Heterotopic Ossification in Trauma

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KEYWORDS

• Heterotopic ossification • Pathophysiology • Classification • Chemical prophylaxis • Radiation • Surgical debridement • Surgical excision

KEY POINTS

- Formation of heterotopic ossification (HO) is poorly understood but is an area of continued scientific investigation.
- Certain injuries and patient populations seem to have increased risk of HO formation.
- Brooker classification is most commonly used; however, the Hastings and Graham classification may be more useful around the elbow.
- Pharmacologic agents and radiation have been used in HO prophylaxis.
- Surgical excision is an option for established, symptomatic HO.

INTRODUCTION

Heterotopic ossification (HO), simply stated, is bone that forms where it does not belong. HO can form after trauma, burns, head injuries, spinal cord injuries, and surgical procedures, such as total hip arthroplasty. HO is categorized into neurogenic, thermal, and traumatic types. Neurogenic HO occurs after traumatic brain injury or spinal cord injury. HO can form after thermal injury and is correlated with the overall body surface that has been burned.[1] Traumatic HO occurs after blunt, penetrating, or explosive injuries. All forms of HO may have common elements of pathophysiology; however, detailed information about the pathophysiology at the cellular or protein level has not yet been determined for each type. All types of HO need 3 essential components: pluripotential cells, molecular signals to cause the cells to differentiate, and the proper microenvironment to form bone. Most likely all forms of HO occur because of some amount of tissue trauma, some degree of ischemia, and activation of pluripotential mesenchymal cells, perhaps in part caused by bone morphogenetic protein (BMP).[2]

New osteoblasts form bone in the soft tissues, especially around joints. Heterotopic bone can cross anatomic planes between muscle and tissue layers and can impinge on, or even enclose, neurovascular structures. Heterotopic bone may cause pain because of compression of overlying skin and subcutaneous tissue or because of compression of adjacent structures. Severe HO can cause restriction of joint motion. There is often accompanying fibrosis around the affected joint. The loss of motion can lead to gait disturbances and inability to perform common daily activities such as sitting or eating. The hips and elbows are the most commonly involved joints after trauma and HO is often related to surgery to repair intra-articular fractures in these joints.[3,4] HO may be more common in men and African Americans.[5] The 2 most commonly used methods to prevent HO are use of nonsteroidal antiinflammatory drugs (NSAIDs) and radiation. Treatment of established HO can range from observation, to physical therapy, to surgical excision.

PATHOPHYSIOLOGY OF FORMATION OF HETEROTOPIC OSSIFICATION

The pathophysiology and basic science of HO formation is incompletely understood. Following injury, cellular and molecular signaling

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differentiate dormant, mesenchymal precursor cells that develop into osseous and/or endochondral cells.[6] HO formation, regardless of the injury mechanism (soft tissue trauma, head injury, and spinal cord injury) occurs in soft tissue. Damage to the skeletal muscle with some level of hemorrhage is a predisposing factor. An ischemic environment and activation of pluripotential cells leads to the formation of ectopic bone. BMP may play a role in the differentiation of pluripotential cells into osteoblasts. Mesenchymal stem cells increase osteogenic BMP-2 and BMP-4 expression. The cells are also affected by oxygen tension, micronutrient availability, and mechanical stimuli, leading to increased osteogenesis and potential HO formation.[2,7] Forsberg and colleagues[8] showed that combat wound inflammatory markers increased HO risk. Interleukin (IL)-3 and IL-13 generated by T lymphocytes during wound healing are inhibitors of osteoblastic differentiation and both were found to be independently associated with increased HO risk. Thirteen genes were upregulated in patients who eventually developed HO.[8] Evans and colleagues[9] sought to characterize the expression of osteogenesis-related gene transcription in 54 high-energy penetrating traumatic extremity combat wounds. Their data supported the theory that ectopic bone formation is initiated shortly following the traumatic extremity insult. HO development was noted to occur in tissue environments with a protracted increased inflammatory process, which likely accounts for higher levels of messenger RNA transcription seen at final debridement.[9] Rossier and colleagues,[10] in the 1970s, noted that histologically HO starts shortly after trauma with the proliferation of spindle cells within the first 7 days. During the second week, immature cartilage and woven bone are seen, with trabecular bone forming 2 to 5 weeks following the initial insult. By 6 weeks, undifferentiated central foci form, with mature lamellar bone being located peripherally. Amorphous calcium phosphate is gradually converted to hydroxyapatite crystals and, by 6 months, spicules of bone can be seen within the muscle planes.[10]

Davis and colleagues[6] examined HO risk through muscle biopsies of soldiers injured by high-energy gunshots and blasts compared with patients who had undergone a hamstring tendon autograft. Patients with gunshot and blast injuries showed significantly increased levels of connective tissue progenitor cells per gram of tissue committed to osteogenic differentiation compared with the hamstring autograft group.

Twenty-five percent of US military personnel who sustain extremity amputations as a result of combat have bilateral amputations. Bilateral amputees (BLAs) were compared with a control group that also sustained blast injuries. The BLA group showed increases in the levels of systemic and local wound proinflammatory cytokines, including IL-6 (serum), tumor necrosis factor alpha (exudate), and IL-1 (exudate). The BLA group also had higher rates of wound dehiscence and HO.[11]

EVALUATION OF PATIENTS WITH HETEROTOPIC OSSIFICATION

Patients with HO typically complain of limited range of motion of the affected joint as well as pain and limited function. In the upper extremity this may cause restricted range of motion in the elbow leading to difficulties with activities of daily living, such as eating and grooming. In the hips HO may result in pain, gait disturbance, limp, and difficulty sitting or using the toilet. A careful history should be conducted to evaluate for past medical history, trauma, head injury, spinal cord injury, and any previous surgery. Examine the patient for range of motion, strength, and any neurovascular abnormalities. The imaging work-up starts with plain radiographs, which are easy to obtain and inexpensive. On the radiograph the extent of the HO can be seen. A computed tomography (CT) scan with three-dimensional reconstruction gives detailed visualization of HO. HO often crosses anatomic fascial planes and can be very close to important neurovascular structures. In patients after open reduction and internal fixation (ORIF) of acetabular fracture, HO is almost always in the location of the previous surgery. Because the Kocher-Langenbeck approach is the most commonly used, HO usually involves the hip abductors and short external rotators. Typically, the sciatic nerve cannot be definitively visualized by CT, but HO is often near the nerve and can occasionally encase the nerve. Other studies, such as bone scans and single-photon emission CT scans, can help with understanding the metabolic activity of the bone, but are not useful in terms of planning a surgical excision because these studies lack the detailed resolution of a CT scan.

HETEROTOPIC OSSIFICATION IN THE UPPER EXTREMITY

HO has been described in the upper extremity, although its incidence is much less common than in other areas of the body. HO of the shoulder has been described following anterior acromioplasty, with an incidence reported from 3% to 30%.[12–15]