Largest international study of rare childhood brain cancer shows early molecular diagnosis and aggressive therapy could improve patient outcomes

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Topics: Research

Summary:

> SickKids researchers offer new insights into the features of ETMR brain tumours and outline potential guidelines for testing and treatment approaches.

The Hospital for Sick Children (SickKids) researchers have published the first clinical management guidelines for patients with a rare and aggressive childhood brain tumour, based on a study of the largest cohort of patients with ETMR in the world. The study was published in The Lancet Child & Adolescent Health on September 29, 2021.

ETMRs (Embryonal Tumor with Multi-layered Rosettes) are an aggressive type of brain cancer found in infants and younger children, first identified as a type of tumour in 2000. The discovery of the C19MC gene as a genetic marker for ETMR by the Huang Lab at SickKids and subsequent insights that showed C19MC is a common genetic feature of several other infant brain cancers has highlighted the need for improved recognition of the disease. While ETMRs are estimated to be one of the most common brain cancers in children less than four, ETMR patients continue to be poorly studied and the disease lacks treatment guidelines.

Together with 140 international collaborators, the SickKids study, co-authored by Dr. Sara Khan, Clinical Fellow, Haematology/Oncology and Dr. Palma Solano-Paez, a former Clinical and Research Fellow, Neuro-Oncology in the Arthur and Sonia Labatt Brain Tumour Research Centre analyzed tumour samples and clinical information from over 200 ETMR patients through the Rare Brain Tumor Consortium (RBTC) . The RBTC is a global clinical registry and repository for rare paediatric brain tumours and was founded by Dr. Annie Huang, Lead Investigator on the study, Senior Scientist, Cell Biology and Staff Neuro-Oncologist at SickKids.

The paper offers detailed data on the genetic features and disease patterns of ETMRs. Although ETMRs are typically considered to develop in the cerebrum – the largest part of the brain – the study findings showed nearly half of the samples were found in various parts of the brain where they may be potentially mistaken for more common brain tumours. Through a systematic review of treatments received by patients, the findings also suggest a substantial proportion of ETMR patients could potentially benefit with a treatment plan that combines surgery and chemotherapy with some radiation.

“Prior to our study, the oncology field lacked basic information about the various ways this rare disease can present and mimic other types of brain tumours in children, so ETMR diagnoses were often made after treatment fails. Our study is the largest and most comprehensive review of ETMR tumours in the world, offering for the first time detailed insights into disease patterns in ETMRs patients as well as optimal medical management using molecular diagnoses and treatment approaches currently available and used in other paediatric brain tumours,” said Huang, who is also a Canada Research Chair in Rare Childhood Brain Cancers.

Survival rates for patients were found to be higher when patients received a molecular diagnosis and were treated promptly with a combination of surgery, high-dose chemotherapy and limited field radiation. The team’s observations also suggested about 30 to 40 per cent of patients who had complete tumour removal and received high-dose chemotherapy treatment survived without radiation. As patients with ETMRs are often very young, these findings suggest physicians may be able to postpone or avoid radiation.

The findings also showed that nine per cent of ETMR patients in the study received no active treatment or treatment was stopped at first sign of tumour growth. The data, Khan says, underscores not only the need for prompt diagnosis but also more detailed genetic studies to help better determine which patients can avoid radiation therapy.

"ETMRs are one of the fastest growing and treatment-resistant brain tumours, with some tumours re-growing quickly after surgery and even during chemotherapy – clinicians don't have much time to act if the patient receives an incorrect diagnosis. We suggest early molecular testing for the C19MC gene should be used in all brain cancers in infants and younger children to avoid delays in aggressive multi-modal treatment and potentially improve the survival of these patients who were previously thought to have very poor outcomes," says Khan.

Solano-Paez notes the guidelines offer a critical patient management framework previously unavailable to clinicians, which could help reduce misdiagnosis and avoid delays in treatment.

"Not only do our findings have immediate implications for children around the world who may have an ETMR, the data could help support the development of clinical trials and more targeted therapies for these rare cancers," says Solano-Paez, who is currently a Pediatric Neurooncologist at the Hospital Infantil Virgen del Rocio in Seville, Spain.

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