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Prognostic and predictive biomarkers in central nervous system tumours: the molecular state of play

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Abstract

Central nervous system (CNS) tumours were one of the first cancer types to adopt and integrate molecular profiling into routine clinical diagnosis in 2016. The vast majority of these biomarkers, used to discriminate between tumour types, also offered prognostic information. With the advent of The Cancer Genome Atlas (TCGA) and other large genomic datasets, further prognostic sub-stratification was possible within tumour types, leading to increased precision in CNS tumour grading. This review outlines the evolution of the molecular landscape of adult CNS tumours, through the prism of World Health Organization (WHO) Classifications. We begin our journey in the pre-molecular era, where high-grade gliomas were divided into 'primary' and 'secondary' glioblastomas. Molecular alterations explaining these clinicopathological observations were the first branching points of glioma diagnostics, with the discovery of IDH1/2 mutations and 1p/19q codeletion. Subsequently, the rigorous characterisation of paediatric gliomas led to the unearthing of histone H3 alterations as a key event in gliomagenesis, which also had implications for young adult patients. Simultaneously, studies investigating prognostic biomarkers within tumour types were undertaken. Certain genomic phenotypes were found to portend unfavourable outcomes, for example, MYCN amplification in spinal ependymoma. The arrival of methylation profiling, having revolutionised the diagnosis of CNS tumours, now promises to bring increased prognostic accuracy, as has been shown in meningiomas. While MGMT promoter hypermethylation has remained a reliable biomarker of response to cytotoxic chemotherapy, targeted therapy in CNS tumours has unfortunately not had the success of other cancers. Therefore, predictive biomarkers have lagged behind the identification of prognostic biomarkers in CNS tumours. Emerging research from new clinical trials is cause for guarded optimism and may shift our conceptualisation of predictive biomarker testing in CNS tumours.

Keywords: Central nervous system; biomarker; ependymoma; glioblastoma; glioma; meningioma; predictive; prognosis.