Radiation Necrosis

Date: December 1st, 2016
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Disclosure statement

Presenter does not have any financial/commercial relationships to disclose
Objectives

- Identify the pathological mechanisms that contribute to radiation necrosis
- Explain the current treatments for radiation necrosis management
- State the possible potential role of stem cell and other novel approaches in radiation necrosis management
- Describe the nursing management of patients undergoing treatment for radiation necrosis

Cancer Treatment-related neurotoxicity

- Central Nervous System
  - Surgery
    - Traumatic
    - Ischemic
  - Radiation
    - Acute
    - Early Delayed
    - Late Delayed
  - Chemotherapy
    - Encephalopathy
    - Intracranial hemorrhage
    - Posterior reversible leukoencephalopathy
  - Myelopathy
  - Paraneoplastic disorders
- Peripheral Nervous System
  - Radiculopathy
  - Plexopathy
  - Myelopathy
  - Neuropathy
  - Myopathy
  - Paraneoplastic disorders

Why is this important?

- Disease symptomology vs. treatment toxicity
- Advances in systemic cancers therapies
- Increased survival
- Potential impact on quality of life
- Provides opportunities for additional research

“Neurological complications should be avoided rather than treated”
David A. Rottenberg, 1991
Case Study

• JD is a 61 year old male with a history of smoking, asthma and a history of seizures that started in 2010. CT scan at that time showed an abnormality in right posterior temporal lobe. Started on Phenytoin and Decadron.
• Seen in 2012 with generalized seizures with an aura of a headache sensation.
• CT scan done revealed an enhancing mass with edema in the right posterior temporal lobe. A CT of the chest also showed a lesion in the right hilar region.

Radiographic Scan
Case Study cont’d

- JD was diagnosed with NSCLC with brain metastasis.
- On 6/12 had SRS for the right parietal-temporal lesion. Currently being treated with Gemcitabine and Carboplatin. On Levatiracetam for seizure management.
- Seen in 8/12, No evidence of brain disease evident with regular follow ups.
- Seen 4/13 with reports of new morning headaches relieved with Acetaminophen.
- MRI showed an enhancing abnormality at the surgical resection site. Compared to previous study, the area grew 38% (unidimensional) or 63% (two dimensional measurement).

Radiographic Scan

May 2013 – still reports seizure. Approx. 10 days ago, had an episode of slurred speech, disorientation and asymmetrical smile. In the emergency room, received increased doses of dexamethasone and Levetiracetam. In addition, his wife reports his auditory hallucinations.

PET showed mild hyper-metabolism in the area of metastasis and surgery. In addition, hyper-metabolism at the right medial temporal lobe is noted.

He experiences significant changes in mood and depression with elevations in dexamethasone doses.
Right parietal craniotomy performed in May 2013. Pathology showed completely necrotic tissue.

Cerebral Radiation Toxicity

- **Acute Injury**
- **Sub-Acute Injury** (early delayed injury)
- **Delayed (late) Injury**

Radiation Necrosis

Radiation Necrosis

- Can occur in cerebral hemispheres and spinal cord
- Incidence - difficult to determine
- Concurrent chemotherapy may play a role
- Increased risk within the first 2 years
- Brain tolerance dose (45-50Gy), increased risk with higher doses
- Stereotactic radiosurgery incidence as high as 50%


Diagnosis

- Radiographic identification is limited
- Metabolic imaging and perfusion scans may aid in discrimination
- Tumor recurrence in conjunction with radiation necrosis delays correct identification
- Histo-pathological diagnosis


Clinical Manifestations

- Asymptomatic vs. Symptomatic
- Increased intracranial pressure
- Cognitive dysfunction
- Focal neurological deficits
Pathophysiology

- Vascular injury
- Inflammatory response
- Radiation Necrosis
- Glial injury
- Enzymatic disturbances
- Neuronal injury

Treatment

Corticosteroids

- Mechanism of action
- Dexamethasone – common
- Improvement of symptoms related to increased intracranial pressure (IICh)
- Decreased mineralocorticoid effect
- Dosing
- Side effects
- Nursing Management
Surgery

- Symptomatic patients
- Increased morbidity
- Nursing Management

Hyperbaric Oxygen Therapy

Tissue Hypoxia

Vascular injury

Necrosis

Mechanism of Action

[Diagram showing the mechanism of action of Hyperbaric Oxygen Therapy]

http://oxfordhbot.com/about-hyperbaric-therapy/
Hyperbaric Oxygen (HBO) Therapy

- Chuba et al, (1997) – 10 children with brain necrosis. All patients initially improved. Four died from disease and 5 of the remaining 6 sustained improvement
- Feldmeier and Hampson (2002) – systematic review supported the beneficial use of HBO in different types of radiation injuries
- Cihan et. al (2009).– Pt with PCNSL developed radiation necrosis who failed steroid therapy and refused surgery. HBO resulted in clinical and radiographic improvement

Hyperbaric Oxygen Therapy

Regimen
- 20-30 sessions at 2-2.24 atm
- 60 sessions (3 months), then 50 sessions (2.5 months)

Advantages
- Reduction in steroid dose
- Symptom and imaging improvement
- Used to treat symptom recurrence


Side Effects

- Ear pain
- Sinusitis
- Lower seizure threshold
- Tumor progression

Biologic Agents

Vascular injury

VEGF expression

Bevacizumab

- Monoclonal antibody against VEGF
- Used to treat a variety of cancers
- Side effects include hypertension, increased risk of thromboembolic events, hemorrhage and hypersensitivity
- Dosage: 5-10 mg/kg every two weeks (up to 4 - 8 cycles)

Retrospective study of 15 patients treated with Bevacizumab (single agent and combination)
- Radiation necrosis diagnosed in 8 patients
- Noted change in post gadolinium and FLAIR images post treatment
Fourteen (14) patients with confirmed radiation necrosis randomized to two treatment groups: Bevacizumab or placebo.

- No response noted in placebo group
- 100% of all patients who received Bevacizumab responded (5/5 randomized and 7/7 cross-over)
- Radiographic and symptom response
- Only 2 patients experienced a recurrence of RN ~ median of 10 months

Laser Interstitial Thermal Therapy (LITT)

- Focused laser energy at target area
- Treatment planning involves 3 zones
- Case reports are promising
- May be an option for high risk patients

Nerve Growth Factor

The future...

From human embryonic stem cells, isolated oligodendrocytes progenitors were transplanted.

Repair major white matter tracts resulting in structural and functional repair.

Behavioral testing showed complete recovery of cognitive function.

Additional transplantation in the cerebellum resulted in recovery of motor deficits.


Human Embryonic Stem Cell-Derived Oligodendrocyte Progenitors Repopulate the Brain and Rescue Behavioral Deficits following Radiation
Nursing Management

- Assess neurological baseline to detect changes
- Monitor for complications from treatment
- Implement home services as needed
- Evaluate compliance with medications and treatment plan
- Educate patient and caregiver regarding self care strategies

Future research...

- Increase knowledge regarding the pathophysiology of radiation necrosis
- Continue to improve technology regarding radiation therapy
- More rigorous research on current treatment options
- Research exploring other possibilities

Summary
References


