dramatic improvement in his left eye vision and cognitive deficits within 24 hours after one dose of Rituximab IV 500 mg/m2. DISCUSSION: In the setting of periventricular lesions and EBV positivity on CSF, EBV-induced DLBCL should be highly considered. CONCLUSION: Misdiagnosis or delay in diagnosis of PCNSL due to the presence of atypical features in disease presentation and radiographic findings could lead to progression of PCNSL.

NCMP-10. DYSGRAPHIA AS THE EARLIEST PRESENTING SYMPTOM OF SEVERE CHIMERIC ANTIGEN RECEPTOR (CAR) T-CELL THERAPY NEUROTOXICITY: A SINGLE CENTER EXPERIENCE

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INTRODUCTION: Chimeric antigen receptor (CAR) T-cell therapy, including axicabtagene ciloleucel (axi-cel; Yescarta®) and tisagenlecleucel (tisa-cel; Kymriah®), are FDA approved for the treatment of adult patients with relapsed or refractory (R/R) diffuse large B-cell lymphoma (DLBCL). Neurotoxicity (NT) associated with CAR T-cell therapy (immune effector cell-associated neurotoxicity syndrome [ICANS]) can be fatal. Timely data, in the form of an abbreviated bedside mini-mental status exam, is thought to lead to earlier identification of NT. However, existing literature validating this method is limited. MATERIALS AND METHODS: In this retrospective study, patients with R/R DLBCL treated with commercial axi-cel or tisa-cel in our center from December 2017 to September 2018 were assessed for NT with the CTCAE v4 criteria and the CAR-T-cell-therapy-associated TOXicity (CARTOX-10) scoring system. RESULTS: Twenty-six patients with R/R DLBCL were treated with CAR T-cell therapy (25 axi-cel/[Yescarta®] and 1 tisagenlecleucel [Kymriah®]). Twenty-three (88%) developed NT with 8 (31%) experiencing severe NT (Grade III-IV). Tremor and dysgraphia occurred in all patients with severe NT. Lower average CARTOX-10 score ($p=< 0.01$), dysgraphia ($p< 0.01$), inattention ($p=.018$), and disorientation ($p=.01$) were significantly associated in patients with severe NT. A trend towards significance was observed between tremor and severe NT ($p=.08$). All patients with severe NT had both dysgraphia and tremor 8/8 (100%) and 2/8 (25%) had concurrent dysnomia. Death occurred in 12/26 (46%) of patients due to disease progression (n=11) and cardiac failure due to myositis (n=1). CONCLUSION: In our limited cohort, dysgraphia, inattention, and disorientation are heralding symptoms of severe NT in adult R/R DLBCL patients treated with commercial CAR T-cell therapy. Dysgraphia was the earliest presenting symptom in patients with severe CAR T-cell neurotoxicity and was likely a manifestation of motor dysfunction rather than a component of dysphasia. Further studies with a larger cohort are needed to validate our findings.

NCMP-11. SPINAL CORD INFARCT AFTER CAR-T TREATMENT

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Cortical and subcortical neurotoxicity from CAR-T therapy is a well described complication in literature, with over 40% of patients experiencing at least one neurologic side effect. However, spinal cord toxicity from CAR-T therapy is less well described. To our knowledge, this is the first reported case of a spinal cord infarct following CAR-T therapy. A 44 year old male with primary refractory DLBCL without CNS involvement, which was refractory to R-CHOP, R-ICE, and hyperCVAD part B underwent CD-19 CAR-T treatment. The day after infusion he developed grade 1 cytokine release syndrome (CRS) with fever and up trending inflammatory markers. Infectious work up was negative and he was treated with tocilizumab and dexamethasone. His fever resolved and markers down trended. On day 5 post CAR-T, he became encephalopathic, developed severe back pain, and was unable to move his bilateral lower extremities. He was treated with 2nd and 3rd doses of tocilizumab, dexamethasone and was started on anakinra. Patient's mental status cleared by day 7 and he was found to have a dermatome sensory level at T10 with flaccid bilateral lower extremity paralysis. MRI Brain was unremarkable, but a spinal MRI showed longitudinally extensive cord edema and diffusion restriction at T10. Due to an initial question of transverse myelitis, he was treated with a 3-day course of IV methylprednisolone, with no improvement in symptoms. CSF studies were unable to be obtained due to his thrombocytopenia. Repeat MRI obtained 10 days after initial imaging showed resolution of cord edema, but continued areas of FLAIR hyperintensity at T10 through the conus. Despite aggressive rehabilitation services, four months later, patient remained paralyzed in his lower extremities with an indwelling foley catheter. He remains in a complete remission.

NCMP-13. ID8 OVARIAN CANCER MOUSE MODEL MIMICS NEUROLOGICAL SEQUELAE OF OVARIAN CANCER IN WOMEN

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OBJECTIVES: Chemotherapy-related cognitive impairment (CRCI) and chemotherapy-induced peripheral neuropathy (CIPN) are neurological complications of cancer treatment. Cisplatin is used to treat ovarian malignancies, and over 70% of women experience CRCI/CIPN during and after platinum-based chemoTx. However, over 30% of non-CNS cancer patients experience cognitive impairment prior to chemoTx. To examine the contribution of cancer itself and additional neurological impairment with chemoTx, we used an ID8 syngeneic mouse model of ovarian cancer and assessed hyperalgesia and cognition +/- cisplatin treatment. METHODS: C57BL/6 female mice were injected intraperitoneally with 10^7 ID8 ovarian cancer cells or 0.9% saline. After 10d of ID8 injections, mice received cisplatin (2.3 mg/kg/day, i.p.) or 0.9% saline (OvT+CIS, OvT+VEH, respectively) for 5d, followed by 5d of rest for 2 cycles. Mechanical and cold hyperalgesia were assessed longitudinally. Cognition was assessed 28d post-chemoTx by the open field test (OFT), novel object recognition (NOR), and novel place recognition (NPR) tasks. RESULTS: OvT+VEH and OvT+CIS mice developed an increased sensitivity to mechanical (>200%, $p< 0.001$) and thermal (cold) stimuli (>78%, $p< 0.004$) starting 14d post-ID8 implantation, vs non-tumor controls (CON). In the OFT, OvT+CIS mice had increased anxiogenic behavior (55%, $p< 0.001$) vs CON, and (46%, $p< 0.05$) vs OvT+VEH. In NPR, OvT+CIS had reduced discrimination (37%, $p< 0.05$) vs CON. OvT+VEH and OvT+CIS showed impaired discrimination (25%, $p< 0.05$ & 33%, $p< 0.01$, respectively) in NOR vs CON, with trending differences between OvT+CIS vs OvT+VEH in hyperalgesia and cognitive tasks. DISCUSSION: This is the first rodent model to demonstrate that ovarian cancer may evoke sensory and neurocognitive changes in the absence of chemotherapy. Future development of the model will address hyperalgesia and cognitive differences between OvT+VEH vs OvT+CIS. This model has potential for translational studies on the treatment of neurological sequelae of cancer and cisplatin-induced CRCI and CIPN.

NCMP-14. WHOLE BRAIN RADIOTHERAPY COMBINED WITH INTRATHECAL LIPOSOMAL CYTARABINE FOR LEPTOMENINGEAL METASTASIS – A SAFETY ANALYSIS AND VALIDATION OF THE EANO-ESMO CLASSIFICATION

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BACKGROUND: Although there is no proven standard therapy for leptomeningeal metastases (LM), treatment often includes intrathecal chemotherapy combined with whole brain radiation therapy (WBRT). Little is known on the toxicity of such combination therapies. We performed a retrospective safety analysis for the combination of intrathecal liposomal cytarabine with WBRT in patients with LM and validated the EANO-ESMO classification in this unique cohort. METHODS: Treatment toxicities in patients diagnosed with LM between 2004 and 2014 were retrospectively analyzed according to the RTOG (Radiation Therapy Oncology Group) and NCI CTCAE V5.0 (Common Toxicity Criteria Adverse Events) toxicity criteria. Diagnostic criteria and treatment response as assessed by EANO-ESMO classification were correlated with survival by Kaplan Meier analysis and Breslow test. RESULTS: 40 patients with LM who were treated with combined WBRT and intrathecal cytarabine, were identified. Ten patients (25%) experienced adverse events ≥ grade 3 according to the RTOG-toxicity criteria, in 22 patients (55%) CTCAE criteria ≥3 grade were detected. Median overall survival (mOS) was 124.0 days [72.9;175.1]. Median time to