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Survival Benefit for Individuals with Constitutional Mismatch Repair Deficiency Syndrome and Brain Tumors Who Undergo Surveillance Protocol. A Report from the International Replication Repair Consortium

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months. CONCLUSION: Our findings showed that pseudoprogression can occur early in the treatment course in CMMRD patients. Identification of this entity is important for appropriate clinical management.

RARE-16. SEVEN CASES OF RETINOBLASTOMA WITH CNS INVOLVEMENTS

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Treatment strategy for trilateral retinoblastoma (TRb: very rare RB with brain tumor) or retinoblastoma with central nervous system (CNS) involvement is not established yet. We retrospectively reviewed our seven cases of these rare almost fatal tumors. Their ages at diagnosis are 0y3m-1y10m (median 1y3m) (Male 4, Female 3). Only one had RB family history. Their affected eyes were bilateral 3, unilateral 3 and no 1. Their CNS involvements were suprasellar tumor 4, pineal tumor 1 and cerebrospinal fluid (CSF) cytology positive 2. Three of the suprasellar tumor patients had spinal metastasis. Four of the seven patients were TRb and one were genetically classified suprasellar retinoblastoma. All of them were treated with chemotherapy and four received high-dose chemotherapy. Three brain tumors of four TRb almost disappeared with chemotherapy. Two of them also received radiotherapy but relapsed. Although one radiation-free long-term TRb survivor developed secondary osteosarcoma, he got remission again and live 5 more years. One CSF positive Rb patient with chiasm invasion died of disease 11 months later. The other patient had no chiasm invasion nor CSF involvement at diagnosis, but his CSF cytology turned to positive after his second cycle of chemotherapy. He got remission with radiotherapy and high-dose chemotherapy, and alive without disease for 4 years. 2-year RFS and 2-year OS of all patients were 40% and 60%. Although our TRb patients responded to chemotherapy, it was difficult to avoid radiotherapy except one. Data accumulation is necessary for better treatment of these cancer-predisposed patients.

RARE-17. SURVIVAL BENEFIT FOR INDIVIDUALS WITH CONSTITUTIONAL MISMATCH REPAIR DEFICIENCY SYNDROME AND BRAIN TUMORS WHO UNDERGO SURVEILLANCE PROTOCOL. A REPORT FROM THE INTERNATIONAL REPLICATION REPAIR CONSORTIUM

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BACKGROUND: Constitutional mismatch repair deficiency syndrome (CMMRD) is a severe cancer predisposition syndrome resulting in early onset central nervous system (CNS) and other cancers. International guidelines for surveillance exist but no study has systematically evaluated the efficacy of this protocol. METHODS: We surveyed all confirmed CMMRD patients in the International Replication Repair Deficiency Consortium. A surveillance protocol consisting of frequent biochemical, endoscopic and imaging (CNS and total body MRI) studies were employed. Survival analyses and efficacy of each method were assessed. RESULTS: Surveillance data were collected from 105 CMMRD individuals from 41 countries. Of the 193 malignant tumors, CNS malignancies were the most common (44%). The surveillance protocol uncovered 49 asymptomatic tumors including 16 glioblastomas and medulloblastomas. Five-year overall survival was 89% for tumors discovered by surveillance, and 61% for symptomatic tumors (p<0.004). Similarly, 5-year survival was 82+/-11% and 24+/-6% for surveillance and non-surveillance of brain tumors (p=0.005). Yearly total body and q6 month brain MRI detected asymptomatic cancers in all but 3 symptomatic CNS gliomas. These were tumors uncovered when time between scans was >6 months as per protocol. Finally, of the low grade tumors identified asymptomatically, 5 were low grade gliomas. All of the low grade gliomas, which were not resected transformed to high grade tumors at a median of 1.6 ± 0.9 years. CONCLUSION: These data support a survival benefit in CMMRD patients undergoing a surveillance protocol. Adherence to protocol and resection of lower grade lesions may improve survival for patients with CNS tumors.

RARE-18. GENETIC EVALUATION IN PATIENTS WITH CHOROID PLEXUS TUMORS

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INTRODUCTION: Choroid plexus tumors (CPT) are rare intraventricular neoplasms of epithelial origin. They usually occur in the 2nd year of life, corresponding to 0.4–0.6% of intracranial tumors in this age group. They are sub classified, according to WHO 2016, in choroid plexus carcinoma (CPC), atypical choroid plexus papilloma (ACPP) and choroid plexus papilloma (CPP). Li-Fraumeni syndrome (LFS) is present in 50% of patients with CPC. In Brazil, the *TP53* p.R337H mutation affects 0.3% of the population in the South/Southeast. OBJECTIVE: Evaluate the incidence of genetic mutations in patients with choroid plexus tumors and therefore the importance of genetic evaluation. PATIENTS AND METHODS: Between 1992–2019, 38 patients were diagnosed with CPT in our institution, 23 with CPC. From 2012, 21 patients were referred for genetic evaluation, 16 of which had CPC (2 had previously CPP). Positive family history for neoplasms was present in 87.5%; 37.5% compatible with LFS, 50% of them with mutations. All the patients with positive, but unspecific, family history of neoplasms, had pathogenic mutation. The molecular investigation of the *TP53* gene in patients with CPC was performed and positive in 56.2%: R337H (5 patients), R110C, R158H, H179R, R196* (1 patient each). Of those with R337H, p53 protein immunohistochemistry resulted in 90–100% positivity. One of the patients with CPP that evolved to CCP had the H179R mutation. Clinical course was similar among them, and with those without mutations. CONCLUSION: These results confirm the need for genetic evaluation in patients with choroid plexus tumors for adequate therapeutic management and long-term follow-up.

RARE-19. PEDIATRIC HIGH GRADE GLIOMA WITH DNA REPAIR PATHWAY ABERRATIONS, CLINICAL CHARACTERISTICS AND OUTCOME

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DNA mismatch repair machinery is an integral part of the human genome and its defect has been involved in tumorigenesis and treatment resistance. Heterozygous monoallelic germline loss of function in MLH-1, MSH-2, MSH-6 or PMS-2 is involved in Lynch syndrome, whereas biallelic mutations cause constitutional mismatch repair deficiency (CMMRD) which is associated with hematologic malignancies and glioblastoma. We report here the clinical characterization and molecular analyses of 7 patients who presented with gliomas and MMR machinery aberrations. Two patients had a clinical diagnosis of NF-1 with dermatologic stigmata, of whom one patient has CMMRD and the other has Lynch syndrome. Two patients had a known family history of Lynch syndrome upon their diagnosis of glioma. Three patients with high-grade glioma and negative family history, 2 had germline mutations in MMR genes, and one had numerous mutations including MMR genes with microsatellite instability. Patients were initially treated with chemotherapy and radiation for high-grade gliomas (HGG); 5/7 had progression. Median time to progression was 12 months (range: 5–52), and median time from progression to death was 7 months (range: 2–25). One patient had low-grade glioma initially but progressed to HGG and is currently on therapy. Another patient treated with temozolomide and radiation is currently receiving maintenance therapy without any disease recurrence. Although the literature data on brain tumors with MMR deficiency is limited, these consistently show that MMRD-associated gliomas are treatment-resistant and have a dismal outcome. Collaborative efforts are needed to better understand this subgroup of pediatric HGG and to define optimal treatment strategy.

RARE-20. MALIGNANT PERIPHERAL NERVE SHEATH TUMOR OF A CRANIAL NERVE IN AN INFANT WITH NEUROCUTANEOUS MELANOSIS

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At one month of age, a female presented with a giant congenital nevus along lower back and thighs and hydrocephalus. A ventriculoperitoneal shunt was placed. An MRI was done at six months, initially reported as normal. At eleven months of age, five months after original MRI, patient presented with dysconjugate gaze and lethargy. MRI showed new 3.8 x 3.7 x 3.4 cm right cerebellopontine angle mass extending into Meckel's cave and foramen ovale along with leptomeningeal disease extending from the mass along the entire length of the spinal cord. Retrospective review of prior MRI revealed subtle leptomeningeal enhancement concerning for neurocutaneous melanosis (NCM). Given the leptomeningeal disease, family elected for open biopsy and debulking of lesion instead of aggressive resection. Histologically, the mass showed hypercellular spindle cell neoplasm with mitotic activity and necrosis mixed with remnants of normal cranial nerve. GFAP was negative, excluding a glioma. HMB-45, MITF, panmelanoma, and Melan-A were negative, excluding melanoma. A negative myogenin stain ruled out ectomesenchymoma. S-100 protein and SOX-10 positivity with variable loss of staining for trimethylation of histone H3 K27 were indicative of malignant peripheral nerve sheath tumor (MPNST). Given the course of the mass, trigeminal nerve MPNST was presumed. Given the poor prognosis of intracranial MPNST and NCM, family elected to forgo treatment and was discharged with hospice. She died 25 days after surgery. Cranial nerve MPNST is rare. MPNST in patients with NCM has not previously been reported to our knowledge.

RARE-21. CANCER SPECTRUM IN GERMLINE SUFU MUTATION CARRIERS: A COLLABORATIVE PROJECT OF THE SIOPE HOST GENOME WORKING GROUP

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BACKGROUND: Little is known about cancer risk associated with pathogenic germline *SUFU* variants. METHODS: Data of all previously published and 25 still unpublished patients with a pathogenic germline *SUFU* mutation were compiled. RESULTS: 124 patients in 67 families were identified, most of them ascertained after the occurrence of a medulloblastoma (MB) or as part of Gorlin syndrome cohorts. Overall, 30 patients were healthy carriers and 94 patients developed a total of 129 tumors (up to 4 tumors/patient): 68 MBs, always as first tumor (median age at diagnosis: 1.5yr [0.1–5]), 22 patients with at least 1 basal cell carcinoma (BCC) (median 10/patient) (median age at first BCC: 43yr, [17–52]), 15 meningiomas (median age 43yr, [13–72]), 7 ovarian stromal/fibrous tumors (median age 12yr [5–34]), and 17 other tumors including 5 sarcomas (median age: 50yr [7–79]). Median age at last follow-up was 30yr. Nineteen patients died, including 11 from MB. Second malignancies were diagnosed