A study refines a molecular marker that accurately predicts the recurrence of aggressive meningiomas

February 17 2023

Credit: Pixabay/CC0 Public Domain

Drs. Akash Patel and Tiemo Klisch, investigators at the Jan and Dan Duncan Neurological Research Institute (Duncan NRI) at Texas

Children's Hospital and faculty at Baylor College of Medicine, have found that the loss of a single copy of CDKNA/B genes can greatly accelerate the recurrence of aggressive meningiomas, portending a poor prognosis for this subset of patients. Their study was published in *Acta Neuropathologica*.

Meningiomas are among the most common brain tumors and account for 39% of all tumors that originate in the brain. Most are benign, although 20% of them are aggressive—they recur quickly and frequently after removal until eventually, the patient succumbs to them. Meningiomas have historically been classified by the World Health Organization (WHO) into grades 1-3 based on their histopathological features with grade I being benign/slow-growing and grade 3 tumors being the most aggressive. Despite the rigor of this classification system, neurosurgeons and patients have long been vexed by the unpredictable behavior of these tumors.

Over the past decade, several groups have identified molecular markers to better classify meningiomas. In 2019, Drs. Patel, Klisch, and others at Duncan NRI and Baylor College developed a molecular classification system (group A-C with C being the most aggressive) that was able to predict tumor recurrence with far greater precision than the WHO grading scale. Last year, recognizing the prognostic value of these molecular markers, WHO included a molecular marker—the loss of both copies of two tumor suppressor genes—as a criterion for grade 3 meningioma classification.

In the present study, Drs. Patel, Klisch, and their collaborators examined 776 meningioma tumors of all grades obtained from patients enrolled in four different institutions. They found that meningiomas lacking CDKN2A/B were exclusively group C tumors but interestingly, were even more aggressive than typical group C meningiomas. While tumors recurred within 47 months (~ 4 years) of surgery in at least half of

typical group C meningioma patients, they recurred much more quickly (within 11-25 months or 1-2 years of surgery) in the subset of group C patients who were also deficient for CDKN2A/B. Furthermore, the team found that the loss of just a single copy of CDKN2A/B resulted in as poor a prognosis as the loss of both copies of these genes.

"Based on these findings, we think in order to accurately prognosticate meningioma patients, the first step should be to identify if they have group C (aggressive) tumors and then to further refine their diagnosis by checking for the loss of one or both copies of CDKN2A/B," said lead author, Dr. Patel who is also a neurosurgeon. "Unfortunately, there is currently no effective cure or treatment for this kind of meningioma, however, knowing that these genes are deficient will alert the oncologist that these patients need vigilant surveillance for early detection of recurrence. Thus, this study emphasizes the need for greater post-surgical care and clinical counseling of this subset of meningioma patients as well as raises the future possibility of having these patients undergo radiation immediately after surgery to reduce recurrence."

More information: A. Basit Khan et al, Even heterozygous loss of CDKN2A/B greatly accelerates recurrence in aggressive meningioma, *Acta Neuropathologica* (2023). DOI: 10.1007/s00401-023-02543-7

Provided by Texas Children's Hospital