

Self-Assessment Module
2017 ASTRO Annual Meeting

Pediatric Brain Tumors-EDU35

Ranjit Bindra, MD, PhD and Shannon MacDonald, MD

1. What is your recommendation for a 12 y/o M with a supratentorial anaplastic ependymoma s/p GTR, negative CSF and spine MRI?
- a) CSI to 36 Gy followed by an involved field boost to total 54 Gy
 - b) Involved field radiation to 54-59.4 Gy
 - c) Chemotherapy for 1 year to delay radiation until the child is over 3 years of age
 - d) Chemotherapy alone and radiation only for tumor recurrence
 - e) Observation

Answer:

- b. Involved field radiation to 54-59.4 Gy

Feedback:

Involved field radiation therapy following maximal surgical resection is standard in the US. CSI has not been shown to be beneficial for localized disease at any age and should not be recommended. Chemotherapy has not been established as a standard treatment following GTR as there is no proven benefit. Omission of radiation has resulted in high rates of relapse. Adjuvant chemotherapy is, however, a question posed in the current COG trial, ACNS0831.

Location:

20

Reference:

Merchant TE, Li C, Xiong X, Kun LE, Boop FA, Sanford RA. Conformal radiotherapy after surgery for paediatric ependymoma: a prospective study. *The lancet oncology*. Mar 2009;10(3):258-266.

Macdonald SM, Sethi R, Lavally B, et al. Proton radiotherapy for pediatric central nervous system ependymoma: clinical outcomes for 70 patients. *Neuro-oncology*. Nov 2013;15(11):1552-1559.

Merchant, TE Current Clinical Challenges in Childhood Ependymoma. *Journal of Clinical Oncology* 35:2364-2369

--- End of Question 1 ---

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2. Which of the following regimens would not be acceptable for management of a localized pure germinoma of the pineal gland for a 17 y/o male?

- a) Carboplatinum/Etoposide for 2-4 cycles followed by whole ventricle radiation to 21 Gy followed by an involved field boost to 30-36 Gy
- b) Whole ventricle radiation to 24 Gy followed by a boost to the involved field to 45-50.4 Gy
- c) Carboplatinum/Etoposide for 4 cycles followed by 18 Gy to the whole ventricles followed by an involved field boost to 30 Gy on the Children's Oncology Group Trial
- d) Carboplatinum/Etoposide for 4 cycles followed by involved field radiation to 36 Gy for a patient with a complete response to chemotherapy

Answer:

d. Carboplatinum/Etoposide for 4 cycles followed by involved field radiation to 36 Gy for a patient with a complete response to chemotherapy

Feedback:

"Pure" Germinoma are highly curable tumors with DFS rates in excess of 90% for both localized and disseminated disease. In the US, chemotherapy followed by reduced-dose radiation is usually recommended for children to reduce late side effects of radiation. Two to four cycles of platinum based therapy, usually carboplatin and etoposide is delivered. If a complete response is achieved, a dose of 21 Gy to the whole ventricles followed by a boost to 30-40 Gy to the primary tumor region is delivered. If a complete response is not achieved, a second-look surgery is recommended (if this can be safely performed) to ensure that a non-germinomatous component is not present and/or higher doses of radiation may be recommended. Some studies have explored the use of chemotherapy followed by involved-field radiation to 30-40 Gy. Early reports showed promising results, but higher rates of ventricular relapse were later reported by Alapetite and colleagues, resulting in a shift back to a larger low dose volume, whole ventricular RT, first followed by an involved-field boost. The current COG protocol, ACNS1123 is investigating the use of pre-RT chemotherapy with four cycles of carboplatin and etoposide followed by very low-dose whole ventricular radiation to 18 Gy and a boost to a total of 30 Gy to the primary tumor for localized pure Germinoma following a complete response to four cycles of Carboplatin and Etoposide.

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Alapetite C, Brisse H, Patte C, et al. Pattern of relapse and outcome of non-metastatic germinoma patients treated with chemotherapy and limited field radiation: the SFOP experience. *Neuro-oncology*. Dec 2010;12(12):1318-1325.

--- End of Question 2 ---

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3. Which of the below characteristics is NOT included in the traditional stratification used for medulloblastoma to classify patients into standard-risk or high-risk groups but has been found to confer a less favorable prognosis and would make an otherwise standard-risk medulloblastoma patient eligible for the recent high-risk COG protocol, ACNS0332 (and ineligible for the recent standard-risk protocol, ACNS0331)?
- a) Age less than 3 years
 - b) + CSF
 - c) Desmoplastic histology
 - d) Anaplastic histology
 - e) Residual disease in the tumor bed measuring 2 cm²

Answer:

d. Anaplastic Histology

Feedback:

For medulloblastoma, maximal safe resection is recommended and additional work up includes MRI of the spine (pre-surgical or 10-14 days after surgery) and a lumbar puncture to obtain CSF (10-14 days after surgery; CSF should be obtained by LP and should not be performed prior to surgery due to risk of herniation). At present, a risk stratification system based on clinical factors divides patients into 2 risk groups, "high-risk" and "standard-risk", with standard-risk defined as children over the age of 3 with ≤ 1.5 cm² of residual disease following surgery and no metastatic disease (grossly or in CSF) and all others considered high-risk. In recent years, diffuse anaplastic histology has been found to portend a poor prognosis and these patients should be considered for high-risk therapy regimens

Location:

15

Reference:

Packer RJ, Gajjar A, Vezina G, et al. Phase III study of craniospinal radiation therapy followed by adjuvant chemotherapy for newly diagnosed average-risk medulloblastoma. *J Clin Oncol*. Sep 1 2006;24(25):4202-4208.

--- End of Question 3 ---

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4. Which of the following is NOT true regarding pediatric low grade gliomas?

- a) They can sometimes be cured with surgery alone
- b) Young patients are often treated with chemotherapy to delay radiation therapy
- c) When using radiation therapy to treat low grade gliomas, a large margin of at least 2 cm is needed around the visible tumor
- d) Radiation often provides durable control rates for this tumor

Answer:

c. When using radiation therapy to treat low grade gliomas, a large margin of at least 2 cm is needed around the visible tumor

Feedback:

Low-grade gliomas can be cured with surgery alone if they occur in a location amenable to surgery with acceptable morbidity, and therefore, many do not require radiation. Tumors that occur in the hypothalamus, thalamus, tectum, optics, and brainstem, often require radiation, as surgical morbidity may be unacceptable in these locations. Histological subtypes of pediatric low-grade gliomas include pilocytic (WHO grade I) and diffuse (WHO grade II), with pilocytic astrocytoma accounting for the majority of tumors in young children. Younger patients are often treated with chemotherapy to delay radiation and for children with Neurofibromatosis chemotherapy alone may be sufficient and spontaneous regression is possible. Packer, et al reported a 68% three-year progression-free survival rate for children treated with carboplatin and vincristine. Additional chemotherapeutic agents have since been studied and also shown efficacy, but 2nd and 3rd line regimens tend to lead to less efficacious and less durable results. For most children with low-grade glioma, chemotherapy typically delays progression, but radiation is usually still required for definitive treatment. When determining the appropriate therapy, one must also consider the cumulative morbidity of multiple regimens and risks of functional loss from progression of tumor. Data also indicates that young children are more likely to respond and have a durable response than older children. Radiation provides durable control with Merchant, et al reporting 10-year progression free survival rates of 74% for conformal focal radiation.

Location: 20

Reference:

Merchant TE, Conklin HM, Wu S, Lustig RH, Xiong X. Late effects of conformal radiation therapy for pediatric patients with low-grade glioma: prospective evaluation of cognitive, endocrine, and hearing deficits. *J Clin Oncol*. Aug 1 2009;27(22):3691-3697.

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Merchant TE, Kun LE, Wu S, Xiong X, Sanford RA, Boop FA. Phase II trial of conformal radiation therapy for pediatric low-grade glioma. *J Clin Oncol*. Aug 1 2009;27(22):3598-3604.

Packer RJ, Lange B, Ater J, et al. Carboplatin and vincristine for recurrent and newly diagnosed low-grade gliomas of childhood. *Journal of clinical oncology : official journal of the American Society of Clinical Oncology*. May 1993;11(5):850-856.

End of Question 4 - - -

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5. In the absence of a clinical trial, which would be the most appropriate treatment for a 5 yo M w/ a GBM s/p GTR?

- a) CSI to 23.4 Gy with a posterior fossa boost to 55.8 Gy
- b) WBRT (30 Gy in 10 fractions) followed by adjuvant CCNU chemotherapy
- c) 60 Gy focal EBRT with concurrent and adjuvant temozolomide (TMZ) chemotherapy
- d) High-dose chemotherapy followed by autologous stem cell rescue
- e) 45 Gy Focal EBRT followed by sequential PCV or TMZ chemotherapy

Answer:

C.

Feedback:

Apart from enrollment on a clinical trial, the standard of care for pediatric high-grade glioma (HGG) is to treat with fractionated EBRT to 60 Gy in 2 Gy fractions (or 59.4 Gy in 1.8 Gy fractions); however, it must be recognized that currently there is controversy over the most optimal management, with the results of ACNS0126 essentially showing no benefit to this “Stupp Style” regimen compared to historical controls (i.e., which included chemotherapy with RT). Choice (A) is the RT treatment for standard risk medulloblastoma. Choice (B) is not a standard glioma treatment regimen. Choice (D) has not shown a benefit in this disease. Choice (E) can be considered in lower grade adult gliomas but is not typically utilized in pediatric HGG.

Location:

Slides 20-25

Reference:

[Unclear standard of care for pediatric high grade glioma patients.](#)

Fangusaro J, Warren KE.

J Neurooncol. 2013 Jun;113(2):341-2. doi: 10.1007/s11060-013-1104-8. Epub 2013 Mar 8. No abstract available.

PMID:23471572

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