Chemotherapy as first line treatment of Optic Pathway Gliomas in Children

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Optic Pathway Tumors in Children

- Accounts for 4-6% of all childhood brain tumors
- 65% of optic pathway tumors - Pilocytic Astrocytoma (PA)
- Equal gender
- Associated with NF1 – 30%
Proptosis & Painless Progressive Visual Loss
Pilocytic Astrocytoma of Hypothalamic Region
Management of OPG

Treatment Strategies

- Observation
- Surgery
- Radiation
- Chemotherapy
- Combination
Observation

• Periodic eye examination
• MRI of the brain
• Consider therapy;
  • *Deterioration of vision*
  • *Imaging evidence of progression*
Surgery

• **Indication**
  
  ➢ Single nerve involvement causing progressive disfiguring proptosis, blindness or both
  
  ➢ Exophytic chiasm tumors causing mass effect or hydrocephalus

• **Relative contraindication**
  
  ➢ Diffuse chiasmal involvement
Radiotherapy (RT)

- Recommended > 10-12 yrs
- Vision preservation/ Visual deterioration / improvement in progressive chiasmal gliomas
- Long term sequel may be devastating esp. in young
Chemotherapy

• Delays / avoids – RT / Surgery particularly in the youngest patients

• Used to treat progressive disease following RT/Surgery/Observation
Chemotherapy Options

- Carboplatin/vincristine
- Thioguanine/procarbazine/CCNU/vincristine
- Carboplatin monotherapy
- Temozolomide
- Vinblastine
- Cisplatin/etoposide
Chemotherapy Response

• Minority - measurable reduction in size
• Majority - stable disease
• Remainder - progress during or after completion of treatment
• Progression free survival (PFS) for chemotherapeutic regimens is 30% to 40% at 5 years
Outcome of OPT

- Favorable prognosis: 80%
- Tumor recurrence: 40%
- Improved/stable vision: 80%
- Significant neurological deficits: 11%
- Hormonal replacement: 15%
Molecular Revolution
Advances in Molecular Diagnostics

• Molecular diagnostics is incorporated into the initial evaluation of PA

Aberrant molecular pathways

Targeted therapy

Improve outcome
Overview of the major known mutations in LGG, other promising targets, and potential therapeutics.
Optic Pathway Tumors
KFSH – Experience
1997 - 2008
Optic Pathway Tumors of Childhood

Distribution by Gender (n=39)

Female, 22, 56%

Male, 17, 44%
Optic Pathway Tumors of Childhood

Distribution by Age at Diagnosis (n=39)

- Below 3 Years: 20 (51.3%)
- 3 to 6 Years: 10 (25.6%)
- Above 6 Years: 9 (23.1%)
Optic Pathway Tumors of Childhood

Treatment Offered at KFSHRC (n=32 Treatment Naïve)
Optic Pathway Tumors of Childhood

Event Free Survival

10 Years EFS: 0.411±0.181
Median Follow-up Time: 10 Years (Approx.)
Conclusion

- Chemotherapy effective esp. in young children

- Integration of molecular genotypes offers the opportunity to tailor therapy
Will these therapies improve on the historic PFS seen with traditional chemotherapy and result in durable complete responses?

Should biology-driven targeted therapy be integrated with, or replace, standard upfront therapies?

Will they actually minimize toxicity?
The important thing is not to stop questioning

Albert Einstein