FINAL CATEGORY: HIGH GRADE Glioma

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HGG-01. DURABLE RESPONSE TO IMMUNOTHERAPY IN AN ADOLESCENT PATIENT WITH CONSTITUTIONAL MISMATCH REPAIR DEFICIENCY CMMRD AND SYNCHRONOUS THREE PRIMARY MALIGNANCES

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BACKGROUND: Familial Cancer Syndrome FCS is of particular concern in Saudi Arabia due to the high rates of consanguinity. Constitutional mismatch repair deficiency Syndrome (CMMRD) is an autosomal recessive FCS with a wide spectrum of malignancies Caused by Biallelic germline mutations in one of 4 mismatch repair genes (MLH1, PMS2, MSH2, and MSH6).

METHODS: we report 13 yr. Saudi boy, previously healthy with multiple café-au-lait (CAL) macules, and Consanguineous parents with a positive family history of Malignancy, presented with progressive headache, vomiting, abdominal pain, weight loss, and macrocytic anemia. MRI Brain showed a Large left hemispheric necrotic mass. MRI abdomen: Circumferential gastric body wall thickening Distal transverse colon intraluminal polypoid mass, and liver hypodense lesion. He had a Resection of the brain tumor and Upper GI endoscopy + colonoscopy with polypectomy: which showed an Ugly gastric ulcer, and multiple colonic polyps. RESULTS: Brain tumor molecular pathology: Gliosarcoma WHO grade 4 with negative IHC expression in PMS2 protein, hypermutant tumor with somatic PMS2 ATRX, TP53, NF1, and PFK3R1 genes mutation. stomach biopsy confirmed invasive gastric adenocarcinoma and Colonic polyp biopsy: Tubulovillous adenoma. Genetic testing Detect pathogenic Biallelic germline PMS2 mutation. He received adjuvant focal Brain radiation therapy 59.4Gy/33 F concurrent with immunotherapy (PD-1) inhibitor Nivolumab, Follow-up Abdominal imaging showed excellent response to immunotherapy with no significant residual lesion. MRI of the brain showed surgical bed multi-cystic lesions with thick nodular enhancement suggestive either of radiation necrosis vs. progressions/pseudoprogression. repeated MRI confirmed further progression of the enhancing surgical cavity lesion which was unresectable. CTLA-4 Inhibitor ipilimumab was added to Nivolumab to optimize therapy. UpToDate our patient is clinically stable on Maintenance Nivolumab with no side effects. CONCLUSION: Our case confirms immunotherapy’s efficacy for treating CMMRD-related cancers, which can improve survival while reducing toxicity from less effective conventional therapies.