GE-01. IDH1-MUTATED PITUITARY ADENOMA CHALLENGES TRADITIONAL CHARACTERIZATION OF MAFFUCCI SYNDROME

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Maffucci syndrome is a rare, non-inheritable condition of mesodermal dysplasia, presenting in childhood with formation of multiple enchondromas and soft-tissue hemangiomas. Approximately, 40% of enchondromas undergo malignant transformation into chondrosarcomas. The underlying genetic etiology lies in somatic mosaicism of mutations in isocitrate dehydrogenase 1 (IDH1) or IDH2, which have been detected simultaneously in both tumors and blood leukocytes of affected patients. We describe a 7-year old male who presented with extensive enchondromatosis and subcutaneous hemangiomas, clinically diagnosed as Maffucci syndrome. Years later, he developed sub-acute dysphasia, dysarthria, and loss of left visual acuity. A brain MRI demonstrated two heterogeneously enhancing lesions, one centered in the left jugular foramen and the other located in the supr-sellar region. Surgical resections of both intracranial tumors were performed over a period of ten months. Histopathological review revealed diagnoses of a grade II chondrosarcoma as well as a non-functional pituitary adenoma after subsequent neuroendocrine studies were unremarkable. Genotypic studies of the tumors were performed to identify common IDH1/2 mutations. DNA sequencing utilized standard Sanger sequencing in conjunction with a target-specific peptide nucleic acid (PNA) to detect IDH1 mutations in tumor tissues. The results demonstrated identical IDH1 mutations (c.394C>T; R132C) in both tumors. This result represents the first genetic evidence to establish causality between pituitary adenoma formation and tumor predisposition in Maffucci syndrome. As neuro-ectodermal tissue, this IDH1-mutated pituitary adenoma challenges the notion that Maffucci syndrome only involves mesodermal tissues. As such, in pediatric patients newly diagnosed with Maffucci syndrome, it may be appropriate to monitor for development of pituitary pathology and neuroendocrine dysfunction. Conversely, in the rare sub-population of pediatric neuro-oncology patients with concomitant non-nervous system tumors, further investigation is warranted to rule out Maffucci syndrome, as there may be considerable risk for malignant transformation as well as additional tumor formation.