Proton Therapy for Craniopharyngioma

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**Background**

- **Craniopharyngiomas** are benign intracranial tumors arising from Rathke’s pouch in the sellar region.
  - They often have a solid and cystic component.
- Although these tumors do not have potential for malignant spread, they can cause complications due to their location and mass effect.
  - Complications include visual disturbances, endocrinopathies, and neurocognitive dysfunction.
- **Epidemiology:**
  - 3-9% of intracranial pediatric tumors
  - >50% of patients are less than 18 years of age
- **Presentation:**
  - Neuroendocrine deficits such as diabetes insipidus or growth defects
  - Visual disturbances including visual field cuts
  - Increased intracranial pressure
  - Behavioral changes
- **Treatment:**
  - Gross total resection (GTR) is the curative modality of treatment, however this is often difficult to achieve given the location of this tumor and its proximity to critical normal structures.
  - 10-30% of patients will have clinical recurrence following a total resection, and patients must thus be followed very closely post-operatively.
  - Studies dating back to 1961 (Kramer, et. al) have shown a high progression-free survival with subtotal resection + post-operative radiation therapy in this disease site.
  - In children who have only subtotal resection (STR) or recurrence after GTR, post-operative radiation is generally recommended. However, radiation may lead to devastating side effects such as short-term memory loss, hypothalamic dysfunction, visual loss, and decline in IQ (Merchant, et, al. 2008).
- Treatment of craniopharyngiomas requires one to consider the delicate balance between post-operative complications with GTR vs. delayed long-term effects of external beam photon radiation therapy including neuroendocrine and vascular events.
- **Proton radiation therapy** can potentially limit long-term side effects traditionally seen with photon radiation. This is due to improved dose conformity and dose distribution, as well as precision because of steep dose fall-off beyond the Bragg peak. These properties allow sparing of normal structures, which may be particularly valuable in the pediatric brain.
- The study presented here was performed in order to evaluate the outcomes of proton radiation in children requiring radiotherapy for treatment of craniopharyngioma after surgical resection at the Midwest Proton Radiotherapy Institute (MPRI).

**Materials and Methods**

- 21 pediatric patients received definitive proton-beam irradiation (PRT) for craniopharyngioma at the Midwest Proton Radiotherapy Institute (MPRI) between 2004 and 2010.
Patient demographics:
- Age 5-21 years (median age 13 years)
  - 13 males, 8 females
- All patients had pathology proven diagnosis of craniopharyngioma by biopsy of surgical resection. (Patients had 1-4 surgeries prior to PRT.)
- All patients received proton radiation with 3 fields: right lateral field, right posterior oblique field, and vertex field. This beam arrangement was used to avoid the left temporal lobe.
- PRT Dose: median 54.0 Cobalt Gray Equivalent (CGE) in a daily fractionated rate of 1.8 CGE per fraction (5 fractions per week)
  - 50.4 CGE in 2 patients (2/3 of these were aged 5 years old)
  - 52.2 CGE in 1 patient
  - 54.0 CGE in 17 patients
  - 57.6 CGE in 2 patients
- GTV was defined by MRI. CTV=GTV+0.5 cm. (expansion also created to account for cyst fluctuation)
- MRI was obtained 1-2 weeks after treatment began for evaluation of possible change in tumor volume, and 3 of 14 patients (21%) required a volume adjustment or cyst drainage.

Results
- Median follow up = 32 months (range 2-65 months).
- No deaths, 100% overall survival (OS).
  - Local control (LC) = 95.2%
  - 1 patient had an in-field recurrence
  - Event-free survival = 90.5%
  - 1 patient with out of field recurrence 2 months after completion of PRT who was then salvaged with surgery
- Side effects:
  - Endocrinopathies, although most had these pre-PRT.
  - All patients had improvement or stabilization of vision after PRT, without further decline of vision.
  - Neurocognitive follow-up continues.
    - 1 patient required special education.

Author’s Conclusions
- Proton radiation therapy after biopsy or subtotal surgical resection in children with craniopharyngioma is well tolerated with minimal acute side effects.
- The local control rates seen in this study parallel previous reports using photon radiation therapy in craniopharyngioma.
- Long-term follow up is needed to examine neurocognitive outcomes in these patients.

Clinical Implications
- Although craniopharyngiomas are benign intracranial tumors, they often can be devastating in children due their proximity to critical structures and the ability to cause symptoms by mass effect.
- Treatment for craniopharyngiomas is also difficult due to tumor location, and can often negatively affect quality of life in these patients, especially in terms of brain and visual development.
- For this reason, it is important to continue to find ways to minimize treatment-related side effects.
- This study was well-designed and aimed to evaluate the efficacy of proton beam radiation in these 21 patients.
- The authors showed that proton beam radiotherapy after partial surgical resection was well tolerated and did not appear to increase the risk of endocrine, neurologic, or visual problems.
  - However, the authors also acknowledge that the study population is small and follow-up is rather short.
Long-term risks of brain radiation including neurocognitive deficits and secondary malignancies have not been covered by the authors in this presentation, and longer-follow-up is needed to address these issues.

Based on this small cohort of patients, postoperative proton beam radiation for treatment of pediatric craniopharyngiomas appears to be acutely safe and efficacious.

Data on long-term side effects associated with this treatment is currently unavailable, however should be the focus of future work in this area.