Improving the survival rates of childhood brain tumours: Translating Discoveries

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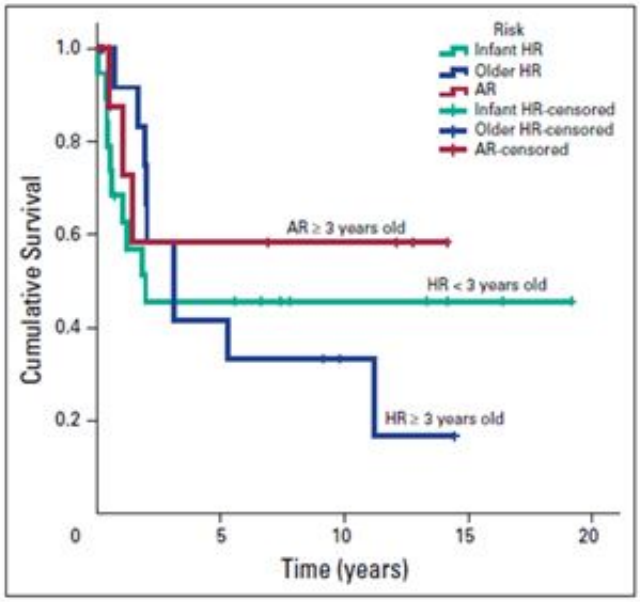

Overall survival of paediatric patients with average-risk (AR) and high-risk (HR) medulloblastoma treated from 1994 to 2013. Credit: American Society of Clinical Oncology

The future of children with brain tumours is very promising. To do nothing is to ignore the very real possibility of a treatment and cure. It is the time now to accelerate clinical and laboratory research in childhood brain tumours.

Brain tumours are the second most common childhood malignancy

worldwide. In Malaysia, a nationwide epidemiological survey from 2010 to 2012 found that brain tumours comprise approximately 15% of all childhood neoplasms. The estimated overall incidence of brain tumours amongst Malaysians aged less than 18 years is approximately 9.9 per million per year. After leukemia, brain tumors are the leading cause of cancer deaths in children. Surprisingly, the public remain unaware of the magnitude of this disease. Brain tumours either can be benign or malignant and different proportions of histological subtypes are present in children compared to adults. Medulloblastoma, low grade glioma and ependymoma are the most prevalent paediatric brain tumours. Meanwhile, in children less than 3 years, a third of brain tumours are of the embryonic type. Malignant brain tumours are highly aggressive and may be associated with systemic metastases.

Timely diagnoses with coordinated multidisciplinary team approaches are known to be pivotal factors that lead to increased overall survival and improved quality of life in children with brain tumours. Surgery represents the first line of treatment when addressing paediatric brain tumours. A retrospective review of paediatric patients with medulloblastoma treated in University of Malaya Medical Centre (UMMC) from January 1994 to December 2013 showed 5-year progression-free survival for patients≥ 3 years was 41.7%±14.2% in the high-risk group and 68.6%±18.6% in the average-risk group, whilst the 5-year overall survival in these two groups was 41.7%±14.2% and 58.3%±18.6% respectively. Children younger than 3 years had 5-year progression-free and overall survival rates of 47.6%±12.1% and 45.6%±11.7% respectively. These rates are significantly inferior to those in developed countries. In our series, we postulate a number of contributing factors for this inferior outcome - these include : limited health care resources, inadequate financial support for diagnostic tests and research activities, absence of molecular subgroup information, lack of multidisciplinary neuro-oncology team in many centres, inadequate long-term follow-up and treatment abandonment secondary to cultural

beliefs.

At the University of Malaya Medical Centre (UMMC), the care and long-term multidisciplinary follow-up for children with brain tumours are co-ordinated by the Paediatric Hematology-Oncology Unit. The UMMC team follows more than 150 brain tumour patients, from infancy through adulthood in outpatient oncology clinics and approximately 10-15 children and adolescents with brain tumours are diagnosed every year. A multidisciplinary neuro-oncology team was formed in 2013 comprising paediatric oncologists, neurosurgeons, radiotherapists, clinical oncologists, neuropathologists and radiologists. The team discusses both paediatric and adult brain tumour cases at a weekly multidisciplinary conference. They provide the most innovative therapeutic solution in a well-structured multidisciplinary approach, while at the same time offering support to the patient and the family. The departments of neurosurgery, radiation oncology and biomedical imaging have recently expanded their services to include more state-of-the-art equipment and medical facilities, such as gamma knife radiosurgery, conformal radiotherapy and intensity modulated radiotherapy. In addition, paediatric oncologists are able to offer evidence based chemotherapy following protocols from the Children's Oncology Group (COG) and International Society of Paediatric Oncology (SIOP).

While historically the prognosis of brain tumours has been bleak, there is good news on the horizon. The molecular era has advanced our understanding of brain tumour disease biology and identified distinct molecular subgroups with gene expression and DNA methylation, allowing better precision in choice of treatment. This is best exemplified in medulloblastoma which is the commonest childhood malignant brain tumour. The current treatment approach for managing medulloblastoma consists of maximal surgical resection, chemotherapy, craniospinal radiotherapy for older children or a radiotherapy-sparing approach using high-dose chemotherapy for children aged

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