Abstract

Bisphosphonate-related osteonecrosis of the jaw (BRONJ) is a rare, serious complication of bisphosphonate therapy. We report here a 69 year old man with a history of multiple myeloma and 5 years of adjuvant zoledronate therapy presenting with loss of light perception, proptosis, ptosis, and impaired abduction of the right eye. This patient was found to have developed an unusually severe presentation of osteonecrosis of the skull base in the setting of bisphosphonate-related osteonecrosis that ultimately led to unilateral blindness. In this extreme case of bisphosphonate related osteonecrosis of the skull base, we reveal the importance of early identification and treatment of these lesions. This is the first description of BRONJ-induced blindness.

Case Presentation

Background:
69 year old man with a history of multiple myeloma 6 years in remission.
• After 5 years of adjuvant zoledronate therapy: diagnosed with osteonecrosis of the right maxilla.

Treatment 1: Caldwell-Luc procedure and maxillary sinus biopsy:
• Intratrabecular necrosis and focal collections of paratrabecular neutrophils.
• Clusters of gram-positive cocci and GMS stain-negative filamentous organisms in necrotic intratrabecular space.

Diagnosis 1: Acute Actinomyces osteonecrosis of the right maxillary sinus.

Clinical course: Patient developed new onset right eye blindness.
• Decreased dimming of vision in his right eye three months prior.
• Initial diagnosis: Glaucoma, treated with travoprost ophthalmic solution.
• Three months later, he demonstrated complete loss of light perception, proptosis, ptosis, and limitation of abduction of the right eye.
• Fundoscopic examination: mild temporal thinning of the right nerve but no pallor. Despite an absence of autonomic or sensory symptoms on left eye, the left optic nerve showed more profound thinning on fundoscopy than the right nerve (Figure 1).

Treatment 2: Despite delay of one week by patient to report total visual loss, urgent aggressive sinonasal debridement, complete FESS, partial maxilloectomy, and optic nerve decompression performed.
• Maxillary sinus filled with chronically inflamed polyloid tissue and necrotic bone debris (Figure 2). Several areas of necrotic bone fragments in the anterior and posterior ethmoid sinuses were removed.
• The posterior orbital apex was exposed to reveal a thickened lamina papyracea, which was removed. The periorbita was traced posteriorly along the optic nerve canal and followed into the sphenoid sinus.
• The sphenoid sinus was opened widely and several necrotic bone chips were removed.
• The optic nerve sheath was opened and extended anteriorly along the orbital apex through the periorbita. The optic nerve and posterior orbital contents did not appear to be under great pressure and no pulsation was observed.

Outcome:
• Placed on 3-month course of amoxicillin. On follow up, patient had regained minimal vision. No evidence of disease progression (Figure 3).

Concluding Remarks

Therapeutic outcomes are optimized by conservative surgery of localized BRONJ lesions, necessitating a timely diagnosis by identification of the early signs of BRONJ. Unfortunately, early signs maxillary BRONJ include nonspecific sinus pain, odontalgia, and altered neurosensory function and thus require the clinician to consider BRONJ when evaluating patients on anti-resorptive and anti-cancer agents. Identification of oro-antral fistula should dramatically raise suspicion of active disease in the maxilla. Diagnosis of maxillary BRONJ should prompt computed tomographic imaging of the paranasal sinuses to ensure prompt therapy and avoid further sequelae.

Key Points

• Clinical definition: >8 week persistence of necrotic bone in the maxillofacial region of patients with a history of bisphosphonate therapy and without radiotherapy of the jaw
• 67% mandible, 33% maxilla
• Exposed necrotic bone is undertakable up to 24% of cases
• Highest incidence in cancer patients treated with long courses of zoledronate
• Associated with invasive dental procedures
• Tooth extraction, root canal
• Other medications associated with BRONJ:
  • Denosumab – anti-RANKL antibody
  • Sunitinib – VEGF receptor tyrosine kinase inhibitor
  • Bevacizumab – anti-VEGF antibody

References


Figures

Figure 1: Magnetic resonance imaging showing a destructive lesion with bony involvement of the right pterygoid and sphenoid wings, soft tissue of the right orbit, and left optic nerve atrophy.

Figure 2: Computed tomography prior to optic nerve decompression demonstrated irregular sclerosis, fragmentation, and expansion of the walls of the right maxillary and sphenoid sinuses, right greater wing of the sphenoid, and right pterygoid body. In addition, enlargement of the right lateral rectus muscle was observed in the inferolateral extracranial compartment of the right orbit extending posteriorly and resulting in compression of the right optic nerve near the orbital apex.

Figure 3: Follow up computed tomography showing post-operative decompression, otherwise unchanged irregular sclerosis, fragmentation, and expansion of the walls of the right maxillary sinus, right sphenoid sinus, right greater pterygoid wing, and right pterygoid body, consistent with sequelae of the patient’s biopsy-proven infected osteonecrosis status post therapy. No evidence of disease progression. Interval near resolution of soft tissue attenuation in the right orbital apex and decreased right lateral rectus muscle enlargement consistent with a response to therapy.