Complications of Radiation Therapy to the Head and Neck

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Lecture Goals

- Understand the use of Radiation in H&N
- Early effects
- Late effects
- Dental Implications
- Treatment protocol for:
  - Candidiasis
  - Xerostomia
  - Dental Extractions in irradiated Jaw
  - Implants in the irradiated Jaw
Radiotherapy

• Therapeutic radiation is delivered by 2 main methods:
  – Electromagnetic (photons):
    x-rays, gamma rays
  – Particulate radiation
    • Electrons
    • Protons
    • Neutrons

• Depth of penetration required is the main criterion used in choosing which energy to employ
Radiotherapy

- **Roentgen** \( \rightarrow \) measure of ionization in air
  - Used for radiation safety

- **Gray (Gy)**
  - Dose absorbed by the tissue (clinically relevant)
  - \( 1 \text{ Gy} = \text{ the absorption of } 1 \text{ joule/kg} \)
  - \( 1 \text{ Gy} = 100 \text{ cGy} = 100 \text{ rad} \)

- There is no absolute resistance to radiation
  - Normal tissue tolerance limits the dose
Radiotherapy

- Brachytherapy
  - Radium
  - Cesium
  - Iridium
Radiotherapy

• Mechanism of action
  – Interacts with atoms and molecules of the cells
  – Produces free radicals
  – Damages DNA
  – Affects all phases of the cell cycle but cells going mitosis are most affected
Radiation

• The sensitivity of cells to radiation is most pronounced shortly before and during mitosis; thus, the effect is greatest in rapidly dividing cells.

• Highly radiosensitive tissues are mucosa, skin, bone marrow, nerve, and muscle tissue.

• Of the bone cells, osteoblasts are more radiosensitive than are osteoclasts and osteocytes.
What orofacial tissues are affected by Radiation therapy?

- Oral mucosa
- Skin
- Subcutaneous tissue
- Cartilage
- Muscles of mastication
- Temporomandibular joint
- Teeth
- Oral flora
- Salivary glands
- Nasolacrimal drainage system
- Bone
- Thyroid and parathyroid glands
- Pituitary gland
- Peripheral and cranial nerves
- Lymphatics
- Paranasal sinuses
Tissue Effect – Early

- Acute skin reactions
- Hyperemia
- Reduced salivary gland function
- Mucositis
- Loss of taste
Tissue Effect – Long Term

• Seem not to occur when the tissues are exposed to less than about 45 Gy

• Chronic damage to skin, muscle, nerves, and bone
Mucositis

• A term given for widespread oral erythema, ulceration and soreness
Mucositis

• Presents with:
  – Pain
  – Erythema
  – Ulceration
  – Bleeding
# Mucositis

## World Health Organization Toxicity Grading

<table>
<thead>
<tr>
<th>Grade</th>
<th>Clinical features</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td>1</td>
<td>Soreness/erythema</td>
</tr>
<tr>
<td>2</td>
<td>Erythema, Ulcers but able to eat solids</td>
</tr>
<tr>
<td>3</td>
<td>Ulcers, but requires liquid diet</td>
</tr>
<tr>
<td>4</td>
<td>Oral alimentation not possible</td>
</tr>
</tbody>
</table>
Mucositis

• May be reduced by:
  – Minimizing doses of radiation
  – Using mucosa-sparing blocks
  – Using Amifostine before therapy
  – Betamethasone mouthwashes
Mucositis

- Opioids (MSO4 etc.)
- Avoiding irritants (smoking, spirits, or spicy foods)
- Good oral hygiene
- Oral cooling using ice chips
- Topical analgesics (especially before meals)
  - 2% lidocaine solution mouthwash
  - Magic Mouth Wash
    - Benadryl, Mylanta, and Carafate and viscous lidocaine in a 1:1:1:1
Mucositis

- The time to healing depends on the dose intensity and is usually complete within 3 weeks after the end of treatment.
Candidiasis
Candidiasis

- Infections by Candida albicans are commonly seen in irradiated patients

- Can be painful
Candidiasis

• Rinses
• Nystatin
• Amphotericin

• Clotrimazole (Mycelex) troches
• Caution troches contain sugars

• Oral/Systemic medications
• Diflucan
Xerostomia
Xerostomia

• Salivary Gland
  – Transient tenderness
  – Occasionally swelling
  – Occurs within a few hours after 1st dose
  – Decrease salivary flow noted within 24 hrs
  – May have ~50% decrease flow after 1st wk
  – Flow continues to decrease throughout treatment course and may become barely measurable at 6 wks.
Xerostomia

- Salivary changes
  - Increased viscosity
  - Decrease pH
  - Increased $[\text{Na}]$, $[\text{Ca}]$, $[\text{Mg}]$
  - Decreased $[\text{HCO}_3]$
Xerostomia

- Persists for several months to year
- May not recover
- Depends on volume of radiated salivary glands, total dose, individual patient
- Causes difficulty with:
  - Swallowing
  - Chewing
  - Talking
  - Denture wear
Xerostomia

• Prevention
  – IMRT
  – Amifostine (Ethylol)
    • Cytoprotective agent
  – RTOG 0244
    • Phase II study of submandibular gland transfer to the submental space prior to therapy
  – RTOG 97-09
    • Phase II study to test the efficacy of the prophylactic use of oral pilocarpine to reduce hyposalivation and mucositis. Closed. No improvement in mucositis but improved salivation
Xerostomia - Treatment

• Sialogogues
  • Pilocarpine (Salagen) 5 mg tid
  • Salivix (Malic acid)

• Salivary replacements
  • Glandosane
  • Luborant
  • Oralbalance
  • Salivace
  • Saliveze
Radiation Caries

• Circumferential cervical decay
• Incisal decay

• Related to:
  – Xerostomia
    • Change in oral flora
    • Pulpal death
    • Dentine dehydration
    • Enamel loss
Prevention of Radiation Caries

- Daily fluoride application
- 0.4% stannous fluoride gel
- 1.1% neutral sodium fluoride
- Tray worn for 5-10 minutes
- Must cover cervical portion of teeth
Osteoradionecrosis
ORN
Pathophysiology of ORN

- Watson & Scarborough (1938)
- Meyer (1970)
  - Triad:
    - Radiation Therapy
    - Local trauma
    - Infection
- Marx’s Theory
  - 3 H’s
    - Hypovascular
    - Hypocellular
    - Hypoxic
What is the Incidence of ORN?

- Recent studies
  - 5% to 15%
  - overall incidence of 5.4%
  - Bimodal distribution
    - 12 months and 24-60 months
Incidence of Osteonecrosis according to radiation dose to bone

<table>
<thead>
<tr>
<th>Dose to Bone (cGy)</th>
<th>Dentulous Pt.</th>
<th>Edentulous Pt.</th>
</tr>
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<tbody>
<tr>
<td>&lt;6500</td>
<td>0/36 (0%)</td>
<td>0/3 (0%)</td>
</tr>
<tr>
<td>6500-7500</td>
<td>8/29 (28%)</td>
<td>1/15 (7%)</td>
</tr>
<tr>
<td>&gt;7500</td>
<td>11/13 (85%)</td>
<td>2/4 (50%)</td>
</tr>
<tr>
<td>Total</td>
<td>19/78 (24%)</td>
<td>3/22 (14%)</td>
</tr>
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Data from Morrish et al., Cancer 1981
Osteoradionecrosis

- Almost all cases occur within the field of radiation
- Most cases associated with a dental extraction
Osteoradionecrosis

FIGURE 1. Location of the most affected areas of ORN on radiographs in 80 patients.
Clinical Features of ORN

- Exposed bone, loss of soft tissue and bone
- Pain and dysphasia/anesthesia
- Soft tissue necrosis
- Trismus
- Pathologic fracture and orocutaneous fistula
Radiographic Features of ORN

- Diffuse radiolucency without sclerotic demarcation

- CT / MRI to evaluate extent of ORN

- Must Biopsy to rule out tumor recurrence
Conservative Management of ORN

- Daily local irrigation (saline, NaHCO3, Chlorhexidine)
- Systemic antibiotics
- Avoidance of irritants
- Good oral hygiene instructions
- Gentle removal of sequestrum
HBO

• Administration of 100% oxygen in a special chamber at 2.4 atmosphere absolute pressure for 90 minutes each session.

• Delivered once a day, 5 times per week
What is the Mechanism of HBO

• Improve tissue healing by:
  – Angiogenesis
  – Inducing fibroplasia and neocellularity
  – Promoting survival of osteoprogenitor cells
  – Promoting the formation of functional periosteum
Controversies regarding use of HBO in ORN

- Hyperbaric Oxygen Therapy for Radionecrosis of the Jaw: a randomized, placebo-controlled, double-blind trial from the ORN96 study group.

Conclusion: Patients with overt mandibular osteoradionecrosis did not benefit from hyperbaric oxygenation
HBO and Osteoradionecrosis

• The influence of HBO on the outcome of patients treated for osteoradionecrosis: 8 year study

• 23 patients
• HBO group – 12.5% cure rate
• Non-HBO group – 86% cure rate

• D’Souza et al. IJOMS 2007
ORN – Fibrosis Theory

• Damage to bone caused by radiation induced fibrosis

• Bone cells damaged by free radicals, acute inflammation and chronic activation of fibroblasts

Treatment ORN– Fibroblast Activation Theory

• Pentoxifyline
  – Vasodilator
  – Anti-TNFα
  – Inhibits dermal fibroblasts

• Vitamin E
  – Anti-oxidant
  – Reduce free radical damage

ORN treatment failure
Fibula Osteocutaneous Free Flap
ORN treatment failure
Dental Management
Pre-Radiation
Dental Management Prior to Radiation

- Complete oral/dental examination and treatment plan
- Any necessary extraction and surgery
- Maintenance of teeth and caries control
- Restoration of restorable teeth
- Prothestic examination to prevent postradiation trauma from ill-fitting dentures
Dental Management Prior to Radiation

- Consider:
  - Condition of the dentition
  - Level of oral hygiene and patient attitude
  - Age of the patient
  - Radiation field and dose
  - Urgency of radiation treatment
Dental Management Prior to Radiation

• Caries control
  – Prophylactic care before and at the end of therapy
  – Oral hygiene instructions
  – Daily administration of fluoride
  – Weekly follow-up during therapy and every 3-4 weeks afterward
Guideline for Extraction Prior to Radiation

• All carious teeth in the field of xrt (>60 Gy) should be extracted except in patients with excellent oral hygiene and dentition
• All questionable teeth should be extracted
• Full bony impacted teeth can be left in place
• Optimal time for extraction is 21 days before beginning xrt
Extractions

• Atraumatic extractions
• perform an alveolectomy
• smooth the bone
• Perform a primary closure
• Allow a minimum of 1 week to 10 days for healing prior to beginning XRT
• Preferable to allow 14 to 21 days
Dental Management
Post-Radiation
Management of patient post radiation

• Obtain records of radiation fields and dose

• Recall for prophylaxis q 3 months

• Daily fluoride treatment for life

• Wait for mucositis to resolve prior to prosthesis placement

• Avoid invasive procedure involving irradiated bone

• HBO vs. Pentoxifylline & Vitamin E
Implants in Irradiated Jaw
• 48 patients
• 271 implants placed
• Implant survival
  – 1 year (99%)
  – 10 year (72%)
• Higher incidence of implant failures
  – Maxilla
  – Posterior oral cavity
• Conclusion
  – Dental implants placed into irradiated bone have a higher failure rate than non-irradiated bone

• HBO for irradiated patients who require dental implants: a Cochrane review of randomised clinical trials

• 1 trial found
• 26 patients HBO vs. non-HBO

• Conclusion – no evidence for or against effectiveness of HBO for improving dental implant outcomes

Radiation induced Malignancies
Radiation induced Malignancies

- Soft tissue Sarcomas
- Thyroid Carcinoma
THANK YOU!