in 21 patients including 13 in MB survivors. Mutations were inherited in 58/66 (88%) of cases in which inheritance could be tested and de novo in 8. In 6/67 families (9%), >2 children were diagnosed with a MB. CONCLUSION: In this large cohort of germline *SUFU* mutation carriers, MB in infants is the most frequent tumor but the spectrum also includes typical Gorlin syndrome tumors (BCC, meningiomas, and ovarian stromal/fibrous tumors) either as first tumors or as second malignancies. This broad tumor spectrum and the high risk of second malignancies justify the implementation of specific cancer surveillance programs.

RARE-22. GERMLINE PATHOGENIC VARIANT C.1552G>A;P.E518K IN DGCR8 CONFERS SUSCEPTIBILITY FOR SCHWANNOMATOSIS AND THYROID TUMORS

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Germline mutations in *DICER1* cause a pleiotropic susceptibility syndrome characterized by the development of pediatric or early-onset tumors including pleuropulmonary blastoma, Wilms tumors, pineoblastomas, multinodular goiter (MNG) and thyroid cancers. Somatic mutations in the other two microprocessors *DROSHA* and *DGCR8* have been found in Wilms Tumors and pineoblastomas. We present here two families with peripheral schwannomatosis and thyroid tumors carrying a germline variant c.1552G>A;p.E518K in *DGCR8*. Family one had six affected members with early-onset MNG and five of them developed schwannomatosis. All five members were heterozygous for the variant. One of the carriers had also been diagnosed with a choroid plexus papilloma at 7 years old. The common second event in all tumors tested was the loss of chromosome 22 at the somatic level. In family two, a 35-year-old male was diagnosed with a peripheral schwannoma at the age of 12. Since then, he has developed seven extra peripheral schwannomas (one of which was an ancient schwannoma) and papillary thyroid cancer. *DGCR8* lies on chromosome 22q, adjacent to the three schwannoma genes: *LZTR1*, *SMARCB1* and *NF2*. The variant, c.1552G>A;p.E518K localizes to the first RNA-binding domain of *DGCR8* and structural modelling predicts that it abolishes proper binding of RNA. It is also a hotspot somatic mutation in Wilms tumors. Using miRNA profiling, we show that this variant disrupts global microRNA production and *DGCR8* mutated tumors show a specific miRNA profile different from *DGCR8* wild type tumors. These findings reinforce *DGCR8* as a novel susceptibility gene for schwannomatosis and thyroid tumors.

RARE-23. NOVEL NF1 MUTATIONS IN TWO OCCURRENCES OF GLIOBLASTOMA MULTIFORM IN A PATIENT WITH CONSTITUTIONAL MISMATCH REPAIR DEFICIENCY SYNDROME

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Constitutional mismatch repair deficiency (CMMRD) syndrome is a rare cancer predisposition syndrome in children. Its main associated tumor types include brain and CNS tumors, hematologic malignancies, intestinal polyps and colorectal tumors, and other malignancies. Tumor genesis within this population is highly complex and poorly understood. We describe a case of a patient with two occurrences of glioblastoma multiforme (GBM), each with unique NF1 mutations. The patient is a female with CMMRD who was first diagnosed with GBM of the right frontal lobe in 2015. She subsequently underwent gross total resection, radiation to the field and concomitant and maintenance therapy with Temozolomide and Everolimus, due to high suspicion for NF-1. Genetic studies didn't show NF-1, instead revealing a diagnosis of CMMRD. Molecular testing of the GBM showed a high mutational burden and an NF1 mutation. Later, screening revealed stage IV colon cancer, for which she underwent subtotal colectomy, partial liver resection and chemotherapy. Molecular testing from the colon cancer found a hypermutant malignancy without mutations in NF1. Surveillance imaging detected a mass at the original site of her GBM, for which she had a resection. Notably, the genetic profile of the second tumor substantially different from the original tumor and the colon cancer sample, but had new mutations in NF-1. These findings highlight the significant variability in the genetic profiles of tumors in the context of CMMRD. It is also worth considering that NF1 is one of the first in a cascade of mutations leading to GBM in these patients.

RARE-24. LARGE CONGENITAL MELANOCYTIC NEVI AND NEUROCUTANEOUS MELANOCYTOSIS: A RETROSPECTIVE CASE SERIES

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Neurocutaneous melanocytosis (NCM) is a rare disease characterized by excessive proliferation and deposition of melanocytes in the leptomeninges and brain parenchyma, occurring in children with large congenital melanocytic nevi (LCMN). Manifestations of NCM range from asymptomatic CNS melanin deposition to cranial neuropathies, seizures, and hydrocephalus. Patients with NCM are at risk for malignant melanoma. We conducted a retrospective, single-institution study of patients with LCMN evaluated at Memorial Sloan Kettering Cancer Center from June 2000 to January 2020. Of 55 patients studied, 15 had no radiographic NCM, and 40 had radiographic NCM at initial evaluation. MRI findings included: focal melanocytosis (33), diffuse leptomeningeal disease (4), solid melanoma (3). Malformations were identified in 13, including arachnoid cyst (4), congenital hydrocephalus (4), Dandy-Walker malformation (3), and tethered cord (1). Twenty-one patients completed imaging once and were followed clinically. Seventeen with serial imaging (10 with focal melanocytosis, 7 with normal MRI) remained stable over a median 24-month follow up (range: 1–124). Six had suspected radiographic progression of NCM without melanoma. Malignant melanoma developed in 11 patients, 5 with focal melanocytosis on initial imaging. Median time from focal melanocytosis identification to melanoma diagnosis was 80 months (range: 18–200). Median age at melanoma diagnosis was 9.9 years (range: 1.1–25.3). Median survival from melanoma diagnosis was 9.1 months (range: 1–60.4). Focal NCM on neuroaxis imaging does not predict time to transformation to malignant melanoma. Serial imaging is not indicated in absence of disease-modifying treatment. Clinical follow up of at-risk individuals is essential in early identification of complications.

RARE-25. RETINAL ASTROCYTOMA MTOR INHIBITOR THERAPY IN TUBEROUS SCLEROSIS MOSAICISM

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INTRODUCTION: Everolimus is an inhibitor of mTORC1 (mammalian target of rapamycin complex 1), it is Health Canada and FDA approved for SEGA and renal angiomyolipoma in the setting of tuberous sclerosis complex (TSC). There is little data available in regards to this treatment of TSC associated retinal astrocytoma (RA). Although the behaviour of RA is often indolent or slowly progressive, aggressive behaviour with retinal detachment and neovascular glaucoma requiring enucleation has been reported in several patients. Definite TSC diagnosis is established when either two major features or one major and two minor features are present. Probable TSC diagnosis is established when one major plus one minor feature is present. METHODS: We report a child with probable TSC mosaicism, with negative serum NGS for TSC but RA and retinal achromic patch on the left. A left retinal peripapillary astrocytoma around optic nerve and very close to fovea was noted. There was concern that if it grew or there were to be any leakage it would cause visual impairment. This lead to therapy with everolimus 4.5 mg/m2/d aiming for level between 5 and 10 mcg/L. RESULTS: This boy has had a gradual reduction of the RA over the last 29 months, with healthy retina in the region no longer occupied by the lesion and preserved vision. He has tolerated therapy well with occasional mouth ulcers. CONCLUSION: mTORC1 inhibition is effective therapy to preserve vision in the setting of retinal astrocytoma and tuberous sclerosis mosaicism.

RARE-26. RETROSPECTIVE ANALYSIS OF PEDIATRIC CHOROID PLEXUS TUMORS

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