LMD-08. PRECISION MEDICINE FOR LEPTOMENINGEAL CARCINOMATOSIS: A CASE REPORT

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Leptomeningeal disease (LMD) is an aggressive late-stage event in cancer. It is rare in gynecological malignancies. We present a case of a patient diagnosed with cervical adenocarcinoma grade III, stage Ib1 who developed LMD treated with immunotherapy based on modern molecular medicine. The patient is 61-year-old female diagnosed with locally advanced cervical adenocarcinoma in November of 2017 and was rendered without evidence of disease after combined chemotherapy and pelvic irradiation. One year after initial treatment, she was found to have a solitary right cerebellar lesion on MRI for which she underwent gross total resection followed by stereotactic radiosurgery to the resection cavity. The pathology of the lesion was consistent with metastatic carcinoma of cervical primary. Next generation sequencing was performed on the brain metastasis tissue and was notable for a high tumor mutational burden (tTMB-high). One year after surgery she developed left arm weakness, and vertical diplopia. She underwent MRI of the brain and spine that demonstrated new nodular enhancement within the folia of the vermis and multi-level leptomeningeal enhancement in the cervical spine, consistent with LMD. She was treated for LMD with radiation to the whole brain and cervical spine. Radiation was followed with single-agent Pembrolizumab due to the reported response in cancer patients with tTMB-high status to immunotherapy. She is currently 6 months from her initial LMD diagnosis and is clinically stable with radiographic improvement. This case presents an extremely rare complication of cervical cancer. It also highlights a unique treatment option for patients with LMD found to have tTMB-high status. Immunotherapy is of particular interest in cases of cervical adenocarcinoma as this cancer commonly has moderately-high TMB. Several studies have investigated the response of leptomeningeal disease to immunotherapy with variable results, though none have evaluated the response of tumors with tTMB-high.

LMD-09. OUTCOMES AND SYMPTOM BENEFIT FROM PALLIATIVE RADIOTHERAPY FOR LEPTOMENINGEAL DISEASE IN BREAST CANCER PATIENTS

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OBJECTIVE: The benefit of radiotherapy (RT) in patients with leptomeningeal disease (LMD) is poorly characterized. This study assessed the overall survival (OS) and clinical improvement of a largely symptomatic cohort of breast cancer patients with LMD, to identify patient subsets most likely to benefit from palliative RT. METHODS: Patients with breast cancer-related classic radiographic LMD (36% cytology-confirmed) were treated with palliative whole brain and/or partial spine RT between 2000–2020 at a single academic institution in this retrospective analysis. OS was calculated from date of LMD diagnosis using the Kaplan-Meier method. A multivariate logistic regression model incorporating ER/PR status, HER2 status, ECOG and steroid use was developed to identify factors associated with symptom benefit, which was ascertained retrospectively by chart review. RESULTS: Among 64 patients, the radiographic distribution of LMD was in the brain (58%), spine (22%), or both (20%). A total of 63% had brain metastases, and 57% of patients had ER+ and/or PR+, 22% HER2+, and 38% triple-negative disease. Of the symptomatic patients (94%), primary symptom domains included cranial nerve deficits (34%), sensory/motor deficits from intracranial disease (25%) or spinal disease (27%), and headaches/nausea (14%), with 42% of patients reporting >1 symptom domain. Two-thirds of patients were on steroids prior to RT, and 13% of patients received intrathecal therapy. OS was 3.75 months. Following a median dose of 30Gy in 10 fractions, 59% of symptomatic patients experienced symptom improvement, with similar improvement rate across domains (12%, 15%, 19%, 14%, respectively); 21% of patients had improvement in >1 symptom domain. Hormone receptor positivity was independently associated with symptom improvement following RT (OR 3.5, 95% CI 1.2–11, p=0.029). CONCLUSIONS: In this poor-prognosis cohort of breast cancer patients with LMD, palliative RT yielded symptomatic improvement, and may be particularly beneficial among better-prognosis patients with hormone receptor-positive disease.

LMD-10. THE ROLE OF IMMUNE CHECKPOINT INHIBITORS IN LEPTOMENINGEAL DISEASE: A SYSTEMATIC REVIEW

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BACKGROUND: Leptomeningeal disease (LMD) is a devastating complication of advanced malignancy with a poor prognosis and limited therapeutic options. Whether immune checkpoint inhibitors (ICIs) alter disease course is unknown. METHODS: We searched PubMed, EMBASE, Scopus, Cochrane, and clinicaltrials.gov according to PRISMA guidelines to analyze the therapeutic role and toxicity profiles of ICIs in the management of LMD. Studies reporting clinical outcome data of patients with LMD treated with ICIs were included. A comprehensive review of clinical characteristics and survival analysis was conducted. RESULTS: We included 14 studies encompassing 61 patients. The median age at LMD diagnosis was 57 years (female=63.9%). Lung cancer (44.3%), breast cancer (27.9%), and melanoma (23.0%) were the most frequent primary tumors. Parenchymal brain metastases occurred in 37 patients, mostly treated with radiotherapy (83.3%). LMD most frequently presented with headache (42.1%) and was diagnosed by MRI findings (leptomeningeal T1-contrast enhancement: 96.7%) and/or positive cerebrospinal fluid cytology (86.5%). Patients received ICIs for a median duration of 7 months (range, 0.5–58.0): pembrolizumab (49.2%), nivolumab (32.8%), and/or ipilimumab (18.0%). The most common concurrent LMD treatments were radiotherapy (54.7%) and steroids (35.7%). Radiological responses at 6-months were complete (33.3%) and partial response (12.5%), stable disease (33.3%), and progression (20.8%). 22 patients developed ICI-related adverse events, mostly mild (100%) and uncommonly severe (15.6%). Median progression-free survival was 5.1 months, median overall survival was 6.3 months, and 12-month survival was 32.1%. Survival was correlated with ICIs (P=0.042), but not with primary tumors (P=0.144). Patients concurrently receiving steroids showed worse survival (P=0.040), with a median overall survival of 1.9 months. CONCLUSION: ICI therapy shows promise and appears to be well-tolerated in patients with LMD. Concurrent use of steroids is associated with worse survival. The role of ICIs in the multimodal management of LMD and their combination with steroids requires further analysis.

LMD-11. PURE SPINAL CORD INVASION IN RECURRENT CLASSIC HODGKIN'S LYMPHOMA - WHAT IS IT?

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We present the case of a 39-year-old male who initially presented in January 2017 with abdominal pain and weight loss. He was eventually diagnosed with stage IVB Classical Hodgkin's Lymphoma. Brentuximab, Vinblastine, and Dacarbazine regimen was initiated with dose adjustments made due to cardiomyopathy and neuropathy. By cycle 5, good response was evident on systemic imaging. He was then lost to follow-up. He represented in December 2020 with near paraplegia, preceded by months of tingling, numbness in both legs, gait imbalance and low back pain. MRI spine in January 2021 demonstrated multifocal abnormal cord signal changes with scattered areas of intramedullary cord enhancement as well as extensive enhancement of the cauda equina (Figures 1,2,3). CNS angiitis as a paraneoplastic phenomenon, mimics a similar clinical and radiographic appearance. Unfortunately none of the cord lesions were amenable to biopsy. Full body PET CT showed florid disease concerning for recurrence. 2 lumbar punctures with limited CSF flow cytometry and cytology analyses were negative. Mediastinal lymph node biopsy revealed Classical Hodgkins Lymphoma. DHAP chemotherapy regimen was initiated, soon after. A 3rd time, high volume comprehensive CSF analysis performed later, was unremarkable. MRI spine, after 2 cycles demonstrated significant improvement(Figures 4,5,6)coinciding with systemic response and clinical improvement. This favored diagnosis of CNS Hodgkin lymphoma over secondary CNS angiitis. CNS Hodgkin's Lymphoma is a rare occurrence1, let alone, pure spinal intramedullary and leptomeningeal metastases. Intramedullary metastases arise from direct hematogenous spread or by, centripetal growth of tumor along spinal nerve roots with secondary invasion of spinal cord[2]. Systemic Hodgkin's Lymphoma rarely affects the spine with a prevalence of 0.2% - 0.5%[3,4]. In an analysis of a large cohort of Hodgkin's patients comprising 14,868 individuals, a prevalence of less than 0.02%, indicating it had been overestimated in the past[5].