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First report of medulloblastoma in a patient with MUTYH-associated polyposis

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Abstract

Aims: The mutY DNA glycosylase encoded by the MUTYH gene prevents G:C→T:A transversions through the base excision repair DNA repair system. Germline biallelic pathogenic variants in MUTYH cause an adenomatous polyposis called MUTYH-associated polyposis (MAP), an autosomal recessive disease (OMIM: 608456), with an increased risk of colorectal cancer. Digestive lesions in this context show an excess of G:C→T:A transversions, individualising a specific mutational signature associated with MUTYH deficiency called signature SBS36. Predisposition to other tumours in patients with germline biallelic pathogenic variants in MUTYH is suspected but remains unclear. We report the first case of medulloblastoma in a patient with MAP, carrying the homozygous pathogenic variant c.1227_1228dup, p.(Glu410Glyfs*43) in MUTYH.

Methods: Whole exome sequencing was performed on the medulloblastoma to enlighten single nucleotide variants of interest, microsatellite status and mutational signature. The objective was to determine the involvement of MUTYH deficiency in the oncogenesis of this medulloblastoma.

Results: The medulloblastoma has the mutational signature SBS36 and driver pathogenic variants in CTNNB1, PTCH1 and KDM6A corresponding to G:C→T:A transversions, suggesting a role of MUTYH deficiency in oncogenesis.

Conclusions: Therefore, medulloblastoma could be a rare manifestation associated with germline biallelic pathogenic variants in MUTYH.

Keywords: MUTYH; medulloblastoma; mutational signature; oncogenetics; whole exome sequencing.