Implications of Androgen-Deprivation Therapy in Patients With Prostate Cancer: A Case Study

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S.R., a 65-year-old male with a history of prostate cancer, went to a cancer center in 2003. He had developed symptoms of bladder outlet obstruction in 1999 and was seen by a urologist. His baseline prostate-specific antigen (PSA) was 44 ng/ml. On physical examination, his prostate was enlarged, and a biopsy in January 2000 revealed adenocarcinoma with a Gleason score of 8. A metastatic workup, including a bone scan and a computed tomography scan of the abdomen and pelvis (CT A/P), was negative for evidence of metastatic disease. S.R. received conformal external beam radiation, and the luteinizing hormone-releasing hormone agonist leuprolide acetate was initiated. Following treatment, his PSA nadired to 0.2 ng/ml, and he did well until 2002, when his PSA started to rise. A reevaluation CT A/P revealed enlarged retroperitoneal and pelvic lymph nodes, and a bone scan was positive for metastatic disease. He underwent a bilateral orchiectomy in November 2002.

S.R. was evaluated at a cancer center soon after his orchiectomy and was treated with multiple chemotherapeutic regimens over the course of 24 months. Most regimens were clinical trials for androgen-refractory metastatic prostate cancer that were available at the center.

Studies have shown that androgen-deprivation therapy in men with prostate cancer can decrease bone mineral density (Diamond et al., 2004; Shahinian, Kuo, Freeman, & Goodwin, 2005). Studies that specifically assessed patients’ bone density after orchiectomy have revealed bone loss within six months of surgery (Agarwal et al., 2005). A dual-energy x-ray absorptiometry (DEXA) scan was ordered for S.R. because his treatment history included hormonal therapy followed by an orchiectomy. The DEXA scan revealed osteoporosis with a T score of −2.7.

Studies have demonstrated improved bone mineral density with bisphosphonate therapy for osteoporosis, data support a benefit of bisphosphonate zoledronic acid in patients with hormone-refractory metastatic prostate cancer. Saad et al. (2002) compared zoledronic acid 4 mg IV to placebo IV every three weeks in patients with hormone-refractory metastatic prostate cancer. The study found that a greater proportion of patients who received placebo had a skeletal-related event compared to those receiving zoledronic acid. A skeletal-related event was defined as pathologic bone fracture, spinal cord compression, surgery to bone, radiation therapy to bone, or a change of antineoplastic therapy to treat bone pain (Saad et al.). Zoledronic acid was initiated for S.R. at a dose of 4 mg via IV every four weeks, which was well tolerated.

After nine months of treatment with zoledronic acid and continued chemotherapy on a clinical trial, S.R. was seen for a routine monthly visit. Oral examination revealed a bony protrusion of the left mandible that was approximately 4 mm in size and was not tender. The remainder of his physical examination was within normal limits.

Clinicians recommended discontinuing bisphosphonate and arranged for S.R. to see his oral surgeon immediately. The oral surgeon confirmed osteonecrosis of the jaw.

Discussion

Case studies continue to report osteonecrosis of the jaw related to bisphosphonate therapy, and patients with cancer appear...
to present a high risk for the complication (Migliorati, Siegel, & Elting, 2006). The etiology of osteonecrosis of the jaw is unknown but is seen as a manifestation of a systemic vascular disorder, the result of local vascular insufficiency and impaired wound healing (Olson, Hellie, & Pienta, 2005). Not all types of bisphosphonates have been implicated in osteonecrosis of the jaw. Pamidronate and zoledronic acid appear to be associated with the highest incidence; however, osteonecrosis of the jaw has been reported in patients taking oral alendronate and risedronate (Katz, 2005; Marx, 2003; Migliorati et al., 2006).

Common clinical features among patients who have developed osteonecrosis of the jaw include:

• History of bisphosphonate therapy
• Concurrent dental procedures (i.e., dental extractions, dental surgeries)
• Previous treatment with glucocorticoids or chemotherapy
• Systemic disorders (e.g., diabetes, peripheral vascular disease, decreased renal function).

Patients often are asymptomatic but may develop severe pain as a result of the infected necrotic bone. If the area around the exposed bone is tender and erythematous, patients should be treated with antibiotics and a chlorhexidine mouth rinse. Osteonecrosis is progressive and may lead to extensive areas of bony exposure. Surgery to remove necrotic bone and close the site with healthy mucosa may be considered, but the surgical procedure could lead to further osseous breakdown and dehiscence (Migliorati et al., 2005). The area of necrosis also could act as a portal of entry for bacteria in patients receiving chemotherapy, which could traumatize the adjacent soft tissues and cause ulceration, forming another portal of entry of bacteria (Migliorati et al., 2005).

S.R. had several risk factors for developing osteonecrosis of the jaw, including previous treatment with chemotherapy and steroids and a dental extraction within three months of diagnosis. Since his initial diagnosis of osteonecrosis, S.R. has been treated with a course of antibiotics, continues daily chlorhexidine rinses, and is followed closely by his oral surgeon. Unfortunately, the area of exposed bone has continued to increase in size, and a continued concern is that he may develop a pathologic fracture of his mandible.

The recent findings that bisphosphonates increase risk for osteonecrosis of the jaw have affected clinical practice. Practitioners initiating bisphosphonate therapy should discuss the increased risk of osteonecrosis of the jaw with patients and communicate with patients’ dentists. Patients should receive a baseline dental examination, followed by routine dental examinations every six months or per dentists’ instructions. Practitioners should perform a thorough oral examination at each clinic visit. In addition, patients should practice good oral hygiene by brushing and flossing, maintain well-fitting dentures, ensure good hydration, and avoid dental surgeries and extractions when possible. The goal of the coordination of care and patient education is the prevention of osteonecrosis of the jaw.

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**References**


