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Molecular staging of intracranial ependymoma in children and adults.

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Abstract

PURPOSE: The biologic behavior of intracranial ependymoma is unpredictable on the basis of current staging approaches. We aimed at the identification of recurrent genetic aberrations in ependymoma and evaluated their prognostic significance to develop a molecular staging system that could complement current classification criteria.

PATIENTS AND METHODS: As a screening cohort, we studied a cohort of 122 patients with ependymoma before standardized therapy by using array-based comparative genomic hybridization. DNA copy-number aberrations identified as possible prognostic markers were validated in an independent cohort of 170 patients with ependymoma by fluorescence in situ hybridization analysis. Copy-number aberrations were correlated with clinical, histopathologic, and survival data.

RESULTS: In the screening cohort, age at diagnosis, gain of 1q, and homozygous deletion of CDKN2A comprised the most powerful independent indicators of unfavorable prognosis. In contrast, gains of chromosomes 9, 15q, and 18 and loss of chromosome 6 were associated with excellent survival. On the basis of these findings, we developed a molecular staging system comprised of three genetic risk groups, which was then confirmed in the validation cohort. Likelihood ratio tests and multivariate Cox regression also demonstrated the clear improvement in predictive accuracy after the addition of these novel genetic markers.

CONCLUSION: Genomic aberrations in ependymomas are powerful independent markers of disease progression and survival. By adding genetic markers to established clinical and histopathologic variables, outcome prediction can potentially be improved. Because the analyses can be conducted on routine paraffin-embedded material, it will now be possible to prospectively validate these markers in multicenter clinical trials on population-based cohorts.

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