

HYPERBARIC OXYGEN TREATMENT OF INTRACRANIAL RADIONECHROSIS

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Background:

With growing utilization of radiosurgery and higher dose radiotherapy regiments, the incidence of radionecrosis is rising, as high as 15% in some reports. Conventional management with systemic steroids carries significant morbidity. If radionecrosis is uncontrolled the patient is subject to further surgical management of high mortality/morbidity risk. The therapeutic value of hyperbaric oxygen therapy (HBOT) in this population is relatively unexplored. We report a single institution experience of HBOT for symptomatic, radiologically evident intracranial radionecrosis.

Methods: Over a 4yr, eight patients with malignant intracranial tumors (4 primary brain tumors and 4 brain metastases) who had previously received radiation therapy were treated at our clinical facility (monoplace 2.0 ATA x 90 min. x 30 Rx) for radionecrosis. Four others were referred but not treated (1 resolved spontaneously 3 became too ill to treat while awaiting treatment). Diagnosis of radionecrosis was based on clinical history and radiological findings. Seven patients had evolving gadolinium-enhancing lesions with areas of central necrosis and surrounding vasogenic edema that corresponded with the irradiated high-dose target volume. Advanced imaging was used to help distinguish radionecrosis from tumor progression in some cases. Clinical response, radiological response and changes in steroid requirements are reported.

Results: No patients had signs of raised intracranial pressure. Neurologic functional level had deteriorated despite steroids in 6 cases, whereas in 2 cases poor steroids tolerance precipitated referral.

Baseline characteristics: Median Interval: radionecrosis to HBOT: 30.5 days (range1-88), Median Interval: radiotherapy to radionecrosis symptoms or imaging evidence: 3.6 months (Range 0.5-7.5)* *if remove outlier (4yr). Median age 50.7yr (range 21-92) Gender: 1 Male: 7 Female

Treatment Tolerance:

- Otic barotrauma = 3 of 8 patients
 - 1 minor & self limiting
 - 2 required typanostomy & tube placement
- Confinement anxiety = 1 of 8 patients; was managed with oral anxiolytic medication
- CNS oxygen toxicity = 2 of 8 patients
 - minor seizures with Jacksonian progression occurring at standard treatment of 2.4ATA both resolved with reduction of pressure [1 when reduced to 2 ATA from an initial 2.4; 1 when reduced to 1.5 ATA]
- Pulmonary oxygen toxicity = 1 of 8 patients (resulted in d/c HBOT after 33 fractions)

CONCLUSION: Early provision of hyperbaric oxygen may achieve acute or gradual improvement to blunt evolving radionecrosis resulting in a clinical improvement and reduce dependency on systemic steroids. In our experience, clinical response was observed soon after starting HBOT, suggesting these problems may be more sub-acute rather than chronic which raises the question of urgency in time to treatment once symptoms develop and possible modification to treatment protocol (ie fewer treatment fractions delivered sooner). Advanced imaging may further improve the diagnosis of radionecrosis and evaluate early response to optimize patient management.

Clinical

no difference identified between primary and metastatic tumor groups

Degree of clinical improvement	Resolved Presenting Sx	Significant Improvement	Moderate Improvement	No change	Deteriorated
Key symptom	Paralysis & Expressive Aphasia	Diplopia (2) Weakness(1)	Weakness(2)	Steroid intolerance	Steroid intolerance
Number of patients	1	3	2	1	1
# of HBOT fractions for response	1	2	9	12	No response
Number of patients	1	3	1	1	2 *

* truncated treatment course in both cases 6 fractions & 14 fractions respectively

Imaging - MRI

Edema and/or ring enhancement **	Significant Improvement Post HBOT	Moderate Improvement Post HBOT	No further progression Post HBOT	Deteriorated Post HBOT
Number of patients	2	2	1	2 (new mets)

** 7 of 8 patients displayed edema and/or ring enhancement

Medication Adverse Effects

Steroid dose reduction	Discontinued or reduced ***	Reduced	Same Dose	Not on steroids
Number of patients	2	3	2	1

*** in one case, drug induced diabetes resolved once off steroid

Discussion: Significant improvement was achieved in the first few treatments for 50% of our patients and correlated with subsequent imaging resolution of the enhancement and vasogenic edema which is inconsistent with angiogenesis however raises the hypothesis of a vascular permeability or immune mediated mechanism of action. Benefits include clinical & functional improvement, reduction or discontinuation of systemic steroids, reduction of associated imaging findings and avoidance of surgical intervention (only one needed in this series). In one case surgical intervention was subsequently required. The majority of patients achieved significant benefit from a well tolerated six week course of HBOT.

Case Report:

History

Patient initially diagnosed with breast cancer in 2002 who subsequently developed brain metastasis treated with radiosurgery in 2010. This survivor was initially assessed in the Hyperbaric Medicine Unit regarding soft tissue radiation injury and progressive neurologic impairment associated with stereotactic radio surgery of the brain 5 months earlier. Onset of symptoms 2 weeks pre-treatment included initial right arm weakness with subsequent facial and right leg involvement then memory deficit & expressive dysphasia. A week later the patient was admitted to hospital due to aphasia paralysis & reduced level of consciousness. The patient was commenced on QID steroids (Decadron 6 mg). A pretreatment MRI showed extent of left hemisphere edema including 0.5 cm midline shift.

Clinical Course

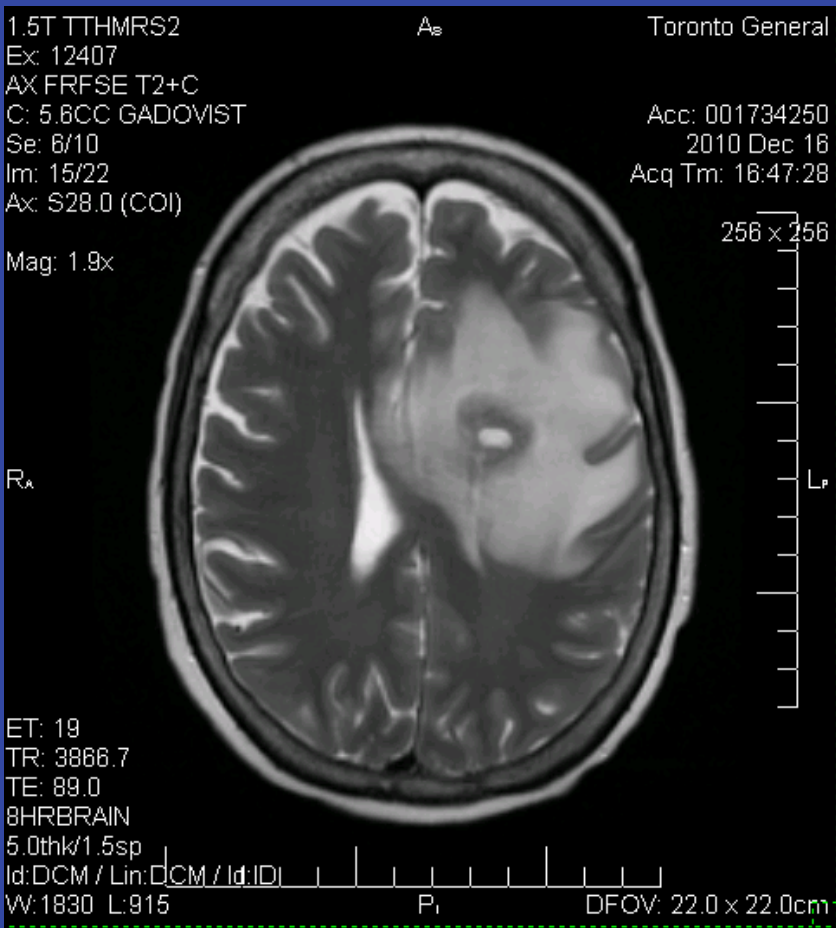
During the patient's initial treatment, she regained some motor function of the right arm & leg. Following 2nd treatment the patient had made significant sustained improvement in resolving the right sided paralysis such that she was able to walk and change clothing with minimal assistance, as well as manage hygiene & feeding independently. The patient was able to converse in detail although some residual word finding difficulty persisted.

Adverse Effects: 30 hyperbaric oxygen therapy fractions were treated with little difficulty aside from eustation tube obstruction managed with tube placement in the TMs.

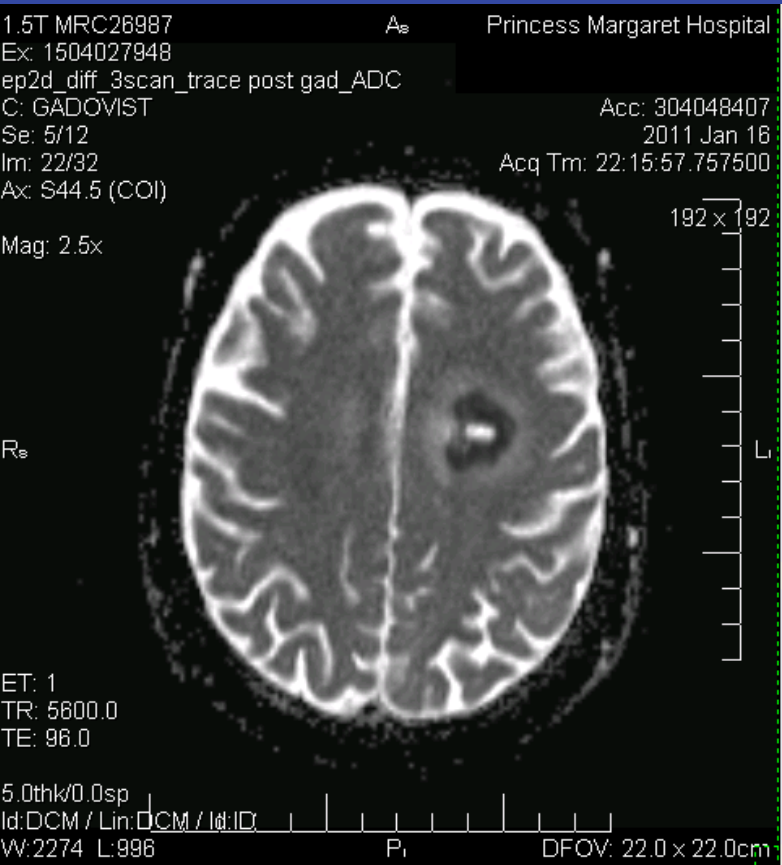
Outcome

Consistent with dramatic clinical recovery, comparison MRI performed after 12 fractions HBOT showed resolution of the previously identified gadolinium-enhanced lesion with central necrosis and surrounding edema in the pre treatment study.

MRI Imaging 5 Days Pre HBOT



MRI Imaging Post 12 fractions HBOT



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