Pedal Heterotopic Ossification Formation: A Case Report

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Abstract: Heterotopic ossification is the abnormal formation of excessive bone in the soft tissue that is exacerbated by trauma, neurological injury or genetic abnormalities. Heterotopic ossification most commonly involves the hip joint after total hip arthroplasties and is less commonly seen in the foot. Heterotopic ossification formation is mainly asymptomatic but when symptomatic it can lead to pain, decreased range of motion, changes in activities of daily living and ulcerations. For the best outcome, surgical resection of heterotopic ossification formation should always be combined with NSAIDs and/or postoperative radiation therapy due to the highly likelihood that heterotopic bone will reoccur.

Key words: Heterotopic ossification formation, pluripotent mesenchymal stem cells, bone morphogenetic proteins, radiation therapy, nonsteroidal anti-inflammatories and ankle-foot orthosis

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Heterotopic ossification (HO) is defined as the abnormal formation of mature lamellar bone in soft tissue (2). HO is extra-articular and occurs outside the joint capsule in connective tissue between muscle planes, but not within the muscle tissue itself. There are two forms of HO: the acquired and hereditary form. The acquired form is the most common and is usually precipitated by trauma to the musculoskeletal system or central nervous system (7). Traumatic HO is usually due to fractures, dislocations, operative procedures or severe burns (2).

The greatest risk factor for HO is a history of HO formation (3). Contributing factors of HO formation include: male gender, proliferative osteoarthritis, ankylosing spondylitis, diffuse idiopathic skeletal hyperostosis, muscle contractures, pressure ulcers and infections (4,5). The clinical signs and symptoms of HO can present itself three to twelve weeks after a musculoskeletal or neurological injury and include increased joint stiffness, limited range of motion, calor, edema and erythema (4).

HO is typically asymptomatic, 80% of the time, but if HO is suspected, a three-phase bone scan should be ordered since it is the most sensitive imaging modality in detecting early HO formation (4). Bone scans can detect HO formation as early as three weeks after insult, while radiographs can take up to four to six weeks (2). If HO formation is confirmed, serial bone scans should be utilized to monitor the maturation process of heterotopic bone. Heterotopic bone usually matures 12-18 months after insult and demonstrates a decrease in metabolic activity and bone formation upon scintigraphic imaging (4,7).

The exact pathophysiology of HO remains uncertain but Chalmers et al. described three conditions necessary for HO formation: osteogenic precursor cells, inducing agents and a permissive environment (4). In response to trauma, an

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inflammatory response is activated which draws pluripotent mesenchymal stem cells to the area of injury (2). The pluripotent mesenchymal stem cells are then induced by bone morphogenetic proteins (BMPs) to differentiate into osteogenic cells, disrupting the balance between bone formation and bone inhibition, leading to excessive bone formation (4). BMPs are released from bone in response to venous stasis and inflammation and have been found to influence chemotaxis, mitosis and differentiation of cells making them potent osteogenic morphogens, especially BMP-4 (2,4,7).

To prevent HO formation, the inductive signaling pathways need to be disrupted to inhibit differentiation of pluripotent mesenchymal stem cells in tissues that are conducive to heterotopic osteogenesis (5). The two primary prophylactic modalities in treating HO are: nonsteroidal anti-inflammatories (NSAIDs) and radiation therapy (RT) (2). NSAIDs directly inhibit the differentiation of pluripotent mesenchymal stem cells into osteogenic cells and indirectly disrupt the inductive signaling pathway by inhibiting a prostaglandin-mediated response (4,5). Along with BMPs, prostaglandins have been found to be a potent co-stimulatory molecule in the induction of HO (5). Meanwhile, ionizing radiation disrupts the responding cells by altering their deoxyribonucleic acid (1).

Methods

A search of the literature was conducted regarding heterotopic ossification until May 2017. References from the appropriate articles were also reviewed to find all reports and outcomes of heterotopic ossification in the literature.

Case Report

This now 70-year-old male, initially presented to his podiatrist’s office over ten years ago for a soft tissue mass that encompassed the dorsal, lateral and plantar aspect of his left fifth metatarsal. Upon physical examination, his pulses were palpable bilaterally, protective sensation was absent bilaterally due to a history of idiopathic peripheral neuropathy, muscle strength was intact to the lower extremities, a cavus foot type was noted bilaterally and a corresponding plantar fifth metatarsal head ulceration was noted on the left without any signs of infection. The patient underwent surgical excision of the left soft tissue mass. The mass was sent for surgical pathology and a TLS drain was placed in the incision site. The surgical pathology of the soft tissue mass read: “purulent inflammation associated with extensive hemorrhage, granulation tissue and fibrosis.” No neoplasm was identified.

For the next four and a half years, the left plantar fifth metatarsal head ulceration failed to heal with conservative care that included: antibiotics, wound care, custom foot orthotics and offloading devices. Conservative and surgical treatment options were routinely discussed with the patient but conservative care was always preferred by the patient until the wound became acutely infected requiring incision and drainage of the left foot along with left fifth metatarsal head excision. Seven weeks post-operatively, HO formation was noted radiographically at the osteotomy site on the left fifth metatarsal but the incision site and ulceration went on to heal uneventfully. Subsequently, the patient ended up developing an ulceration to the plantar fifth metatarsal head on his right foot and chose to proceed surgically by excising the right fifth metatarsal head. The incision site and ulceration went on to heal until three and half years later when HO formation around the osteotomy site lead to re-ulceration. The patient underwent an exostectomy of the right fifth metatarsal where a power sagittal saw and pulse lavage were used. Within nine months postoperatively, the patient ended up undergoing a revisional exostectomy due to recurrent HO formation at the right fifth metatarsal shaft. Again, a power sagittal saw and pulse lavage were used but Surgicel and topical thrombin were used to obtain hemostasis and a TLS drain was placed. Six months post-operatively, HO formation was again noted to the shaft of the right fifth metatarsal. To avoid another surgery, the patient was given a script for indomethacin 25 mg three times a day and a short leg articulated ankle-foot orthosis (AFO). The patient was unable to tolerate indomethacin and his ulceration increased in size with the short leg articulated AFO. Other treatment options were explored and discussed but the patient elected to undergo his third exostectomy and targeted radiation therapy that would occur the day after surgery. Again, a power sagittal saw, Surgicel and topical thrombin were used intraoperatively. The incision site was copiously irrigated and a drain was placed. One day post-

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operatively, the right foot was irradiated with 7 Grays in one fraction. The incision site and ulceration went on to heal until seven months post-operatively when his right plantar ulceration reoccurred without any new radiographic signs of HO formation. He was again treated with local wound care and a new short leg articulated AFO. Correction of his cavus deformity has been discussed but the patient has been reluctant to proceed.

**Discussion**

In the 20% of cases that HO formation becomes clinically significant, surgical intervention is usually required to restore normal anatomy and function (2,7). Prior to surgical intervention, the maturation of the heterotopic bone should be confirmed to limit or prevent intraoperative complications and HO reoccurrence (7). Intraoperatively, stripping of the periosteum should be kept to a minimum, iatrogenic trauma to the periarticular soft tissue should be avoided and all devitalized tissue should be debrided to limit or prevent the reoccurrence of heterotopic bone (1). It is recommended that bone saws be used over bone cutting forceps to limit the amount of bone fragments in the surrounding tissues (3). Irrigation is necessary to remove bone fragments from the surrounding tissues during and after bony resection. Hemostasis should be as complete as possible and a drain should be placed to minimize hematoma formation (1,3). Hematomas are a common complication of partial ray resections and are a risk factor for HO formation. A study by Boffeli et al., found the incidence of HO formation to be 75% after a partial ray resection (3).

After surgical resection, prophylaxis against HO reoccurrence includes NSAIDs and/or RT. Indomethacin is a commonly prescribed NSAID for the prevention of heterotopic bone. To be most effective, 25 mg of indomethacin should be taken three times a day for 5-6 weeks (2). A meta-analysis by Pakos and Ioannidis found RT to be more effective than NSAIDs, in preventing clinically significant HO, when the radiation dose exceeded six Grays (Gy). When the RT dose was six Gy or less, RT and NSAIDs were equivalent in terms of the rate of HO formation. Their research also found preoperative RT to be significantly less effective than NSAIDs, while postoperative RT became increasingly superior to NSAIDs with increasing RT doses (6).

Pluripotent mesenchymal stem cells only remain radiosensitive for four days after extravasation into the surrounding tissue so for postoperative RT to be effective, the area of interest should be irradiated within four days post-operatively (3).

**Figure 1.** Bilateral fifth metatarsal head resections with evidence of heterotopic ossification formation postoperatively

**References**


Figure 2. Resected heterotopic ossification formation from the right 5th metatarsal