Title

RARE-36. BORTEZOMIB WOKE UP A PATIENT WITH ANTI-NMDA RECEPTOR ENCEPHALITIS REFRACTORY TO STANDARD THERAPY AND LONG TERM FOLLOW-UP

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and time to treatment failure (TTF; metastasis or death). Additionally, we have analyzed amplification of PD-L1 gene by FISH, translocation between promotor region of CIITA and PD-L1 by PCR, and mutation in 3'-UTR by immunohistochemistry with antibody recognizes C-terminus (clone; SP-142) of PD-L1. PD-L1 was expressed in most of tumor cells. The intensity of PD-L1 expression was negatively associated with MFS (p=0.04), and diffuse pattern of PD-L1 expression showed trends towards shorter TTF compared with partial expression (p=0.08). Notably, with the combination analysis of PD-L1 and CD8(+) TIL, the diffuse PD-L1 expression with less CD8(+) was significantly associated with shorter TTF (p=0.005). However, there was no significant relevance between the expression of those immune-checkpoint molecules and OS or PFS. Although neither amplification of PD-L1 gene, 9p24.1, nor translocation between CITTA and PD-L1 were observed, difference in immunohistochemistry with two different anti-bodies was observed. In intracranial SFTs/HPCs, tumor immunity mechanism associated with PD-1/PD-L1 may play an important role in their extracranial metastases, and mutation in 3'-UTR may be a cause of PD-L1 activation in SFT/HPC.

RARE-35. MRI FINDINGS AT PROGRESSION IN ADULT PATIENTS WITH MEDULLOBLASTOMA

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Progression (PD) in medulloblastoma (MB) represents a diagnostic challenge due to imaging heterogeneity among/within patients. SHH (Sonic hedgehog)-MB is thought to recur mostly within the tumor bed (TB). In children, DWI restriction (DWIr) is more sensitive than contrast enhancement(CE) for first PD. Whether this is applicable to adults is unknown. METHODS: Retrospective review of adults (age ≥18) with MB enrolled to Natural History study at NCI-NOB. Descriptive statistics of imaging at diagnosis and PD(CE, T2/FLAIR signal without CE, DWIr) and imaging patterns for each PD. RESULTS:14 adults with MB: 5 diagnosed in childhood (8–16 yrs), 9 as adults (18–45 yrs); Subtypes: 7 SHH, 3 non-WNT/non-SHH, 4 unknown. Eleven experienced ≥1 PD (6/7 SHH, 2/3 non-WNT/non-SHH, 3/4 unknown); median PD of 5 (range 1–9). Median age at first PD 31 years (range 10–46) with 5 first PDs >5 years after diagnosis. In 10 patients with available baseline MRI, 9 had CE, and 8 DWIr (2 without DWI sequences). Of 48 total PDs, the commonest patterns were: brain LMD alone (n=14), TB alone or distant brain parenchyma alone (each n=7), distant brain parenchyma with brain LMD (n=6), and TB with either distant brain parenchyma or LMD (n=3). Of the 82 PD lesions, 23% (n=14) of brain lesions lacked DWIr, and 37% (n=23) had T2/FLAIR signal without CE. PD tissue confirmation obtained at 18 time points:16 cases with confirmed recurrence had heterogeneous characteristics; in 12 with brain PD: CE in 5, T2/FLAIR without CE in 3 (unknown: 4). 2 CE lesions revealed meningioma (one-atypical meningioma- had DWIr). CONCLUSIONS: Imaging findings in adult patients with MB are highly heterogeneous. Despite high specificity of DWIr for PD in children, it failed for 23% of brain lesions across multiple patients. Most SHH-MB had PD outside the TB, unlike what is widely accepted in the literature.

RARE-36. BORTEZOMIB WOKE UP A PATIENT WITH ANTI-NMDA RECEPTOR ENCEPHALITIS REFRACTORY TO STANDARD THERAPY AND LONG TERM FOLLOW-UP

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OBJECTIVE: To report a case with refractory NMDA encephalitis in comatose for 18 months, who was treated successfully with bortezomib. BACKGROUND: Anti-NMDA encephalitis is a rare autoimmune encephalitis. Standard therapy include corticosteroid, IVIG or plasma exchange, cyclophosphamide, rituximab, and tumor removal. Refractory cases are very severe and often stay in ICU on ventilation for several months to years. Bortezomib for the treatment of refractory anti-NMDA receptor encephalitis was reported. We have applied the treatment to our refractory case and successfully woke up the patient. And we have followed up the patient for 3 years. METHODS: Case report. RESULTS: A 40 yo male was diagnosed as anti-NMDA encephalitis. Standard therapy was applied. After stabilization, the patient was eventually discharged to ICU at a long term care subacute hospital. The patient was brought back for more Rituxan or steroid or IVIG therapy. The condition had not improved at all. Eighteen months in comatose, the patient had worsening NMDA titer in CSF to 1:640. Decision was made to start bortezumib as reported with modification: 1.3 mg/m2 bortezomib were administered on days 1, 8, 11 and 14 and allowed two weeks off therapy. After first cycle, the patent started to talk first word "hurt." After 6 cycles, the patient sat up and started riding bicycles for physical therapy. The NMDA titer in CSF was reduced to 1:40 at the end of 6 cycles. One year later, the patent stood up and ambulated with a walker. One and half year later, the patient walks without assistance and his speech and cognition have significantly improved with good communication with family members and staff. CONCLUSIONS: Proteasome inhibitor bortezomib might be considered to be the third line therapy as early as possible if the first line and second line are ineffective to treat anti-NMDA receptor encephalitis.

RARE-37. TREATMENT OF H3K27M MUTANT GLIOMAS WITH PANOBINOSTAT

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Panobinostat (PBST) is a histone deacetylase inhibitor with biologic rationale in the treatment of gliomas harboring H3 K27M mutation.

METHODS: We performed a retrospective medical record review of adult patients with H3 K27M mutant diffuse midline glioma treated with PBST at Mayo Clinic (Rochester, MN). RESULTS: Four patients were identified with a mean age 40 years (range 22–62 years). Tumor location was: spinal cord (thoracic n=1, cervical n=1), brainstem (n=1), and thalamus (n=1).Two patients underwent biopsy alone while two underwent a partial resection. Three patients were treated with radiation (36–54 Gy) immediately prior to PBST monotherapy, and one patient was treated with PBST monotherapy without preceding radiation. All patients were otherwise chemotherapy naïve and did not receive any concurrent chemotherapy with PBST. PBST was dosed at either 10 mg (n=1) or 20mg (n=3) administered on days 1, 3, 5, 8, 10 and 12 of 21 day cycles. The mean duration of PBST therapy was 5 months (range 2–11 months). PBST was well tolerated overall. One patient experienced an objective response per RANO criteria. Two patients continue on therapy (5 cycles, 12 cycles) with stable disease. One patient rapidly progressed after 2 cycles of PBST therapy. In contrast with the patients who derived benefit from PBST, this patient was younger (22) and had multifocal disease with leptomeningeal involvement at treatment onset. The average progression free survival post PBST initiation was 8 months. CONCLUSION: This single institution case series shows promise that PBST may have therapeutic benefit in adult patients with H3 K27M mutant diffuse midline glioma.

RARE-38. CNS LYMPHOMA INVOLVING HYPOTHALAMIC-PITUITARY AXIS

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BACKGROUND: It is rare for CNS lymphoma which involves the hypothalamic-pituitary axis. It could result in misdiagnoses such as pituitary adenoma, craniopharyngioma, or glioma. We report clinical findings of eight cases of either primary or secondary lymphoma involving the hypothalamic-pituitary axis(H-P axis). METHODS: We retrospectively reviewed 488 patients who were diagnosed as CNS lymphoma from 2000 to 2017 in our institute. There were eight patients (8/488, 1.6%) who had H-P axis involvement in radiographic findings while six patients received chemotherapy. We analyzed patient characteristics, pathologies, clinical features, laboratory findings, imaging, and treatment outcome. RESULTS: The mean age was 48-year-old (range 18~80) and male to female ratio was 5:3. We performed endonasal TSA for four patients, endoscopic biopsy for two patients, and stereotactic biopsy for two patients. There were six patients of diffuse large B-cell lymphoma and two patients of MALT lymphoma. Seven patients were PCNSL and one patient was metastasized lymphoma. All patients had hormone imbalance whereas three patients had visual disturbance and one patient had diabetes insipidus. Initial serum LDH was 337±167IU/L(range 169~567 except one patient). MRI finding was different from the usual pattern which was low SI in T1 and high SI with perilesional edema in T2, on the other hands, our patients group revealed that five patients(62.5%) had iso SI in both T1 and T2, and only two patients(25%) showed perilesional edema in T2. Median OS and PFS of six patients who received chemotherapy were 34.8 months(range 0.9~93.7) and 33.0 months(range 0.9~93.4), respectively. Two patients(25%) died in 26 days and 51 days after diagnosis because of pneumonia and cardiac arrest, respectively. And one patient lost to follow up after diagnosis. CONCLUSION: CNS lymphoma involving H-P axis is rare, however, we need to understand its unique characteristic.

RARE-39. COMBINATION OF TUMOR TREATING FIELDS (TTFIELDS) WITH LOMUSTINE (CCNU) AND TEMOZOLOMIDE (TMZ) IN NEWLY DIAGNOSED GLIOBLASTOMA (GBM) PATIENTS - A BI-CENTRIC ANALYSIS

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