Genetic Alterations Associated With Progression and Recurrence in Meningiomas.


Molecular Pathology Research Unit (EPM, YCM, PM, ARL, MM, BM) and Department of Pathology (MM), Virgen de la Salud Hospital, Toledo; Department of Pathology, Xeral-Cíes Hospital Complex, Vigo (CF); Department of Pathology, Hospital Clinic, Universitat de Barcelona, IDIBAPS, Barcelona (TR); Department of Pathology, MD Anderson Internacional, Madrid (JFG); Research Unit, IdiPAZ, Hospital Universitario La Paz, Madrid (JAR); and Department of Neurosurgery, Puerta de Hierro Hospital, Madrid (ARL), Spain.

Abstract

ABSTRACT: Meningiomas are the most common primary brain tumors; they arise from the coverings of the brain. Although meningiomas are generally benign, some are more clinically aggressive, as reflected by their histopathological features or by their unexpected recurrence. We hypothesized that recurrent histologically benign meningiomas might have genetic features in common with those showing a more aggressive histology. By comparing gene expression profiles associated with meningioma progression and recurrence in 128 tumor samples (i.e. 83 benign World Health Organization [WHO] Grade I, 37 atypical WHO Grade II, and 8 anaplastic WHO Grade III) from 121 patients, we identified a 49-gene signature of meningioma aggressivity. This signature classified the tumors into 2 groups showing different clinical and pathological behaviors. The signature was composed of genes involved in the cell cycle (TMEM30B, CKS2, and UCHL1) and other pathways previously described as being altered in meningiomas, that is, WNT (SFRP1 and SFRP4) and transforming growth factor-β pathways (LTBP2 and LMO4). Overall, gene downregulation was observed in advanced and recurrent samples versus benign and original ones. We propose that this gene repression may be caused by gene promoter hypermethylation, as in the case of UCHL1 and SFRP1, suggesting that this epigenetic event, together with loss of specific chromosomal regions, may play an important role in meningioma progression and recurrence.

PMID: 22964784 [PubMed - as supplied by publisher]