Intra-Arterial Chemotherapy As Treatment for Glioblastoma Multiforme and Retinoblastoma

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History and Background

- Intra-arterial chemotherapy (IAC) was not used to treat glioblastoma multiforme (GBM) until the 1950s and 60s when the blood-brain barrier (BBB) was identified.[1]
- The membrane separating endothelial cells from the brain is selectively permeable, and most chemotherapies cannot pass through the BBB. [1]
- In 1990, a treatment protocol using IAC to treat retinoblastoma was created by Akihiro Kaneko.
- IAC is now regularly used to treat intraocular retinoblastoma.[2]
- When chemotherapy is injected into an artery that feeds directly to the tumor, chemotherapy concentration within the tumor increases while systemic exposure decreases.

Methods

A literature review was conducted using PubMed and searches using the keywords “Interventional neuro oncology,” “intra-arterial,” “retinoblastoma,” “intravenous,” “glioblastoma multiforme,” and “chemotherapy.” Information was gathered and summarized for a review article.

Glioblastoma Multiforme

- Intracranial malignant tumors are typically treated with surgical resection and adjuvant chemotherapy and radiation.[1]
  - This treatment plan leads to a low 2-year survivial rate.
- Because IAC would increase chemotherapy concentration within the tumor, it is likely that chemotherapy would be more effective if injected intra-arterially.
- Because of the blood-brain barrier, temozolomide, is the most common IAC drug because of its ability to pass through the BBB[6]
- Therefore necessary to disrupt the BBB in order for chemotherapy to reach tumor.[1]
- The BBB can be disrupted by creating a reversible osmotic opening, but this creates an all or nothing pathway.

a)

b)

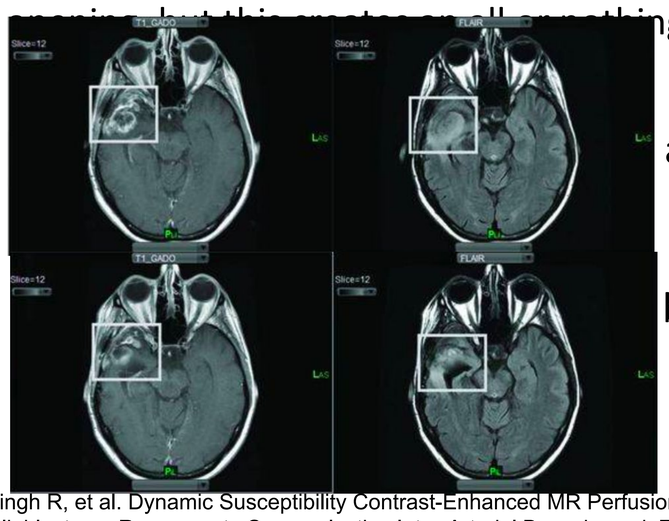

Figure 1.

a) Lesions GBM patients before IAC

b) Decreased size of lesions following IAC

Singh R, et al. Dynamic Susceptibility Contrast-Enhanced MR Perfusion Imaging in Assessing Recurrent Glioblastoma Response to Superselective Intra-Arterial Bevacizumab Therapy. *AJNR Am J Neuroradiol*. 2016;37(10):1838-1843. doi:10.3174/ajnr.A4823

Retinoblastoma

- Intra-arterial infusion of chemotherapy is regularly used to treat retinoblastoma, especially unilateral retinoblastoma.[2]
- Can also be used for bilateral cases, although that is less common.[2]
  - Controversial because increases risks of vascular toxicity
- Intravenous infusion is used for bilateral retinoblastoma.[2]
- IAC is used more often because chemotherapies can be effectively infected into the ophthalmic artery.
- However, the surgery for the ophthalmic artery infusion is a very expensive and complicated procedure.[2]
- Advantages of intravenous chemotherapy: protects from metastasis, minimizes long-term development of subsequent cancers.[5]
- Advantage of intra-arterial: better tumor control and lower systemic toxicities, can be used when other treatment modalities fail.[5]
- IAC can be used following recurrence and previous IAC.[2]

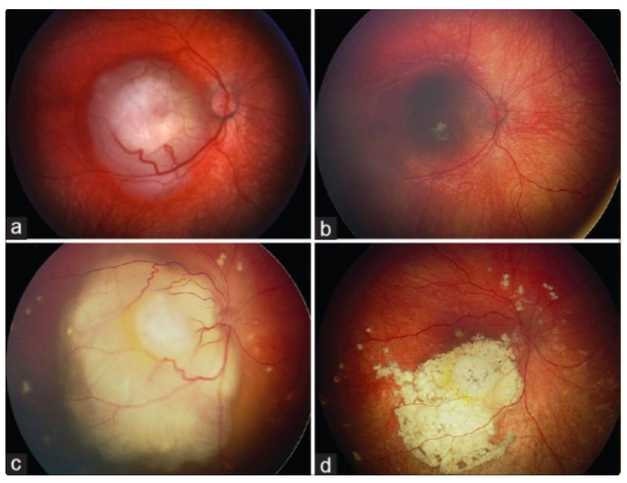

Figure 2.

a. Unilateral retinoblastoma with macular involvement

b. Retinoblastoma following IAC. Macula has been preserved.

c. Unilateral retinoblastoma with detached retina

d. After IAC, retina has reattached and tumor has shrunk.

Ancona-Lezama D, Dalvin LA, Shields CL. Modern treatment of retinoblastoma: A 2020 review. *Indian J Ophthalmol*. 2020;68(11):2356-2365. doi:10.4103/ijo.IJO_721_20

Conclusions

- IAC, while already a standard treatment modality for Retinoblastoma, is not standard for glioblastoma multiforme or other malignant intracranial tumors.
- The general advantage of IAC is increased tumor control by superselective access to the tumor via arteries.
- However, due to the expensive and complication of IAC surgery, the treatment is not always feasible.
- Additionally, the process of disrupting the BBB has not been perfected.
- In order to disrupt the BBB, the correct formula and concentration of hypertonic solutions must be used, but the correct one differs on a patient-by-patient basis, making it difficult to calculate.[1]
- Despite the regularity with which IAC is used for retinoblastoma, the cost of the surgery still makes IAC difficult.
- IAC is the future of interventional neuro-oncology because as infusion processes and BBB disruption methods are advanced, IAC will likely be more often used.
- IVC creates so much systemic toxicity, that if that can be avoided by superselective intra-arterial cerebral infusion, it will be.
- In the coming years, more research should be done on alternative BBB disruption methods as well as how to more easily infuse chemotherapies into cerebral arteries.

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Acknowledgements

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