

## American College of Physicians Dental Pearls for The Internist: A Case-Based Approach

Mark Drangsholt, DDS, PhD, DABOM  
Professor and Chair, Department of Oral Medicine  
University of Washington School of Dentistry  
Immediate Past-President, American Board of Oral Medicine

David Dean, DDS, MSD, DABOM, FDS RCSEd  
Graduate Program Director, Department of Oral Medicine  
University of Washington School of Dentistry  
Medical Director, Oral Medicine service  
Seattle Cancer Care Alliance

### Declarations

- We are not physicians ☺
- We have not conflicts of interest to disclose
- All recommendations are consistent with current literature & standard of care within Oral Medicine/Orofacial Pain

## Xerostomia + Recurrent Parotid Gland Swelling

### CASE

#### Case

- 64-year-old female
- Referred to OMCS by her dentist
- Chief concern: Recurrent swelling in the left parotid gland

### CASE

#### Case

- Initial swelling episode took place 10 years ago
- For many years episodes occurred infrequently & resolved spontaneously within 48 hours
- Over the last 3 months, frequency has increased to one episode every 2 weeks
- Concurrent malaise + low grade fever during most recent episode (treated with po penicillin, sour candies, & parotid massage)

#### Highest yield xerostomia questions

- Do you sip liquids to aid in swallowing dry foods?
- Does the amount of saliva in your mouth seem to be too little, too much, or you don't notice it?
- Do you have difficulties swallowing dry foods?
- Does your mouth feel dry when eating a meal?

Fox, et al. (JADA, 1987)

**CASE**

- Past medical history
  - Arthritis
  - Asthma (controlled)
  - Depression
  - Hypertension
  - Hypothyroidism
  - Insomnia
  - Uterine cancer
    - s/p hysterectomy

**CASE**

- Past medical history
  - **Arthritis???**
  - Asthma (controlled)
  - **Depression???**
  - Hypertension
  - **Hypothyroidism???**
  - **Insomnia???**
  - Uterine cancer
    - s/p hysterectomy
- Additional questions
  - Osteoarthritis or Rheumatoid?
    - Secondary Sjögren Syndrome?
    - ANA panel?
  - Primary or iatrogenic? (e.g. I-131)
  - Depression & insomnia
    - Is she being treated with medication?
    - Antidepressants & sedatives decrease salivary function

**CASE**

- Medications
  - Albuterol
  - Benazepril
  - Fluoxetine
  - Levothyroxine
  - Ranitidine
  - Trazodone
- Adverse medication reactions
  - None

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**CASE**

## Physical exam

- Head & neck
  - (-) swelling or asymmetry
  - (-) lymphadenopathy
  - (-) sinus pain (maxillary or frontal)
  - (-) thyromegaly
  - (-) TMJ dysfunction
  - (-) pain in muscles of mastication or cervical muscles

**CASE**

## Physical exam

- Intraoral
  - (+) decreased expression from the bilateral parotids
    - saliva expressed from the left parotid was **cloudy**
    - adherent **white material** inferior to the left parotid papilla
  - (-) mucosal abnormality
  - (-) dental or periodontal pathology
  - (-) pharyngeal abnormality

## Consider objective salivary measurement

- Stimulated & unstimulated salivary flow
  - Unstimulated (WNL >0.5ml/min)
  - Stimulated (WNL = 1-1.5ml/min)
  - Sjögren's unstimulated <0.1ml/min

No food/drink for 2 hours prior to exam



## CASE

### Plan

Conservative hyposalivation protocol  
 -stay well-hydrated with frequent sips of water  
 -sugar-free salivary stimulants  
 -coating agents (e.g. Biotene, Xerostom, Aquoral, Mouthkote, etc.)  
 -warm saline rinses

Milking of salivary gland (as tolerated).  
 -5minutes, 2x/day

Hot water holds (if swelling returns)

Systemic Antibiotic Therapy in the future if signs of infection return.

Consider referral for sialography to assess ductal system.

Consider referral to [redacted] for cannulation of the left stenosed duct.

Provided instructions for contacting clinic while I am out of the country (if signs of infection return).

## Conservative Dry Mouth Management

- Adequate hydration (frequent sips of water)
- Salivary stimulants (sugar-free candies, mints, gum, etc.)
- Normal saline rinses (3/4 TSP salt in 32 oz. water)
- Coating agents (3M xerostomia relief spray [Rx only] vs. OTC: Biotene, Xerostom, Xylimelts, OraMoist, MouthKote, etc.)



## Medications to increase salivary flow

- Sialagogues
  - Cevimeline (Evoxac®) – 30mg TID\*
  - Pilocarpine (Salagen®) – 5mg TID-QID\*\*

\*FDA approved for Sjögren Syndrome only

\*\*FDA approved for Sjögren Syndrome & radiation-induced hyposalivation

## Sialagogue hacks...

- Warn patients about potential flushing & sweating
- Titrate up to minimize side effects
  - Sample instructions:  
Begin with 30mg dose before bed, after 5 days add a second dose in the morning. After an additional 5 days increase to recommended 30mg TID
- **3-month trial** required to maximally assess benefit

## Sialagogue therapy

- **Contraindications**
  - **Narrow angle** glaucoma
  - **Uncontrolled** asthma

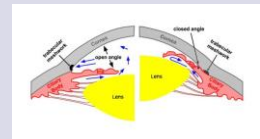


Figure © Webeyeclinic.com

## Sialagogue therapy

### • Cautions

- Arrhythmia, **Beta blocker** use, &/or other significant cardiac disease (e.g. MI, angina)
- Respiratory illnesses (controlled asthma, mod/severe COPD)
- Gallstones/Kidney stones
- Hepatic impairment
- Anti-cholinergic meds (diphenhydramine, bupropion oxybutynin, etc.)

## Medication-related Osteonecrosis of the Jaw (MRONJ)

### CASE

#### Case

- 68-year-old male
- Referred to SCCA Oral Medicine clinic by his oncologist
- **Chief concern:** Exposed bone on the lingual surface of the left mandible

### CASE

#### Case

- Identified roughness on the inside of his mandible “a few months back”
- Reports some irritation on the side of his tongue, but has been otherwise asymptomatic
- Was waiting for oncology visit in Seattle to have the lesion assessed (lives in rural Alaska)
- Stage IV prostate cancer + 24 months of denosumab therapy

### CASE



© SCCA

## Medication-related osteonecrosis of the jaw (MRONJ)

- 1) Current or previous treatment with **anti-resorptive or antiangiogenic agents**;
- 2) Exposed bone (or bone that can be probed through a fistula) in the maxillofacial region that has persisted for **more than 8 weeks**; and
- 3) **No history of radiation therapy** or **obvious metastatic disease** to the jaws.



© SCCA

## Principal medications associated with MRONJ

- Bisphosphonates
  - Inactivate osteoclasts
  - IV nitrogen-containing bisphosphonates (e.g. Zometa®) have highest risk
- Denosumab
  - Anti-RANK-L antibody
  - Prevents pre-osteoclast fusion to form osteoclasts



### Medication-Related Osteonecrosis of the Jaw—2014 Update



- Used to prevent hypercalcemia & decrease risk for fracture in patients with Multiple Myeloma + metastatic bony cancer
  - MRONJ risk in cancer patients exposed to Zometa® = **50-100X** higher than placebo<sup>(1)</sup>
    - Incidence ranges from **0.7% - 6.7%** <sup>(2,3)</sup>
    - **~1%** when limited to Level 1 studies<sup>(2, 4-6)</sup>

1 AAOMS Position Paper (2014)  
 2 Coleman et al. (Breast Cancer Res Treat, 2011)  
 3 Vahisevanos et al. (J Clin Oncol, 2009)

4 Qi et al. (Int J Clin Oncol, 2013)  
 5 Mauri et al. (Breast Cancer Res Treat, 2009)  
 6 Scagliotti et al. (J Thorax Oncol, 2012)



### Medication-Related Osteonecrosis of the Jaw—2014 Update



- Denosumab (Xgeva®)
  - RANK-L inhibitor
  - Used in the setting of bony metastasis (e.g. breast cancer, prostate cancer) + Multiple Myeloma (approved 1/2018)
  - MRONJ risk comparable to Zometa®

1 Fizazi et al. (Lancet, 2011)  
 2 Stopeck et al (LJC supplements, 2009)  
 3 Henry (J Clin Oncol, 2011)

## Remember...

- There are **two different forms** of both zoledronic acid (Zometa® & Reclast®) & denosumab (Xgeva® & Prolia®)
- Lower dosing in osteoporosis = Lower risk for MRONJ  
 “The risk for ONJ among patients [with osteoporosis] treated with either zoledronate or denosumab (0.017 – 0.04%) **approximates the risk for ONJ of patients enrolled in placebo groups (0%-0.02%)**”



AAOMS Position Paper (2014)

## CASE

### MRONJ - Management

- Keep area as clean as possible
  - Decreases infection risk
  - Promotes “re-growth” of gingiva beneath area of exposed bone → promotes sequestration
- Avoid invasive surgery (unless stage 3)
  - Removing mobile sequestra & smoothing bone is OK

### MRONJ - Assessment

- Symptoms
  - Pain
  - Drainage and/or bad taste/bad breath
  - Numbness/Paresthesia
- Signs
  - Local inflammation (erythema, edema)
  - Bleeding and/or purulence on probing
  - Signs of progressive infection
    - Fever, lymphadenopathy, swelling, limited opening
  - Tissue trauma

Mawardi et al. (UpToDate, 3/2018)

### MRONJ - Stage 1

- Clinical characteristics
  - Exposed & necrotic bone
  - No signs of infection
  - Asymptomatic
- Management
  - OHI (keep bone clean)
  - Chlorhexidine 0.12% (dip & brush + rinse)



### MRONJ - Stage 2

- Clinical characteristics
  - Exposed & necrotic bone
  - Evidence of infection
  - Symptomatic



### MRONJ - Stage 2

- Management
  - Stage 1 interventions
  - Systemic antibiotic therapy
    - Amoxicillin (500mg TID)
    - Clindamycin (300mg QID)
    - Metronidazole (500mg TID-QID)
  - Consider culture + sensitivity



### MRONJ - Stage 3

(or “what you see if you google osteonecrosis of the jaw”)

- Clinical characteristics
  - Evidence of infection (Beyond region of alveolar bone)
  - Osteomyelitis (to inferior border of Mn/Mx sinus)
  - Oro-antral communication
  - Extraoral fistula
  - Pathologic fracture



Photo: Eckardt A et al. (*Anticancer Research*, 2011)

### MRONJ - Stage 3

- Management
  - Antibiotic therapy
  - Surgical intervention
    - Resection
    - Debridement



**CASE**

## Plan - Diagnostic testing

- Consult with Oncologist
  - “Will the patient’s health support a drug holiday?”
  - Oncologist elected to hold denosumab
- Follow-up/assessment every 4-12 weeks based on signs & symptoms

Is stopping the medication likely to be beneficial?

## Drug holidays

- Limited evidence for drug holidays in cancer therapy prior to EXTs, but oncologist may consider if MRONJ present
- More likely to be effective in patient’s taking denosumab

**Half-life = 6 months vs. 10-15 years**

AAOMS Position Paper (2014)

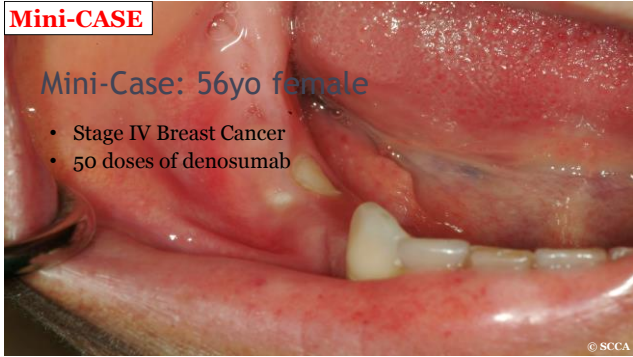
**CASE****CASE****CASE**



**Mini-CASE**

Mini-Case: 56yo female

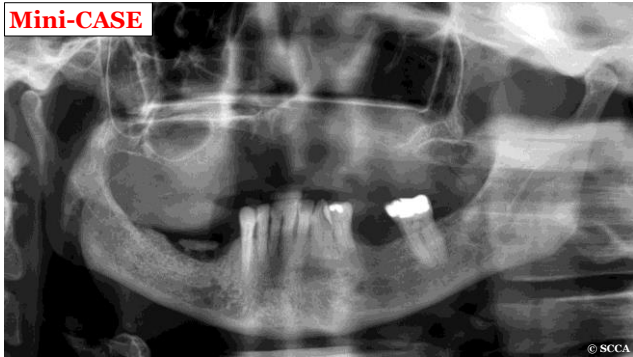
- Stage IV Breast Cancer
- 50 doses of denosumab



**Mini-CASE**



**Mini-CASE**



Questions?

ddean2@uw.edu