Radiation Induced Brain Injury

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Radiation to the brain in therapeutic dose can cause significant injury.

Pathophysiology:

	Hypothesis	Site	Outcome
1	Vascular hypothesis	Vessels	Ischemia and secondary white matter necrosis
2	Parenchymal hypothesis	Oligodendrocyte	Oligodendrocyte type 2 astrocyte fails to maintain myelin sheaths
3	Microglia	Microglia	Production of reactive oxygen species
4	Astrocytes	Astrocytes	Acute cellular swelling and chronic hypertrophy hyperplasia
5	*Neurons*	*Neurons*	DNA damage

Broadly classified as (a) acute effects, (b) early delayed effects, (c) late effects

(a) Acute effects: occur during or shortly after the radiation exposure which is secondary to edema and disruption of the blood–brain barrier (BBB).

	Clinical manifestation	Management
1.	Fatigue characterized by lack of improvement by rest	Methylphenidate 10 mg BD, escalating to 30 mg BD [1, 2] Side effect: Anxiety and insomnia
2.	Dizziness	Fludrocortisone 0.1 mg OD All these drugs cause hypertension, hypokalemia

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	Clinical manifestation	Management
3.	Increased intracranial pressure	Dexamethasone 8 mg TDS with PPI If not controlled mannitol infusion 1 mg/kg every 8 h Acetazolamide 250 mg BD
4.	Hair loss	Regrowth occurs
5.	Skin erythema	During radiation saline dressing, steroid skin cream may be applied Once radiation is completed topical emollients should be used

(b) Early delayed effects: Occurs 6–12 weeks after radiation exposure; due to transient demyelination.
   1. Generalized weakness.
   2. Somnolence.

   Somnolence evaluation

1. Subjective methods include.
   (a) Visual Analog Scales (VAS).
   (b) Epworth Sleepiness Scale.
2. Objective methods include.
   (a) Physician rated scale.
   (b) Littman Somnolence Syndrome (LSS) scale.
   (c) Electro-Encephalographic (EEG).

   These are reversible.

   Oral dexamethasone is used 4–8 mg TDS with PPI.

(c) Late effects: more than 1 year after radiation exposure leads to irreversible neurological consequences.
   1. Cognitive deficits.
   2. Necrosis of brain.
   3. Seizures.
   4. Cranial neuropathy.

   Management policy for late delayed effects:

- Oral dexamethasone is prescribed most common: Initial dose of 4 mg BD for mild symptoms and 4 mg QID or 8 mg TDS for moderate to severe symptoms.
- If life-threatening symptoms appear dose of dexamethasone 10–25 mg bolus followed by 4–10 mg QID.
- The patients should receive PPI along with dexamethasone therapy to reduce chances of gastritis.
- After symptomatic improvement dexamethasone should be tapered by 50% dose every third day starting 5–7 days after therapy initiation.
- For prolonged steroid therapy or if symptoms arise of oral thrush anti-fungal therapy should be used. Fluconazole 200 mg for first day subsequently 100 mg daily for 6 days should be used.

- Cognitive dysfunction occurs with total doses 20 Gy in adults and 24 Gy in children (conventional fractions).

11.1 Necrosis of Brain

1. Incidence of radiation necrosis varies widely as it is difficult to estimate the true diagnosis. The authors who used histopathology as the method of diagnosis concluded incidence 5–7%, whereas by radiological modality the incidence ranges from 20% to 25%.
2. Risk factors.
   (a) Dose-volume: As the lesion size increases, deliverable dose should be reduced accordingly to limit the risk of toxicity.

Lesion size (mm)	Safe dose (Gy)
≤20	24
21–30	18
31–40	15

   (b) Previous radiation exposure increases the chances of radiation necrosis.

Modality	Risk (%)
Previous SRS	20
WBRT	4
No WBRT	3

   (c) Certain parts of brain are at higher risk of radiation necrosis. Frontal cortex has highest risk while the brainstem has least chances. Few studies have also highlighted that superficial lesions are at a lower risk.
   (d) Margin for defining Planning Target Volume should be minimized with help of image guidance.
3. Diagnosis and investigations for patients with suspected RN.
   (a) While certain enhancement patterns described in the literature as "Swiss cheese," "soap bubble" or "cut green pepper" was initially thought to favor radiation necrosis, these have only a 25% positive predictive value.
4. Management:
   - Not always an irreversible process.
   - Oral corticosteroid is the preferred first line.
   - VEGF inhibitor: bevacizumab appears to be a promising agent [3].
   - Oral pentoxifylline and vitamin E are also being attempted.
   - Laser interstitial thermal therapy (LITT) also appears to be a promising approach [4].
   - Surgical resection can be an option in selected cases [5].

References

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