Osteonecrosis of the Jaw - MRONJ

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Objectives

- Define and describe the different agents that have been associated with MRONJ?
- Define and describe the clinical and radiographic presentation of MRONJ?
- Describe the risk factors associated with MRONJ?
- Describe the evidence-based management strategies for MRONJ
  - Preventive
  - Treatment

Antiresorptives: Rationale for use

- Osteoporosis
  - Potential to impact 54 million Americans (55 percent > 50 years).
  - 50% of women and 25% of men over 50 will sustain an osteoporosis-related fracture
  - 34 million more with low bone mass, which increases risk for osteoporosis.

http://nof.org/articles/4
Antiresorptives: Rationale for use

- Osteoporosis is responsible for more than 1.5 million fractures annually, including:
  - 300,000 hip fractures
  - 700,000 vertebral fractures
  - 250,000 wrist fractures
  - 300,000 fractures at other sites.
- The estimated national direct care expenditures for osteoporotic fractures is $18 billion per year in 2002 dollars.
- Bisphosphonates reduce risk of vertebral and hip fractures by 60%.

Bone Health and Osteoporosis: A Report of the Surgeon General

Antiresorptives: Rationale for use

- Cancer
  - + osteoclast activity by osteoclast stim. proteins (RANKL) and PTH-related peptide.
  - Bone metastases are associated with pain, fractures, spinal cord compression, and hypercalcemia of malignancy.
  - The goals of treatment for bone metastases are to prevent disease-related skeletal complications, palliate pain, and maintain quality of life.
  - Multiple myeloma, bone metastasis related to breast, prostate, lung, and renal cell cancer.
- Paget's disease
  - Accelerated bone turnover with overgrowth
  - Goal of treatment is to interrupt uncontrolled bone remodeling.

Antiresorptive Medications Associated with ONJ

<table>
<thead>
<tr>
<th>Medications</th>
<th>Action</th>
<th>Medical Use</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bisphosphonates</td>
<td>Osteoclast Inhibitor via mevalonate pathway</td>
<td>Osteoporosis Bone Metastasis Multiple Myeloma Antitumor</td>
</tr>
<tr>
<td>Denosumab</td>
<td>RANK-RANKL Pathway Inhibitor</td>
<td>Osteoporosis Bone Metastasis</td>
</tr>
<tr>
<td>Anti-angiogenics</td>
<td>VEGF Inhibitors</td>
<td>Advanced Tumors</td>
</tr>
<tr>
<td>SU5416, Sorafenib</td>
<td>Receptor tyrosine kinase inhibitor (TKI)</td>
<td>Renal cell carcinoma and GIST</td>
</tr>
</tbody>
</table>
Bisphosphonate: Mechanism of Action

- Analogue of inorganic pyrophosphates
- High affinity for bone with increased bone formation or resorption
- Internalized by osteoclasts and inhibit activity
- Estimated half-life in bone 10-12 years

Bisphosphonate: Other mechanisms

- Anti-angiogenesis properties
- In-vitro anti-tumor effects
  - tumor cell apoptosis
  - tumor cell adhesion to ECM
  - tumor invasion
- Morgan GJ. Lancet Dec 2011;376:1989-1999. First-line tx with zoledronic acid...
  - Overall survival improved independently of prevention of skeletal-related events, showing that zoledronic acid has treatment benefits beyond bone health. (12% improved progression-free survival vs. clodronic acid)
  - Support immediate treatment with zoledronic acid in patients with newly diagnosed multiple myeloma, not only for prevention of skeletal-related events, but also for potential antimyeloma benefits.

Denosumab: Mechanism of Action

- Monoclonal antibody against RANK ligand
- RANKL key activator of osteoclasts
  - Via tumor-secreted growth factors and cytokine → Skeletal related events (SRE)
- Elimination half-life 25-32 days
- Does not bind to bone
- Osteoclastic activity is suppressed while in circulation, but is reversible when cleared from circulation
Anti-angiogenesis

- Bevacizumab (Avastin): Humanized antibody to vascular endothelial growth factor (VEGF)
  - Interfere with normal blood vessel formation- osteosclerosis
  - Half life- 20 days
- Sunitinib (Sutent) and Sorafenib (Nexavar): blocks VEGF tyrosine kinase
  - Half life- 40-60 hours

Osteoporosis- Comparative Effectiveness

- Meta-analysis of 116 placebo-controlled or head-to-head trials assessed alendronate, risedronate, ibandronate, zoledronic acid, raloxifene, denosumab, teriparatide, vitamin D, and calcium
  - Any of the drugs were likely more effective than vitamin D or calcium
  - Raloxifene was not as strong as the evidence for the other drugs
  - Differences in vertebral and nonvertebral fracture risk reduction among any of the bisphosphonates, denosumab, or teriparatide were not consistent or statistically significant

SRE- Comparative Effectiveness

- Denosumab to ZA for SRE
  - Denosumab improvement delay and treatment SRE (prostate, breast and combined solid tumors)
  - 19% delay in time to first SRE and time to develop moderate and severe pain

MRONJ incidence

<table>
<thead>
<tr>
<th>Study</th>
<th>Denosumab NMI</th>
<th>Zoledronate NMI</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>NTH031046/85</td>
<td>1,820</td>
<td>20 (0.94%)</td>
<td>98</td>
</tr>
<tr>
<td>NTH033378/85</td>
<td>682</td>
<td>31 (0.45%)</td>
<td>96</td>
</tr>
<tr>
<td>Total</td>
<td>1,914</td>
<td>31 (0.16%)</td>
<td>97</td>
</tr>
</tbody>
</table>

CNI = Number needed to harm, since these are head-to-head comparison trials, the incidence of osteonecrosis of the jaws in the control populations was assumed to be zero. NMI = number of metastatic patients treated the treatment.

Alpha value is set to $= 0.05$. Alpha values reported from original cancer reports [7-9].

ClinicalTrials.gov NCT00121444, sponsored by Sagent Inc and Amgen Inc.
ClinicalTrials.gov NCT00138988, sponsored by Amgen Inc.

MRONJ incidence

- **Zolendronate**
  - Cumulative incidence 0.7 – 6.7%
  - 50-100x higher that cancer patients tx with placebo
- **Denosumab**
  - 0.7-1.9%
- **Bevacizumab**
  - 0.2%
  - 0.9% (with zolendronate)
  - 55/800,000 (British and French regulatory agencies)

**Denosumab**

  - 8893 patients with a variety of solid tumors from 7 randomized controlled trials (RCTs) were included for the meta-analysis.
  - The overall incidence of ONJ in cancer patients receiving denosumab was 1.7 % [95 % CI: 0.9-3.1 %].
  - Also, the use of denosumab was associated with significantly increased risk of ONJ in comparison with bisphosphonates (BPs)/placebo treatment (RR 1.61, 95 % CI: 1.05-2.48, P = 0.029).
  - Subgroup analysis based on controlled therapies demonstrated an increased risk of ONJ in denosumab therapy, when compared with BPs (RR 1.48, 95 % CI: 0.96-2.29, P = 0.078) or placebo (RR 16.28, 95 % CI: 1.68-158.05, P = 0.017).
MRONJ Incidence

- Tyrosine Kinase Inhibitors (sunitinib)
  - Case reports
  - 27/100,000 patients (British and French regulatory agencies)
- Raloxifene (nonsteroidal benzothiophene-selective estrogen receptor modulator)

Oral Care Study Group Systematic Review: IV bisphosphonates


Weighted prevalence of BON by study design and bisphosphonate type

<table>
<thead>
<tr>
<th></th>
<th>Sample Pop.</th>
<th>Mean Wgt. Pres.</th>
<th>Confidence Interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>All Studies (11)</td>
<td>39,124</td>
<td>6.1%</td>
<td>0.3-11.9%</td>
</tr>
<tr>
<td>Cancer cohort documented follow-up (5)</td>
<td>927</td>
<td>13.3%</td>
<td>1.6-23.1%</td>
</tr>
<tr>
<td>Cancer cohort undocumented follow-up (2)</td>
<td>8,029</td>
<td>0.7%</td>
<td>0.7-1.74%</td>
</tr>
<tr>
<td>Epidemiologic study (6)</td>
<td>28,308</td>
<td>1.2%</td>
<td>0.5-1.1%</td>
</tr>
<tr>
<td>Zoledronic acid only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All studies (5)</td>
<td>10,380</td>
<td>8.8%</td>
<td>3.4-13.9%</td>
</tr>
<tr>
<td>Cancer cohort documented follow-up (3)</td>
<td>927</td>
<td>9.8%</td>
<td>4.4-17.4%</td>
</tr>
<tr>
<td>Cancer cohort undocumented follow-up (2)</td>
<td>8,029</td>
<td>7.4%</td>
<td>5.8-9.7%</td>
</tr>
<tr>
<td>Epidemiologic study (1)</td>
<td>624</td>
<td>16.0%</td>
<td>NA</td>
</tr>
<tr>
<td>Pamidronate only</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All studies (3)</td>
<td>10,380</td>
<td>7.3%</td>
<td>0.5-19.2%</td>
</tr>
<tr>
<td>Cancer cohort documented follow-up (2)</td>
<td>927</td>
<td>18.0%</td>
<td>0.22-6.8%</td>
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<tr>
<td>Cancer cohort undocumented follow-up (2)</td>
<td>8,029</td>
<td>14.4%</td>
<td>2.4-14.4%</td>
</tr>
<tr>
<td>Epidemiologic study (1)</td>
<td>624</td>
<td>4.1%</td>
<td>NA</td>
</tr>
<tr>
<td>Zoledronic acid + Pamidronate</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>All studies (5)</td>
<td>5,756</td>
<td>21.0%</td>
<td>5.7-30.3%</td>
</tr>
<tr>
<td>Cancer cohort documented follow-up (3)</td>
<td>927</td>
<td>24.6%</td>
<td>2.2-48.7%</td>
</tr>
<tr>
<td>Cancer cohort undocumented follow-up (2)</td>
<td>8,029</td>
<td>23.1%</td>
<td>0.15-100%</td>
</tr>
</tbody>
</table>
### BON prevalence by type of cancer

<table>
<thead>
<tr>
<th>Cohorts with documented follow-up</th>
<th>Multiple Myeloma</th>
<th>Breast</th>
<th>Prostate</th>
<th>Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>86764 (11.3%)</td>
<td>7480 (8.8%)</td>
<td>4449 (8.2%)</td>
<td>141 (100%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Epidemiological studies</th>
<th>Multiple Myeloma</th>
<th>Breast</th>
<th>Prostate</th>
<th>Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>692479 (2.8%)</td>
<td>237213 (0.7%)</td>
<td>1754 (0.1%)</td>
<td>51491 (0.3%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cohorts with undocumented follow-up</th>
<th>Multiple Myeloma</th>
<th>Breast</th>
<th>Prostate</th>
<th>Lung</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>190993 (2.7%)</td>
<td>344742 (2.3%)</td>
<td>4516 (1.9%)</td>
<td>00380 (0%)</td>
</tr>
</tbody>
</table>

### Studies of ONJ cases
- 11 studies
- 614 total ONJ cases reported
  - 69 (11%) Non-cancer
  - 547 (89%) Cancer
    - Multiple Myeloma= 245 (45%)
    - Breast Cancer= 166 (30%)
    - Prostate= 30 (5%)
    - Lung= 9 (2%)
    - Other= 97 (18%)

### Frequency of Bisphosphonate Use

<table>
<thead>
<tr>
<th>Bisphosphonate</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zoledronic acid</td>
<td>196 (31.9%)</td>
</tr>
<tr>
<td>Zoledronic acid + Pamidronate</td>
<td>190 (30.9%)</td>
</tr>
<tr>
<td>Pamidronate</td>
<td>117 (19.1%)</td>
</tr>
<tr>
<td>Alendronate</td>
<td>60 (9.8%)</td>
</tr>
<tr>
<td>Residronate</td>
<td>5 (0.8%)</td>
</tr>
<tr>
<td>Clodronate</td>
<td>3 (0.5%)</td>
</tr>
<tr>
<td>Zoledronic acid + Ibandronate</td>
<td>2 (0.3%)</td>
</tr>
<tr>
<td>Ibandronate</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Not reported</td>
<td>40 (6.5%)</td>
</tr>
</tbody>
</table>
Pain from ONJ

- 4 Studies reported level of pain from ONJ
- 172 ONJ cases
- 81/172 (47%) with report of pain
  - Study one= 9/91 (9.9%) with pain
  - Other 3 studies=72/81(89.9%) prevalence of pain

MRONJ: Clinical Presentation

- Presence of exposed bone weeks with h/o or current an use
- Asymptomatic bone exposure to painful, purulent discharge
Case 1

- CJ is a 42 y female h/o of multiple myeloma and painful exposed bone in previous extraction site
- Had tooth #18 extracted 10/01
Case 1

- Returned 11/05 for stem cell transplant clearance
- A 2x2 mm bony spicule noted extraction site #18
- Removed bony projection with anesthetic/rongeurs on 11/05 and cleared for stem cell transplant clearance
- Previous use of monthly zometa after 2001 was first noted (approved by FDA in Aug, 2001) in 11/05
- Returned 4/06 with purulence in area, treated with peridex

Case 1

- 05/06 non-erythematous, non-edematous area 4x5 mm exposed bone
- Swelling of mandible on 06/06
- Referred to Oral Surgery
- Returned on 09/06 with no swelling noted, but #19 radiolucency, scheduled for RCT #19
- Patient reports has been off zometa since 2005
- Returned 11/9/06 with swelling for one week. Purulent discharge. Placed on Pen VK and peridex will follow-up in 2 weeks.
MRONJ- Differential Diagnosis

- Osteomyelitis
- Fibro-osseous disease
- ORN
- Cancer
  - Metastases
  - Recurrence
  - Primary
Osteoradionecrosis

Definition

ORN is characterized by a nonhealing area of exposed mandibular and maxillary bone of at least 6 months duration in a patient who has been treated with radiation therapy (RT) for cancer.

Prevalence

- Weighted prevalence in conventional RT = 7.4%
- Weighted prevalence in intensity modulated RT = 5.2%
- Weighted prevalence in RT and chemotherapy = 6.8%
- Weighted prevalence in brachytherapy = 5.3%
  - Note: The majority of cases involve the mandible
MRONJ: Radiographic Presentation
- alveolar bone loss or resorption not attributable to chronic periodontal disease
- changes to trabecular pattern—dense woven bone and persistence of unremodeled bone in extraction sockets
- regions of osteosclerosis involving the alveolar bone and/or the surrounding basilar bone
- thickening/obscuring of periodontal ligament (thickening of the lamina dura and decreased size of the periodontal ligament space

MRONJ- Stages AAOMS – 2014 update
0: No exposed bone
I: Exposed and necrotic bone
  - Asymptomatic and no infection
II: Exposed and necrotic bone
  - Pain and erythema with or without purulent discharge
III: Exposed and necrotic bone
  - Pain, infection and …
  - Bone exposure beyond region of alveolar bone resulting in pathologic fracture, E/O fistula, oral antral/oral nasal communication or osteolysis extending to inferior border of mandible or sinus floor

MRONJ: Risk Factors
- 74% mandible vs. 22.5% maxilla and both 4.5%
- Chronic steroids and older age
- Denture use in cancer patients exposed to ZA= 4.9 (1.2-20.1) (Kyrgidis A. et al. J Clin Oncol 26:4634, 2008)
- Pre-existing inflammatory disease
- Anemia and diabetes
Tooth Extraction and MRONJ

- 52-61% of MRONJ patients reported tooth extraction as the predisposing event
- Case-control study of cancer patients exposed to ZA
  - Tooth extraction increased risk of ONJ = 16.4 (3.4-79.6)
- Longitudinal cohort study of cancer patients exposed to IV BP
  - Tooth extraction 33x increased risk ONJ
- Estimates for developing ONJ after tooth extraction among cancer patients exposed to intravenous BPs ranges from 1.6 to 14.8%.


BON: Why only the jaws?

- Alveolar bone remodels 10X rate of skeletal bone with greater uptake of bisphosphonates
- Minor trauma to thin mucosa
  - Posterior lingual mandible
  - Use of dental prostheses
- Bacterial infection of teeth and periodontium
- Trauma and infection overwhelm bone remodeling capacity
- Antiangiogenic properties of bisphosphonates?

Prevalence by Oral BP Duration (years)

Figure 1: Prevalence of ONJ by Bisphosphonate Duration - PROBE Study 2007

Prevalence of ONJ by BP Duration

Prevalence of ONJ (%)

<table>
<thead>
<tr>
<th>Oral BP Duration (years)</th>
<th>0</th>
<th>0.05</th>
<th>0.01</th>
<th>0.2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>0.05</td>
<td>0.01</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Duration of Medication Therapy

- Cancer patients exposed to zolendronate or denosumab, the incidence of developing ONJ:
  - 0.6 (ZA) and 0.5% at 1 year
  - 0.9 (ZA) and 1.1% at 2 years
  - 1.3 (ZA) and 1.1% at 3 years

Prevention of MRONJ

- Dental Screening Pre-Tx

Dental Screening Visit prior to Bone Modifying Agent
Key Medical Information

- Type of cancer and location
- Staging
- Treatment protocol (toxicities)
  - Surgical resection
  - Chemotherapy
  - Radiotherapy
  - HSCT
  - Combination
- Prognosis
- General medical health status
- Time to initiation of therapy

Key Dental Information

- Prior dental history
- Current oral hygiene status
- Motivation to maintain dentition
- Social history
- Oral disease

Pre-Cancer Treatment Visit

- Thorough Clinical Exam
  - Extraoral
    - Observe for asymmetries, swelling or skin lesions
    - Palpate for nodes, salivary glands, TMJ, muscles of mastication and neck muscles
  - Intraoral
    - Soft tissue
    - Hard tissue
    - Periodontal
    - Removable Appliances
Pre-Cancer Treatment Visit

- Radiographic Exam
  - Panoramic and PAs/BWs
  - Impacted teeth, retained root tips, latent osseous disease
  - Current Radiographs

Dental Treatment prior to Cancer Therapy

- Radiation for H&N Cancer and IV bisphosphonate Treatment
  - More long-term oral complications
  - Removal of teeth at risk for future complications
    - All hopeless teeth
    - Other teeth deemed at risk for future failure
  - Root canal therapy vs. extraction
  - Calculus removal, prophylaxis
  - OHI
  - Restorations (pre- vs. post-tx)

What is a hopeless tooth?

- Pocket depths 5 mm or greater, excessive mobility, purulence on probing
- Periapical inflammation present (and endodontic treatment not possible or not desired)
- A tooth is broken-down, non-restorable, non-functional or partially erupted and the patient is noncompliant with oral hygiene measures
- Patient has no interest in saving tooth/teeth
- Tooth is associated with an inflammatory (e.g., pericoronitis), infectious or malignant osseous disease
Dental Treatment prior to Cancer Therapy

- Chemotherapy
  - Acute oral complications and minimal long-term oral complications
  - Remove teeth with active infection and/or symptomatic
    - Swelling, purulence
    - Symptomatic teeth
  - When to do nothing?
    - Antibiotics and pain management

- HSCT
  - Similar to CT, but with more long-term oral complications
  - Longer immunosuppression with more risk for infection
  - Allogeneic HSCT with chronic immunosuppression and GVHD risk
  - Remove teeth with active infection and/or symptomatic

- Where does preventive dental care fall?
  - Denosumab- osteoporosis (1 dose every 6 months)
  - Denosumab- prevention of SRE in metastatic disease
  - Bevacizumab
  - Sunitinib
  - Sorafenib
Logistics of pre-antiresorptive dental treatment

- Extractions with minimal trauma at least 2 weeks (ideal 3) before start of antiresorptive therapy
- Confirm next round of CT
- Confirm current labs- ANC and platelets

Future Care of Patients on Bone-Modifying Agents

- Close follow-up, but especially in first year with H&N CA patients
- Oral hygiene protocol
  - Brushing, flossing and fluoride
  - Daily prescription fluoride (rinse, gel +/- trays)
    - Compliance is key
  - Xylitol
  - High risk: Add in-office fluoride varnish and chlorhexidine
- Dietary counseling

Diagnostic Tests

- Serum CTX (Marx, RE)
  - Bone turnover marker (Carboxy terminal octapeptide fragment)
  - Is fragment of bone collagen type 1 cleaved by osteoclasts
  - Risk Levels (Marx RE)
    - 300-600 pg/mL  Normal
    - 150-299 pg/mL  None or minimal
    - 101-149 pg/mL  Moderate
    - ≤ 100 pg/mL  High
- AAOMS- 2014 update
  - The use of CTX has not been validated
  - Use of systemic markers of bone turnover is not recommended
Drug Holidays?

- Various Recommendations with NO evidence to support that interrupting bone-modifying agent will decrease risk of MRONJ
- Few recommendations for osteoporosis
- No data for IV BP
- 6 months- Denosumab

### Antiresorptive Therapy for Osteoporosis

<table>
<thead>
<tr>
<th>Organization/Group</th>
<th>Year</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>AAOMS:</td>
<td>2009</td>
<td>d/c oral BP 3mo prior and 3mo after dental surgery</td>
</tr>
<tr>
<td>ADA Council on Scientific Affairs :</td>
<td>2011</td>
<td>&lt; 2yrs on BP or denosumab to continue treatment during dental surg</td>
</tr>
<tr>
<td>International ONJ Task Force</td>
<td>2013</td>
<td>Drug holiday for &gt;4 yrs BP and RA, steroids, DM</td>
</tr>
<tr>
<td>FDA</td>
<td>2011</td>
<td>No substantial data to guide decisions regarding a drug holiday</td>
</tr>
<tr>
<td>AAOMS</td>
<td>2014</td>
<td>Theoretical benefit for &gt;4 yrs. Use drug holiday of 2 months &amp; wait for healing</td>
</tr>
</tbody>
</table>

**History of oral bisphosphonates: Dental Manag. ADA Recommendations**

- Osteoporosis (ADA Expert Panel)
  - Inform patient of low risk of BON
  - Document discussion of risk and benefits and treatment options
  - Discuss alternative treatments
  - Obtain patient’s written acknowledgement of discussion and consent for treatment
**History of oral bisphosphonates: Dental Manag. ADA Recommendations**

- **Elective treatment plan**
  - Treat one sextant or tooth 1st
  - 2 month follow-up treated with chlorhexidine 2x/d
  - If no BON, then treat other sextants
- **Presence of periapical disease, severe periodontitis**
  - Treat immediately

**Treating MRONJ: AAOMS 2014**

- Bone will remain exposed and does not currently recommend discontinuation of IV bisphosphonate
- **Stage 0**
  - Pain and/or infection management
- **Stages I**
  - No treatment vs. chlorhexidine
- **Stages II**
  - Chlorhexidine 3x/d
  - Pain control
  - Penicillin
  - Quinolones, metronidazole, clindamycin, doxycycline and erythromycin
  - Microbial cultures
  - Operative therapy as needed

**Treating IV-BON: Marx**

- **Stage III**
  - Chlorhexidine 3x/d
  - Pain control
  - Penicillin
  - Quinolones, metronidazole, clindamycin, doxycycline and erythromycin
  - Surgical debridement/resection as needed
Management of ONJ cases - Migliorati, 2010

- 13 studies reported management strategies for 658 ONJ cases
  - Bisphosphonate stopped = 106 (16.1%)
  - Conservative therapy = 100 (15.2%)
  - Antibiotics = 393 (59.7%)
  - IV antibiotics with hospitalization = 4 (0.6%)
  - Unspecified surgery with antibiotics = 45 (6.8%)
  - Simple bone sequestrectomy = 154 (23.4%)
  - Extensive surgical debridement = 84 (12.8%)

- Response to therapy
  - ONJ resolved completely = 79 (12%)
  - Stable ONJ = 215 (32.7%)
  - Progressing ONJ = 43 (6.5%)
  - Died of Cancer = 12 (1.8%)
  - Not clearly specified = 309 (47%)

Bisphosphonate Osteonecrosis (BON)

- Update
    - 40 txs HBO with conv therapy of surgery and antibiotics vs. conv therapy only
    - 46 patients:
      - HBO: 17/25 improved (68%)
      - Conv: 8/21 improved (38%) (p=0.43)
    - HBO may be a useful adjunct for more severe cases: underpowered study.
    - 347 BRONJ patients treated operatively. 59% improvement (BRONJ staging), 30% no change, 11% worsening.
    - Positive result with maxillary, resective surgery, no additional steroid tx. (multivariate analysis)

Bisphosphonate Osteonecrosis (BON)

- Update
  - Pentoxifylline and Tocopherol
  - Platelet Rich Plasma

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Bisphosphonate Osteonecrosis (BON)
Other Treatment Strategies

- Teriparatide — (human parathyroid hormone peptide 1–34) increases bone remodeling and density
  - Bone formation exceeds bone formation
  - Increase number and action of osteoblasts

Case 1

- LN 87 y female treated for multiple myeloma affecting the anterior maxilla
- Diagnosed 3 years ago
- On Aredia for approximately one year duration
- Receiving palliative care and pain management

Case 1

- Referred for 2nd opinion regarding extraction of anterior lower teeth, which thought to be exacerbating upper exposed bone
Case 2

- Management strategy

- DM is a 55 y female with h/o breast cancer 1989 and metastasis in 2005
- Patient treated with Zometa from 2/05-9/05. Not in medicines listed by patient.
- Patient reports pain with upper teeth, has not received routine dental care
Case 2

- Management strategy
Case 3 - History
- 54 year-old male for oral and dental evaluation prior to chemoradiation therapy
- Past Medical History:
  - SCCA right tonsil and neck, Chronic lower back pain, Depression, Osteoarthritis
- Medications:
  - Ambien, Oxycontin, Vicodin, Diazepam, Zoloft
- Social history:
  - Tobacco - 1 pack year history; quit 35 years ago
  - Alcohol - ~1 beer/week
  - Drugs - Denies

Case – Dental History
- Has had routine dental care for last one year, but went for many years without care
- Had multiple crowns and bridge placed 2 years ago

Case- Dental Findings
- The patient has fair oral hygiene. He has 9 remaining teeth in the maxilla and 12 remaining teeth in the mandible.
- Patient had localized plaque deposits, especially in the lower anterior.
- Multiple teeth with periodontal pockets ≥ 5 mm (5, 6, 9, 10, 11, 12, 15, 19, 20, 28, 29).
- Teeth with class I mobility include: lower anterior teeth
- Caries examination: #15
Case - treatment plan

- Extractions?
- Dental Cleaning / localized SRP?
Questions?

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