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METB-02. GENETIC COUNSELLING IN SOTOS AND NS1-RELATED OVERGROWTH SYNDROMES PREDISPOSING TO BRAIN TUMORS
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BACKGROUND: Sotos and many other overgrowth syndromes are among the rare tumor predisposition syndromes that might be under-recognized in pediatric neuro-oncology practice. NSD1 gene (5q35), belonging to the histone lysine methyltransferases family, is involved in the majority of Sotos patients who exhibited haploinsufficiency and loss-of-function variants of the gene, but also in other overgrowth entities such as Beckwith-Wiedemann syndrome. Somatic mutations in this gene are likewise responsible of numerous cancers, particularly brain tumors. Here, we aim to assess the neurologic cancer risks and provide genetic counseling for appropriate clinical follow-up in Sotos syndrome. METHODS: From our genetic counseling database at the medical University of Sfax (Tunisia), we selected among patients presented for genetic management of overgrowth syndromes, those with Sotos syndrome. RESULTS: Only two Tunisian consanguineous pedigrees were enrolled in this study. Two boys were diagnosed with typical Sotos syndrome based on the three major clinical manifestations: specific facial dysmorphism, mental retardation and excessive growth including advanced bone age and macrocephaly. Chromosomes 5 in both pedigrees did not show structural abnormalities. During genetic counselling, parents were informed about the molecular testing options and the advantage of the exome sequencing. Furthermore, they were informed about the rate of cancer predisposition (3%) and the gains of neurologic and neuro-oncologic management, particularly regarding the intellectual disability and the increased risk of developing neural crest tumors, astrocytoma, glioma/ glioblastoma and neuroblastoma cancer, during childhood. CONCLUSIONS: Neurological pediatric malignancies are described in patients with Sotos syndrome, but the genotype-phenotype correlation is still unclear. It is suggested that NSD1 disruptions in Sotos patients trigger specific patterns of DNA methylation alterations leading to the development of cancer. Accurate molecular exploration is needed in the heterogeneous Sotos condition in order to improve the management according to the implicated gene and to benefit in the future from targeted therapies.