Commentary (Paulino): Current Management of Childhood Ependymoma

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Dr. Merchant provides a comprehensive overview of intracranial ependymoma in children. As he points out, most of the current information regarding childhood intracranial ependymoma has come from single-institution retrospective reviews. Of the prognostic indicators mentioned in the article, both young age and subtotal resection are widely accepted. Children less than 3 years old have a worse prognosis than older children, possibly because of more aggressive tumor biology, reluctance to give postoperative radiotherapy, or use of lower doses of radiotherapy. Regarding the degree of surgical resection, assessment by postoperative imaging is more important than the neurosurgeon’s perspective on whether a gross total or subtotal resection has been performed.[1,2]

Tumor grade is a controversial prognostic factor. Our experience and that of others indicate a worse outcome for high-grade or anaplastic ependymomas[3,4]; however, cooperative group studies and other single-institution reviews have not verified this finding.[2,5] One problem concerning tumor grade is the lack of agreement among individual pathologists. In a study from the Children’s Cancer Group, 22 (69%) of 32 cases had a discrepancy in the diagnosis on central review.[2]

Radiotherapy Volume
Perhaps one of the more controversial topics in ependymoma until recently has been the volume of irradiation. Studies from the 1970s to early 1980s reported a better outcome among patients receiving wide-field irradiation (craniospinal and whole-brain radiotherapy).[6] With the advent of better imaging and surgical techniques, current evidence indicates that the predominant pattern of failure is local, regardless of tumor grade or location.[2-3,5] For infratentorial ependymomas, the entire posterior fossa does not need to be treated.[7] Our current recommendation for a nondisseminated ependymoma is local radiotherapy. Craniospinal irradiation has more toxicity and may protract treatment duration, which can affect eventual outcome.[8,9] Craniospinal radiotherapy is reserved for the less than 10% of children with neuraxis dissemination.

Radiotherapy Dose
Studies that have shown a dose response level for ependymoma indicate a dose threshold of 45 to 50 Gy.[10,11] More recent studies suggest that dose escalation in subtotally resected tumors may be beneficial. As Dr. Merchant correctly points out, the Pediatric Oncology Group (POG) study 9132 used hyperfractionated radiotherapy to a total dose of 69.6 Gy (1.2 Gy twice daily). The 4-year event-free survival rate was 50%, compared to 24% in an earlier POG study that used a lower total dose of conventional radiotherapy.[12]

A study from the Children’s Hospital of Philadelphia showed a 74% 5-year progression-free survival rate for a group of children who had received adjuvant chemotherapy.[13] Of the 19 children, 10 had undergone subtotal resection and 16 had received hyperfractionated radiotherapy to a dose ranging from 65 to 72 Gy. It is unclear whether the higher doses of radiotherapy or the use of chemotherapy was responsible for the better outcome.

No Adjuvant Treatment
Although no randomized study has been conducted, based on retrospective studies, the standard adjuvant treatment after surgical resection for ependymoma is postoperative radiotherapy. Recently,
Hukin and colleagues challenged this dogma with a study in which 7 of 10 children (mostly with supratentorial ependymomas) treated with imaging-verified gross total resection received no further therapy and did not relapse. Of the three children who relapsed, two were salvaged with reresection and radiotherapy.[14]

Our experience showed that of five patients with infratentorial tumors who had imaging-verified gross total resection and did not receive any further treatment, four were locally controlled at 36 to 127 months after surgery.[7] In addition, Palma and colleagues reported long-term survival of four patients with supratentorial ependymomas treated with surgery alone.[15]

The above findings indicate that there may be a subset of patients who do not require adjuvant treatment. A proposed future study of the newly formed Children’s Oncology Group will look at surgery alone for low-grade, supratentorial tumors that have been completely resected.

**Chemotherapy**

I agree with Dr. Merchant regarding the role of chemotherapy. The only randomized trial that used adjuvant radiotherapy, with or without chemotherapy, did not show a benefit for chemotherapy.[16] The Children’s Hospital of Philadelphia study used chemotherapy and higher doses of radiotherapy, but these results are difficult to interpret.[13]

One recent study reported that giving chemotherapy to younger children resulted in the avoidance of radiotherapy in 40% and 23% of children at 2 and 4 years after the initiation of systemic treatment.[17] The real question is whether these same patients needed adjuvant therapy at all, since most of them had supratentorial tumors that had been completely resected.

**References:**


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