Stereotactic radiosurgery for primitive neuroectodermal tumors

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The authors report a single-institution retrospective review of their experience treating children with recurrent primitive neuroectodermal tumors (PNETs) by using stereotactic radiosurgery (SRS), specifically Gamma Knife surgery (GKS). Over a 17-year period, they collected 7 patients whom they treated with 15 GKS sessions. All of these children had undergone prior resection, multimodality chemotherapy, and craniospinal irradiation. These patients underwent 9 treatments for local recurrences and 6 for distant intracranial metastases. All 7 eventually died of their disease, but the authors concluded that the GKS treatments were well tolerated and contributed to prolongation of survival. They divided their patients’ outcomes into 2 groups: in 2 children the disease progressed early and the patients were dead within 5 months, whereas the other 5 seemed to have an initial response to the GKS treatments, and then their disease progressed. Four of these 5 were treated a second time. In 6 of the 7 children the tumor progressed locally, and in 6 of 7 it also progressed with disseminated disease. The 5 who seemed to respond to treatment enjoyed a median survival of 30 months.

There are a number of take-home messages that can be gleaned from this publication. The first is the fact that GKS is well tolerated by children who have previously undergone craniospinal irradiation and chemotherapy. Given that all of these children were treated with other salvage therapies in addition to SRS, one cannot comment on how SRS impacted survival time. Furthermore, no information is provided as to the patients’ quality of life at this stage of their disease (that is, whether the authors were actually prolonging their living or merely prolonging their dying). This is particularly true when one considers that 4 of 5 children with a third recurrence were again treated with SRS. The value of that retreatment has to be questioned, but cannot be evaluated from the data presented. Second, as is already recognized, in infants and younger children the tumors tend to progress more rapidly and to be more resistant to all therapeutic modalities. Whether this represents a cohort with more biologically aggressive disease is speculative. Given that the time course of the retrospective review extends back to 1989, it might be interesting to perform a fluorescence in situ hybridization analysis of their pathological specimens for the INI-1 gene to see how many children actually had an atypical teratoid rhabdoid tumor. Third, as has been our experience, the children who have the longest survival times are the ones who have had maximal repeat resection of their local recurrence, followed by SRS to the tumor bed or to a small residual nodule. Those who merely have SRS for lumps will have poorer responses and shorter survival times. In this series, the children undergoing GKS alone survived for 15 months, whereas those who underwent repeat resection followed by GKS enjoyed a median survival of 33.5 months. Finally, 6 of 7 children showed dissemination at the time of treatment failure, despite high-resolution MR images that demonstrated no evidence of metastatic disease, and despite negative cytological findings in CSF sampled just prior to SRS. This underscores the fact that we are in need of more sensitive surveillance tools for the detection of micrometastatic disease.

Ultimately, all of these children suffered disease progression and died. They had 1 or 2 GKS treatments as part of their salvage therapies, and the treatment was well tolerated, but could hardly be deemed cost effective. The final lesson of this series is that recurrent PNET after prior multimodality therapy is a systemic illness, not a localized disease. Even though all of our available tests might suggest that the recurrence is local, 6 of 7 children ultimately died of disseminated disease; therefore, using a focal therapy such as SRS may offer some degree of palliation, but only systemic therapy will afford the chance of a cure.

Reference

We thank Dr. Boop for his comments on our report, in which we evaluate the potential role of SRS in the treatment of recurrent pediatric PNETs in which conventional management has failed. As he points out, GKS is well tolerated and perhaps most effective when it follows maximal repeat resection of a local recurrence. This approach may be particularly suited to infants and younger children, who appear to have a more biologically aggressive and treatment-refractory disease. Although patients were selected for SRS based on the best available medical evidence and after failure of standard management, unrecognized micrometastatic disease may indeed have been the source of delayed distant progression. In addition, local disease may progress if such tumors are relatively resistant to radiation doses that are compatible with satisfactory risk to adjacent critical brain structures.

We agree that better surveillance tools are required to select patients appropriately, based on who is more likely to benefit from radiosurgery. To date, our experience in more than 9300 patients undergoing GKS has not allowed us to define a better modality than high-resolution MR imaging performed at the time of referral of the patient.

Although a focal approach such as GKS may offer palliation, it is difficult to quantify its potential benefit when other salvage therapies are being administered at the same time. In our patients, multimodal conventional management had already failed. In the apparent absence of effective alternative therapies, GKS was the best and potentially only option. As Dr. Boop certainly knows from personal experience, it is always difficult to tell parents “We have nothing more to offer your child.”

We did not assess the impact of radiosurgery on the quality of overall survival in this study; certainly the outpatient nature of this procedure and the minimal additional risks were well received by the parents of our patients. We completely agree with Dr. Boop that additional investment is needed to develop systemic therapies that may provide even more benefit for these difficult tumors. It is our hope that until better treatment strategies are developed, GKS will be considered as an important but palliative additional tool in the fight against treatment-resistant medulloblastomas. (DOI: 10.3171/2008.11.PEDS08387)