Paediatric ependymomas: should we avoid radiotherapy?

Although ependymomas account for only 10% of all childhood brain tumours, this tumour type is particularly common in young children. Because of the potentially severe long-term effects of radiation on the developing central nervous system, over the past 20 years, several studies have focused on the feasibility of using postoperative chemotherapy to delay or even avoiding radiotherapy.

In this issue of *The Lancet* Oncology,[1] Grundy and colleagues present new findings that suggest up to 42% (95% CI 32–53) of young children with ependymomas could benefit from such a deferral strategy. Other attempts at delaying or avoiding radiation have been less successful: between 1986 and 1990, the Pediatric Oncology Group undertook the first large collaborative study of children younger than 3 years with intracranial ependymoma.[2] Depending on their age at diagnosis, children were given either 12 months or 24 months of chemotherapy, and radiation was started after the last cycle of chemotherapy. Despite systematic use of radiation at the end of the chemotherapy period, the 5-year progression-free survival with this approach was only 27%. More recently, a French group reported a disappointing 22% (13–43) 4-year progression-free survival in 73 patients treated with postoperative chemotherapy only.[3] That the results of Grundy's team are better than these two reports, and also than findings from the Children's Cancer Group[4] and Head Start[5], suggests that their strategy is the most effective so far.

However, why their protocol should be more successful is unclear. The absence of data for response to chemotherapy is a major limitation in the interpretation of these promising results. Phase II studies of chemotherapy in ependymoma have shown disappointing results, and the benefit of chemotherapy in tackling this disease remains essentially unproven.[6] Assessment of response to chemotherapy was not a principal component of this study, and the undertaking of a comprehensive radiological review might have been limited by technical and administrative barriers. However, the international paediatric oncology community might remain unconvinced as long as these survival data are not supported by radiological evidence of response to chemotherapy, in particular to methotrexate, considered by the authors as one of the main agents in the success of the trial.

The absence of information on the neurocognitive abilities of children who went through this study is another major limitation. Strategies aimed at avoiding radiotherapy have been recently challenged by the results of a pilot study from St Jude Children's Research Hospital, TN, USA, in which children with intracranial ependymoma aged 12 months and above were treated with postoperative conformal radiation.[7] In this study, the progression-free survival at 3 years for children younger than 3 years was 69·5% (SD 8·6). At a median follow up of 38 months (range 12·4–75·6), there were no significant changes in IQ, memory, academic achievement, adaptive behaviour, and visual-auditory learning, and all neurocognitive outcomes were within normal limits. Children younger than 3 years had a significantly lower IQ compared with older children; however, this difference was already present at the time of the first evaluation and serial assessments showed a gradual increase in IQ scores over time.

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For this reason, most North American institutions have abandoned deferral strategies that use chemotherapy; postoperative conformal radiotherapy is considered the best standard of care for all children with intracranial ependymoma from the age of 12 months onwards. A study by the Children's Oncology Group of more than 300 children with intracranial ependymoma is near completion.[8] This study will provide valuable information on the safety and efficacy of conformal radiotherapy in young children.

Where do we go from here? Fundamental differences in the approach to treatment between Europe and North America mean a randomised study is virtually impossible. Although the follow-up in the St Jude study was shorter, the event-free survival data favour conformal radiation.

Does this mean that there is no room for strategies like that of Grundy's team? The ball is in their court. To justify the continuation of such a strategy, the study needs to prove that there are young children that will not be left with impaired neurocognitive abilities as a result of prolonged chemotherapy. In addition, more work needs to be done to identify patients who are likely to benefit from a chemotherapy-only strategy. In the multivariate analysis, the study failed to identify prognostic factors for survival in non-metastatic patients. Further studies should be directed to the identification of biological

predictors of behaviour. Two recent retrospective studies have suggested that a combination of molecular and clinical markers could provide an accurate means of predicting prognosis in ependymoma.[9,10] Additional studies of ERBB2 and ERBB4 co-expression[9] or hTERT expression[10] in Grundy and colleague's cohort would provide additional insight and could help identify this subgroup of patients.

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Preparing mothers and fathers for death of their child


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In this issue of *The Lancet Oncology*, Valdimarsdóttir and colleagues[1] describe a analysis of a population-based dataset on parents' perceptions of intellectual and emotional awareness of their child's fatal cancer. The researchers focused on parents who reported a short awareness (less than 24 h) before their child's actual death. Adequately preparing parents intellectually and emotionally for the death of their child is associated with the parents' future well-being as bereaved survivors, according to Valdmirsdóttir and co-workers.[1] This finding confirms an earlier report that suggested parental perceptions of inadequate information (and absence of a caring attitude from health-care staff) during the time of their child's death in a paediatric intensive-care unit could predict the intensity of long-term parental grief.[2] Further evidence linking parent experience at the time of their child's death with the style of care given by health-care professionals, and subsequent parent well-being was reported by Contro and colleagues;[3] the group documented that parental perceptions of their child's unrelieved suffering while dying affected the parents' well-being for years later.

Providing parents with adequate information about their child's impending death and relieving the child's suffering directly connect the work of health-care professionals to the well-being of parents—what we do at the time of the child's dying continues to affect parental health up to at least a decade later. But Valdmirsdóttir and co-workers' findings highlight an additional consideration for health-care professionals who are dealing with parents in this situation: the need to prepare the mother and father in both similar and different ways because they are similarly and differently affected by factors related to intellectual and emotional awareness of the child's impending death.

Although mothers and fathers report similar intellectual and emotional awareness scores by time before their child's death, the effects of awareness factors differ by the sex of the parent.[1] This finding has important clinical implications and contrasts with reports about mothers and fathers of children in treatment for cancer or in survivorship who do not differ significantly from each other in coping behaviours.[4-6] During treatment or survivorship, parents are jointly focused on maintaining family integrity and an optimistic outlook.[4,7] Why would the effect of differences in the sex of the parents not occur during treatment, but emerge after the death of the child?

The similarities in factors that affect the awareness and well-being of mothers and fathers enhance our understanding of this end-of-life experience for bereaved