ABSTRACT

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Refining M1 stage in medulloblastoma: criteria for cerebrospinal fluid cytology and implications for improved risk stratification from the HIT-2000 trial.

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BACKGROUND: Medulloblastoma is the most common malignant paediatric brain tumour, and cerebrospinal fluid (CSF) dissemination (M1 stage) is a high-risk prognostic factor. Criteria for CSF evaluation and for differentiating M0 from M1 stage are not clearly defined, and the prognostic significance of M1 stage in this context is unknown.

PATIENTS AND METHODS: CSF investigations from 405 patients with medulloblastoma of the prospective multicenter trial HIT-2000 (HIirnTumor-2000) were reviewed. Data from 213 patients aged ≥4 years were related to 5-year progression-free (5y-PFS) and overall survival.

RESULTS: Patients with cytological tumour dissemination only (M1 stage only) aged ≥4 years (n = 18) and patients with radiologically detected metastases (M2/3, n = 85) showed a worse 5y-PFS than M0 patients (n = 110) without signs of metastatic disease (5y-PFS 61.1% and 59.6% vs 80.7%; $p < 0.02$ and $p < 0.01$, log rank). Patients with positive samples drawn early after surgery who turned negative within 14 days postoperatively (n = 9) and patients with atypical cells (n = 6) showed a 5y-PFS similar to M0 patients. No tumour cells were detected in samples containing <10 nucleated cells. Analysis of cytological criteria showed a better predictive value for tumour cell clusters than ≥2 individual tumour cells.

CONCLUSION: Based on our results, we suggest that CSF medulloblastoma staging should be performed 14 days postoperatively by lumbar puncture, and specimens should contain at least 10 nucleated cells. Cytological tumour dissemination alone (M1 stage only) appears a high-risk prognostic factor associated with an

outcome comparable to M2/M3 stage. Tumour cell clusters seem to have a greater impact on prognosis than single tumour cells. This should be validated further.

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