Intra arterial Chemotherapy in Brain Stem Gliomas

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Intra-arterial Chemotherapy (IAC)

• IAC has the advantage of superselective administration of the drugs avoiding collateral effects.
• We need experience with use of catheters and microcatheters to get the target.
• Intra arterial therapy allows elevated concentrations of the drug in the site of tumor.
**Intra arterial chemotherapy with ACNU and radiotherapy in inoperable malignant gliomas.**


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IAC in inoperable Malignant Gliomas

• We perform selective IAC from Internal Carotid Artery.
• Three courses of intra arterial chemotherapy (IAC) with ACNU, at intervals of six weeks.
• Haematological, neurological anf ophtalmological toxicity were acceptable.
• Nitrosureas (ACNU) crosses the blood brain barrier.
• Problem: Vascularization of Glioblastomas.
Hypervascular tumor. Right carotid artery angiogram shows displacement of the branches of the middle cerebral artery. The tumor blush is indicated by the arrows.
IAC for Retinoblastoma

- Retinoblastoma presents a unique vascular supply (Ophthalmic artery).
- Not blood brain barrier (BBB)
- Superselective catheterysm is possible.
- These peculiar supply allows high concentration of intratumor drug.
- MELFALAN is used in this tumor with good results.
Brainstem vascular anatomy

**UPPER COMPLEX**
- SCA
- Midbrain
- CN III, IV, V
- Cerebellomesencephalic Fiss.
- Superior Cerebellar Ped.
- Tentorial Surface

**MIDDLE COMPLEX**
- AICA
- Pons
- CN VI, VII, VIII
- Middle Cerebellar Ped.
- Cerebellopontine Fiss., Petrosal Surface

**LOWER COMPLEX**
- PICA
- Medulla
- CN IX, X, XI, XII
- Cerebellomedullary Fiss.
- Inferior Cerebellar Ped.
- Suboccipital Surface
Intra-arterial chemotherapy for brain stem glioma: report of four cases.

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Abstract

Four patients with pontine gliomas were treated with radiation and intra-arterial chemotherapy using ACNU, cisplatin, and/or carboplatin. All underwent biopsy and were histologically proven to have gliomas. Even though three were benign histologically, all appeared malignant on neuroimaging. Two patients had complete remissions; the others had partial responses; three patients died, 36, 14, and 15 months after the primary diagnosis. One patient, now in complete remission, has been alive for 24 months. There was no neurotoxicity except for transient nausea and vomiting. Intra-arterial chemotherapy is effective against brain stem gliomas, producing remission with minimum side effects.
Intra-arterial carboplatin and intravenous etoposide for the treatment of recurrent and progressive non-GBM gliomas.

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Abstract

Recurrent and progressive non-GBM gliomas are a diverse group of brain tumors that often respond poorly to adjuvant chemotherapy treatment. Regional intra-arterial (IA) administration of chemotherapy may result in increased tumor uptake of drug, with improvement in response rates and time to progression (TTP). Twenty-five patients with recurrent or progressive non-GBM gliomas were treated with IA carboplatin (200 mg/m2/d) and intravenous (IV) etoposide (100 mg/m2/d) for 2 days every 4 weeks. Patients ranged in age from 22 to 68 years (mean 37.8). All but one patient had received standard irradiation, and eight patients had attempted prior chemotherapy. Five of 25 patients had objective responses (20%), while another 15 patients had stable disease (60%), receiving a total of 318 IA treatment procedures. There was one complete response (4.0%), three partial responses (12.0%), one minor response (4.0%), 15 stable diseases (60.0%), and five progressive diseases (20.0%). The median TTP was 24.2 weeks overall and 32 weeks in responders. Overall median survival was 34.2 weeks. Therapy was well tolerated, with mainly hematologic toxicity. Two patients had embolic complications. Although these are preliminary results, IA carboplatin and IV etoposide have modest activity against recurrent and progressive non-GBM gliomas and warrants further study.
• Selective IAC from vertebral artery.

• Moderate permeability of the blood brain barrier.

Low dosis of drug in the tumor
Osmotic blood-brain barrier disruption chemotherapy for diffuse pontine gliomas.

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Abstract
The prognosis for patients with diffuse pontine gliomas (DPG) remains poor. New aggressive innovative treatments are necessary to treat this disease. From 1984 to 1998, eight patients (4M/4F), median age 11 years, with DPG were treated with monthly osmotic blood-brain barrier disruption (BBBD) chemotherapy using intraarterial carboplatin or methotrexate and intravenous cytoxan and etoposide. Patients presented for a median duration of 6 weeks with increased intracranial pressure, long tract signs, diplopia, ataxia, and nausea/vomiting. DPG was demonstrated on magnetic resonance (MR) imaging in seven patients and on CT in one. Two patients had biopsies that showed an astrocytoma and an anaplastic astrocytoma. Three tumors enhanced on MR imaging after contrast administration. Three patients had radiation therapy before BBBD chemotherapy and four afterwards. Two patients had chemotherapy (tamoxifen, topotecan) before BBBD chemotherapy and two afterwards. In general, patients were evaluated with MR imaging every 3 months to monitor for a response to treatment. The median number of chemotherapy cycles that were administered by BBBD was 10, mean 10. Three patients also received one, two, or three cycles of intraarterial chemotherapy without BBBD. One patient that was started on carboplatin was converted to methotrexate, and five that were started on the methotrexate protocol were later converted over to carboplatin. One patient received monthly methotrexate followed by 14 days of procarbazine and one patient started on methotrexate was switched to navelbine. MR imaging demonstrated two partial responses, five patients with stable disease, and one with disease progression. The median time to tumor progression was 15 months with the range from <1 to 40 months. The median survival from the time of diagnosis was 27 months, ranging from 7 to 80 months. The median survival time from the first BBBD or intraarterial treatment was 16.5 months, ranging from 5 to 69 months. One patient was lost to follow-up with an unknown date of death. Although the sample size is small, the TTP and survival times are longer than those previously reported in other DPG series. In addition, the ability to demonstrate stable disease or partial responses in DPG on MR imaging argues for the therapeutic benefit of BBBD chemotherapy. The enhanced delivery of chemotherapy afforded by osmotic BBBD supports the further examination of this treatment modality for patients with DPG.
• Selective IAC from vertebral artery.

• Increase permeability of the blood brain barrier.

Increasing the drug concentration intratumor (but it is not enough)
This report mentions a treatment in a 43 years old man with Malignant BSG.

They describe:

- Previous occlusion of the basilar tip with catheter balloon.
- Disruption of BBB with Manitol Infusion.
- Superselective administration of Bevacizumab in DBSG.
• Previous reports of IAC in BSG.
• Experience in IAC of glioblastomas and Retinoblastomas.
• Final treatment of an advanced stage of pediatric malignant BSG (nine years old).
Protocol

- One hour previous IAC: dexametasona IV 0,35mg /Kg.
- Seizure medication.
- General anesthesia.
- Sistemic Heparin Na 1mg/Kg (after bifemoral puncture).
- 20% mannitol (37°C ).
- Melfalan 4mg/m2 to 1ml/min. (5mg total dosis).
• We pretended to perform more IAC sessions.

• Unfortunately the patient get worse after some weeks.
• We propose this method to treat Malignant Brainstem glioma as a different way to access to this tumor.
• The successful of this treatment requires the hands of an experienced team in pediatric interventional neuroradiology.
• It is important to be familiarized with the vascular anatomy of this region.
• It needs a large cohort of patients to demonstrate the effectivity of the procedure.
• Which chemotherapeutic agent???? Oncolytic Virus???