

Webinar – Patients treated with antiresorptive medicine

Host

The Danish Dental Association (Tandlægeforeningen)

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Speakers

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Reservations

All reservations of the correct reproduction of the course material in the notes are taken by the author.

Dental Insights

Webinar – Patients treated with antiresorptive medicine

Definition of MRONJ

MRONJ = Medication-Related Osteonecrosis of the Jaw

First described patient case in the British Medical Journal in 1899 in the form of "phosphonate-induced dead jaw" in phosphorus miners and match factory workers.

Characteristics of MRONJ:

- Exposed bone or bone that can be probed through fistula intra- or extraorally for more than 8 weeks.
- Patient who has received antiresorptive therapy alone or in combination with immunomodulatory or antiangiogenic therapy.
- No radiation to the jaws.

MRONJ was first described by Dr. Robert Marx in 2002, first published article in 2003.
Dr. Morten Schiødt described the first case at Rigshospitalet in 2005.

Patients who receive MRONJ

- Patients undergoing treatment for osteoporosis, osteopenia, Paget's disease or osteogenesis imperfecta.
- Cancer patients without metastases (adjuvant treatment). Often breast, prostate, multiple myeloma, some lung and kidney cancer.
- Cancer patients with metastases (high-dose). Often breast, prostate, multiple myeloma, some lung and kidney cancer.
- Some patients with rheumatoid arthritis, psoriasis, Chron's disease (treatment with immunomodulatory therapy or methotrexate).

Dose, interval and treatment period have an impact on MRONJ.

Medications that can cause MRONJ - both IV and tablet form (many of these medications might not be included in the patient's medication list)

- Antiresorptive drugs, low-dose (patients with osteoporosis): bisphosphonates and other drugs, e.g. Alendronate and Denosumab (Prolia).
- Antiresorptive drugs, adjuvant (cancer patients without metastases): Zolendronic acid and Denosumab (XGEVA).
- Antiresorptive drugs, high dose (cancer patients with metastases): Zolendronic acid, Pamidronate, Clodronate, Ibandronic acid, Denosumab (XGEVA).
- Immunomodulatory drugs: tyrosine kinase inhibitors and monoclonal antibodies (many of the drugs ending in -nib, -mab) and methotrexate and Romosozumab.

Local risk factors for the development of MRONJ

- Poor oral hygiene
- Infection with apical or marginal periodontitis
- Anatomy: often lingual, retromolar, mandibular tori
- Dentoalveolar surgeries in the oral cavity, most commonly tooth extractions (62-82% of MRONJ cases occur after tooth extractions - Saad et al 2012, Aljohani et al 2017, Hallmer et al 2018)
- Poorly fitting dentures

Development of MRONJ

- Infection due to necrosis around the tooth
- Tooth extraction
- MRONJ

Systemic risk factors for the development of MRONJ

- Other medication: chemotherapy, steroid (e.g. prednisolone), methotrexate
- Diabetes, anemia, immunocompromised
- Smoking

Classification of MRONJ severity ("staging system")

- **At risk:** Generally all patients on antiresorptive, antiangiogenic or immunomodulatory therapy.
- **Stage 0 (non-exposed):** No exposed bone, but non-specific symptoms and clinical/radiologic findings of tooth, jaw or sinus pain with no odontologic cause. Sinus membrane may be reactive. Altered neurosensory function. Loose teeth without marginal pathology. Intra- or extraoral swelling. 50% of these patients develop stage 1 MRONJ.
- **Stage 1:** Exposed necrotic bone or fistula with palpable bone. No symptoms. No inflammation or infection. Radiologically, empty extraction alveolus is seen.

- **Stage 2:** Exposed necrotic bone or fistula with palpable bone. Symptoms. Signs of inflammation or infection. Radiologically, empty extraction socket.
- **Stage 3:** Exposed necrotic bone or fistula with palpable bone. Symptoms. Signs of inflammation or infection. In addition, 1 of the following:
 - Exposed necrotic bone extending beyond the alveolar region.
 - Pathologic fracture.
 - Extraoral fistula.
 - Oroantral or oronasal communication.
 - Osteolysis extending to the basis mandibularis or the base of the maxillary sinus.

Radiologic changes in MRONJ

- Alveolar bone loss or resorption not due to chronic periodontal disease (osteolysis).
- Altered trabecular bone structure in the form of sclerotic bone, lack of healing in relation to extraction sockets.
- Altered periodontal ligament: thickened, blurred, reduced.

Ruggiero et al 2022, 2014. AAOMS position paper on MRONJ. Fedele et al 2010.

Treatment of MRONJ

- Conservative treatment
 - Removal of sequestrants.
 - Obturator prosthesis.
- Surgical treatment
 - 3D scanning.
 - Block resection or continuity resection of the necrotic area with primary closure.
 - Removal of other non-preservable teeth with primary closure.
 - Patient-specific splint can be implanted to avoid pathological bone fractures in the future.
 - Can be difficult to make removable prosthesis afterwards due to new anatomy.
 - After good healing, implants and prosthetics can be inserted, e.g. hybrid prosthesis.
 - Changed facial profile and appearance.

The Danish Patient Safety Authority (STPS) has published new guidelines in 2021 regarding MRONJ.

Orthodontics (e.g. Invisalign) also affects the osteoclasts, so it is important to register if the patient is receiving antiresorptive treatment! This is not described in the STPS guidelines.

Referral of patients on antiresorptive treatment for oral surgery

- **GREEN - Low-dose treatment for up to 4 years** (without having received other immunomodulatory medication!) → own dentist, preferably in the period between two injections. NOTE: hospital prescribed preparations are not always listed on the FMK!
- **GUL - Adjuvant treatment or low-dose treatment for more than 4 years** → primary care specialist dentist or hospital department of maxillofacial surgery. Rigshospitalet provides patients with prophylactic antibiotics for tooth extraction with primary closure.
- **RED - High-dose treatment** → maxillofacial surgery hospital ward.

The good referral describes

- The problem being referred for
- Previous treatment, diagnosis and date
- Patient's general condition and any diagnoses

- Medication
- X-rays
- Clinical photos

In the future, there will be more elderly citizens and thus more patients with osteoporosis and thus more patients with MRONJ.

Patients with MRONJ due to low-dose treatment

- 13.3% also received methotrexate
- 6.7% also received steroid treatment (e.g. prednisolone)
- 48.9% were smokers

Take home message

- Thorough history of conditions and medications, if possible!
- Check after tooth removal/surgery for healing after 4 weeks after extraction.
- Referral if no healing after 4 weeks.
- Feel free to call at-risk patients for more frequent examinations.

Good questions for low-dose risk patients

"Do you have osteoporosis?"

"Do you have prostate cancer?"

"Do you have a history of breast cancer?"

Healthcare needs to pay more attention to MRONJ

Doctors need to be more informed about the MRONJ risk. There is a need for much better collaboration between doctors and dentists, especially general practitioners. All doctors should have received a guideline on antiresorptive treatment.

If the patient refuses resection of exposed necrotic bone, the patient can prophylactically rinse with chlorhexidine and receive antibiotics for local infection.

That was Dental Insights. Thank you for being here. ❤️

Dental love, Anne Mette