

## CLINICAL CHALLENGES

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### Osteonecrosis of the Jaw in a Patient Receiving Bisphosphonate Therapy

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#### Case Study

Mr. M, a 66-year-old man, was diagnosed with stage IV hormone-refractory prostate cancer four years ago. At that time, he presented with metastatic disease to the lumbar spine, hip, and pelvic region and received site-specific radiation therapy to alleviate his pain. He initially was treated with leuprolide acetate injections every three months, bicalutamide by mouth daily, and IV bisphosphonate infusions once a month. After six months of hormonal therapy, his prostate-specific antigen (PSA) level began to rise and his treatment was changed to docetaxel and estramustine starting two days prior to receiving docetaxel. He tolerated the regimen very well, with greater than 50% reduction in his PSA. After the fourth cycle of docetaxel and estramustine, the PSA level began to rise and his treatment was changed to paclitaxel, estramustine, and carboplatin (TEC). Monthly infusions of zoledronic acid were continued. Because his PSA level continued to rise following five cycles of TEC, Mr. M agreed to a new treatment plan of docetaxel, carboplatin, estramustine, and zoledronic acid IV.

During a chemotherapy follow-up visit, Mr. M complained of a sudden onset of right lower jaw pain that he described as a "toothache." Zoledronic acid infusions were placed on hold, chlorhexidine 0.12% antiseptic rinse was prescribed, and a dental consult was

ordered. Dental x-rays were negative for any dental abnormalities, and four views of the mandible were unremarkable. The following week, Mr. M complained of persistent right lower jaw pain radiating to his right ear with a new onset of headache, photosensitivity, and occasional dizziness. A neurologic consult was ordered. A computed tomography scan of the brain showed scattered sclerotic lesions to the skull base consistent with blastic metastases. A magnetic resonance imaging (MRI) scan of the brain was normal, but an MRI scan of his cervical spine revealed spondylosis from C4–5 through C6–7 without bony metastases. Temporal arteries and temporomandibular joints were normal. On physical examination, Mr. M had no scalp or sinus tenderness and no oral lesions were noted. The neurologic examination also was normal. The clinical impression was that the patient had trigeminal neuropathic pain, and he was placed on gabapentin.

Mr. M returned two weeks later with painless purulent drainage from the site of a previous tooth extraction on the lower right side of his mouth. A wound culture was obtained, and empiric antibiotic therapy with clindamycin was ordered because the patient was allergic to penicillin. A maxillofacial surgeon was consulted. A maxillofacial computed tomography scan with contrast was performed and revealed osteomyelitis or osteonecrosis of the right mandibular ramus.

#### What is osteonecrosis of the jaw?

No consensus definition exists for osteonecrosis of the jaw (ONJ), and its pathobiologic mechanisms are not clearly understood (Ruggiero et al., 2006). ONJ is a rare, osseous pathologic complication that causes temporary or permanent loss of blood supply to the jaw bone, resulting in necrosis, or death, of the bone. The incidence of ONJ ranges from 1%–21% in patients treated with bisphosphonates (Assouline-Dayane, Chang, Greenspan, Shoenfeld, & Gershwin, 2002; Bamias et al., 2005). The condition usually is diagnosed clinically, based on visual inspection of the oral cavity and, in some cases, review of radiographic studies (Ruggiero et al.).

#### What are the risk factors for osteonecrosis of the jaw?

The exact mechanisms that induce necrosis of the jaw remain poorly understood; however, cancer and certain cancer treatments have been linked as risk factors (Assouline-Dayane et al., 2002). ONJ has been reported in the literature since the 19th century (Ruggiero et al., 2006). An increasing body of literature suggests that the use of bisphosphonates, especially IV formulations, may be associated with ONJ (Ruggiero et al.; Woo, Hellstein, & Kalmar, 2006). The most important risk factors for the development of ONJ are the type and total dose of bisphosphonate and history of trauma, dental surgery, or dental infection. Although osteoblastic function is reduced during bisphosphonate therapy, the continuous mineralization process results in hard, brittle bone (Ruggiero et al.; Woo et al.). Zoledronic acid, an aminobisphosphonate,

#### Do You Have an Interesting Clinical Experience to Share?

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