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More precise characterization of brain tumors improves diagnosis and therapy

An international study with about 3000 patients confirms the validity of a new classification system for meningiomas. It combines tissue characteristics (histology) with molecular analyses and thus improves therapy planning.

Researchers from the Department of Neuropathology (Medical Director Prof. Dr. Andreas von Deimling) at Heidelberg University Hospital (UKHD) and the German Cancer Research Center (DKFZ) together with international colleagues have published the results of this prospective study in the Journal of Clinical Oncology.

In Germany, about 7,000 people are diagnosed with a tumor of the brain or spinal cord every year. One third of those affected suffer from a meningioma, which displaces surrounding brain tissue and presents with headaches and other neurological symptoms. Meningiomas are the most common brain tumors in adults and vary in disease progression from benign to highly aggressive and fatal. A reliable classification at diagnosis is crucial for the further course of therapy.

Meningioma classification is relevant for therapy

For diagnosis, meningiomas are currently classified by histology, i.e. the appearance of their cells under the microscope, into grade 1 (benign) to grade 3 (malignant). Ninety percent of cases are considered benign and can usually be removed completely by surgery. Whether the patient is thus cured or whether the tumor grows back quickly is often difficult to decide with the classic histological examination of tissue samples - the current WHO classification. "Precise risk assessment is extremely important for therapy and its adaptation in the course of the disease," says PD Dr. Felix Sahm, managing senior physician of neuropathology at the UKHD and a scientist at DKFZ. Currently, grade 2 and 3 meningiomas often require subsequent radiotherapy. "With the current classification based purely on histological criteria, aggressively growing meningiomas cannot be reliably distinguished from benign cases," reports Sahm, a project leader and scientist in the German Consortium for Translational Cancer Research (DKTK). As a result of inaccurate classification of the tumor, relapses repeatedly occur with tumors that are classified as too harmless and are mistakenly not irradiated. On the other hand, some tumors that are classified as too aggressive may be irradiated unnecessarily.

New classification system uses histological and molecular markers

The researchers therefore developed a new classification system based on histological and molecular characteristics that can be used to classify meningiomas much more accurately.

The new classification system is based on three pillars: the previous WHO grading based on tissue characteristics, the methylation status of the genetic material and copy number variations. The methylation status describes to which sections of the DNA small biochemical groups are attached, and the copy-number variations (CNV) show the different frequency of occurrence of different DNA sections in the genome. Both play important roles in gene readout and production of cellular building blocks. The combination of classical tissue characteristics and the molecular fingerprint of the tumor is converted into an algorithm-supported evaluation - the so-called score - and provides indications of how the individual meningioma will develop in the course of time. In this way, it is now possible for the first time to distinguish between tumors that appear identical in their DNA structure, but nevertheless take a different course of disease.

Validity of the score confirmed

In recent years, the Heidelberg researchers have already been able to demonstrate the development and validity of the new classification system based on methylation status in retrospective analyses of stored tumor samples. In their current publication, they combine the advantages of molecular analysis with the microscopic findings, and show over a study period of four years that the score is also meaningful in a forward-looking manner, i.e. prospectively, with freshly isolated tissue samples

and can support diagnostics as well as therapy planning.

Publication

Maas SLN, Stichel D, Hielscher T, et al. Integrated Molecular-Morphologic Meningioma Classification: A Multicenter Retrospective Analysis, Retrospectively and Prospectively Validated. J Clin Oncol. 2021;JCO2100784.
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