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## Management of Heterotopic Ossification with Bisphosphonates after Hip Hemiarthroplasty in Patients with Contraindications to Standard of Care Prophylaxis

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### Introduction:

Heterotopic Ossification (HO) is the production of bone outside of normal physiologic location on the skeleton. This is mostly caused by a disruption of normal bone formation, leading to production of bone in soft tissue. Some etiologies include, but aren't limited to, surgery, neurologic injury, and genetic disease. The effects of HO can include functional and gait deficits, limited range of motion, and pain. One of the most common etiologies for the formation of HO is following a total hip arthroplasty (THA). The rates of HO following total hip arthroplasty that have been reported are variable (2-90%).<sup>1</sup>

There are methods to provide HO prophylaxis successfully via NSAIDs, single dose radiation therapy, or combination therapy.<sup>2,3</sup> However, there are no alternative therapies for HO prophylaxis for patients with contraindications to NSAIDs and radiation therapy. This report seeks to suggest methods to prevent HO outside standard of care therapies for this subset of patients.

### Case Description:

One month post left hip hemiarthroplasty, a 78-year-old Jehovah Witness man with history of diabetes, hypertension, chronic kidney disease, anemia, and thrombocytopenia presented with functional and gait deficits. The patient had sustained femoral neck fracture after a fall at home secondary to hypertensive encephalopathy. Left hip X-ray revealed a femoral neck fracture. The patient received a left total hip arthroplasty, and was subsequently admitted to acute inpatient rehabilitation.

The patient developed intolerable pain three weeks after his admission to inpatient rehabilitation, and he became non-weight bearing on his left leg. Prior to this development the patient was able to walk 25-30 feet in therapy. Repeat X-rays were negative. CT without contrast was performed on the hip at that time which demonstrated left sided prosthesis with no loosening. The CT also showed scattered areas of bone formation seen in the soft tissue at the inner and outer margin of the hip. Heterotopic bone formation was also noted involving the piriformis, gemelli muscles, obturator internus, quadratus femoris, distal insertion of the iliopsoas, and gluteus maximus.

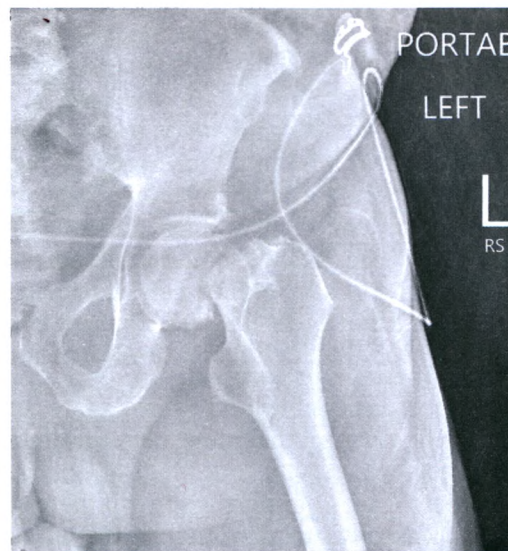


Figure 1: Pre-operative left hip radiograph- transcervical neck fracture of femur.

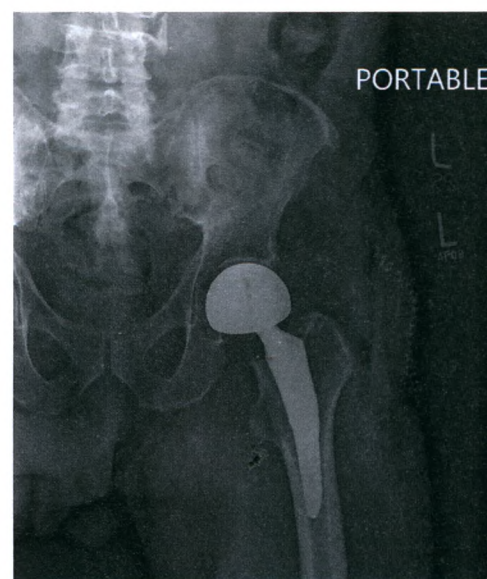


Figure 2: Post-operative radiograph of left total hip arthroplasty.



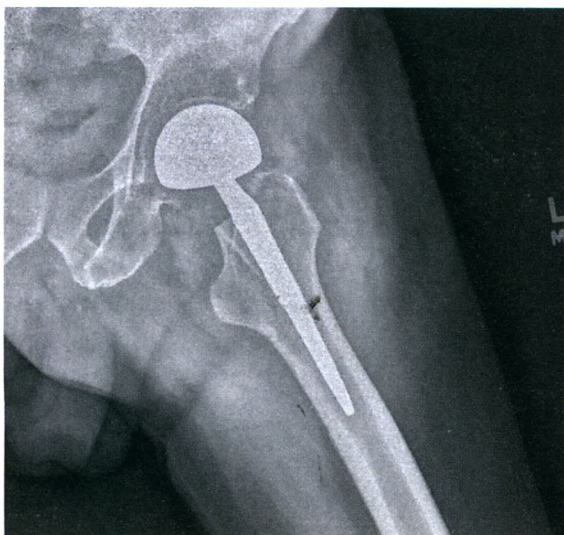


Figure 3: Degree of HO three weeks after admission to acute inpatient rehabilitation (X-ray).



Figure 4: Degree of HO three weeks after admission to acute inpatient rehabilitation (CT).

## Discussion:

This patient's symptoms of progressive functional and gait disturbance due to pain are consistent with HO as demonstrated by CT. The patient was unable to receive NSAIDs for prophylaxis due to a past medical history of chronic kidney disease. In addition, the patient had not received radiation therapy in the recommended perioperative period from 24 hours prior to surgery to 72 hours post-op. The patient's past medical history of anemia and thrombocytopenia were also contraindications to radiation therapy. The patient's thrombocytopenia was also a contraindication to low dose aspirin therapy.

A literature review study had looked into evidence of alternative therapies for heterotopic ossification prophylaxis and treatment using a modified Sackett Scale.

## Treatment

Bisphosphonate studies show cohort study Level 2 evidence in the treatment of HO if the diagnosis is made early (3-6 weeks post-op). Bisphosphonates, however, are unlikely to be as effective if treatment is started when radiographs are positive. There is also a case series Level 4 evidence that bisphosphonates stops secondary HO after surgical resection of HO.<sup>5</sup>

Another study was done to assess the potential benefits and adverse effects of bisphosphonates in CKD patients with osteoporosis. Results showed that nephrotoxicity and drug accumulation is uncommon and of little clinical significance when lower doses of bisphosphonates are used in CKD. It was demonstrated that bisphosphonates were safe as long as renal function was closely monitored with administration in Stage 1-3 CKD for osteoporotic patients.<sup>6</sup> If bisphosphonates can be safely used in CKD patients with osteoporosis,

there may be a safe way to administer bisphosphonates in patients with mild-moderate CKD to treat HO.

A retrospective study was performed in which the management of five cases with bisphosphonate therapy after surgical excision of primary HO had prevented the need for a second surgery. No recurrences were seen in this small study. Furthermore, none of the patients had side effects including nephrotoxicity. It is suggested that the bisphosphonates not only inhibit the mevalonate pathway in osteoclasts, but also act as an anti-inflammatory by interacting with IL-1, IL-6, and TNF.<sup>7</sup> The exact mechanism of HO prevention is unknown, but correlations exist such that more research should be done with larger sample sizes to demonstrate the efficacy of bisphosphonates for HO prophylaxis and treatment.

## Treatment Plan:

The primary treatment plan in place for this patient was conservative management. The patient was placed on passive ROM therapy without additional prophylaxis or treatment. The use of passive ROM therapy remains controversial. Some studies suggest that passive ROM therapy may increase the incidence of HO due to microtraumas. However, other studies emphasize the significance of ROM exercise to maintain mobility and function. A study by Garland demonstrated that 64% of affected joints maintained or gained ROM with joint manipulation and passive ROM therapy.<sup>8</sup> The risk/benefit ratio of joint manipulation favors joint manipulation in patients for HO prophylaxis.

## Conclusion:

Heterotopic ossification is a complication that causes decrease in extremity range of motion and an increase in patient pain after trauma, neurological injury, or genetic



disease. Although there are few alternative therapies for HO prophylaxis and treatment, these studies show some promise for subsets of patients who have contraindications to NSAID and radiation therapy. More research is needed to assess the benefits of these alternative treatments within therapeutic windows to assess toxicity and adverse effects.

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