Heterotopic Ossification Following Upper Extremity Injury

Shailesh Agarwal, MD, Shawn Loder, BS, Benjamin Levi, MD*

KEYWORDS

• Heterotopic ossification • Burn injury • Elbow • Upper extremity

KEY POINTS

- Heterotopic ossification (HO) is the formation of ectopic bone within or involving soft tissues, including joint spaces, nerve, and/or muscle.
- HO occurs in patients following trauma, and often develops in the elbows of patients with severe burn injuries, even without direct injury to this anatomic site.
- HO causes restricted motion and subsequent joint contractures, chronic pain, and open wounds.
- Diagnostic approaches to HO are limited primarily to clinical presentation and radiography.
- Prophylactic measures against HO include nonsteroidal antiinflammatory drugs and radiotherapy, although these may have adverse consequences with imperfect outcomes.

INTRODUCTION

Heterotopic ossification (HO) is the pathologic formation of extraskeletal bone within soft tissues or joints. HO occurs in 2 patient populations: those who have severe trauma and those who have genetic mutations in the bone morphogenetic protein (BMP) signaling pathway. The latter are a minority of patients with an extremely debilitating disease process, representing approximately 500 individuals nationwide. However, patients with trauma, including musculoskeletal injury, spinal cord injury (SCI)/traumatic brain injury (TBI), and burns represent a much larger population of patients at risk for HO. Patients with any of these injuries may develop HO in the upper extremities, even if the extremities are uninjured from the initial trauma.

HO presents a substantial barrier to patient recovery after major trauma, burns, and surgical procedures. These patients have often already undergone procedures related to the initial traumatic insult, and may present 6 or more months later with signs that indicate HO, including localized pain or discomfort, reduced range of motion, and open wounds. However, current therapeutic modalities are limited in their ability to prevent HO, and surgical excision to remove the osseous lesion is unable to address chronic sequelae of HO, such as pain and joint contractures. Furthermore, even after successful excision, patients are at risk for recurrence because of the local inflammation caused by surgery.

The elbow is the most common anatomic location of HO in patients with burns, even in the

Disclosures: B. Levi was supported by funding from National Institutes of Health/National Institute of General Medical Sciences grant K08GM109105-0, Plastic Surgery Foundation, the Association for Academic Surgery Roslyn Award, American Association for the Surgery of Trauma Research & Education Foundation Scholarship, and American College of Surgeons Clowes Award. S. Agarwal was supported by the Coller Society Research Fellowship, NIH Loan Repayment Program, National Institutes of Health, F32AR06649901A1, and Plastic Surgery Foundation.

Section of Plastic Surgery, University of Michigan, 1500 East Medical Center Drive, Ann Arbor, MI 48109, USA
* Corresponding author. 1150 West Medical Center Drive, MSRB2 A574, Ann Arbor, MI 48109.
E-mail address: blevi@umich.edu

Hand Clin 33 (2017) 363–373
http://dx.doi.org/10.1016/j.hcl.2016.12.013

absence of burns to the upper extremity.[1–3] However, diagnosis of HO at this site can be particularly challenging, because the elbow can become stiff after trauma because of prolonged inactivity or direct injury. Cognitive decline caused by prolonged sedation can further compromise successful rehabilitation in these patients.[4] Although there are several surgical approaches to remove HO in the upper extremity, none is able to completely restore preinjury function.[5]

EPIDEMIOLOGY AND RISK FACTORS

HO occurs in patients following musculoskeletal injury and extensive burns. A recent review of nearly 3000 patients with burn injuries from 6 high-volume centers found that 3.5% of patients developed HO.[6] Included patients were 18 to 64 years old with total body surface area (TBSA) greater than 20%; 65 years old or older with TBSA 10% or greater; or any patients with burn injury to face/neck, hands, or feet.[6] Patients with the highest odds of developing HO had greater than 30% TBSA burns and patients with upper extremity burns requiring grafting had nearly 100 times higher odds of developing HO. Overall, elbow HO has been reported to occur in 0.1% to 3.3% of patients with burns.[7–9] A systematic review of reports describing excision of HO in the elbow found that 28% (174 out of 626) of cases were in patients with burns, 55% (343 out of 626) of cases were in patients with trauma, and 17% (109/626) were in patients with TBI.[10] Studies of patients with burns have found the elbow to be the most commonly involved joint, with formation approximately 3 months after the initial injury.[1–3] These findings provide further evidence that HO may form in the elbow after a variety of injuries.

In patients with elbow fractures, those who underwent surgery more than 1 week after injury or had mobilization of the elbow delayed by more than 2 weeks were at the highest risk for HO, with 7% (55 out of 786) of patients developing HO.[11] Another review of 124 patients with elbow fractures found clinically relevant HO, defined as being class 2 or greater using the Hastings and Graham classification scheme, in 21% (26 out of 124) of patients.[12]

HO is also reported in the lower limbs of patients with polytrauma, including blast injuries, as in those sustained by military members. A review of injured military personnel with amputations found that more than 60% of the 213 residual limbs had HO.[13] A separate study by the same group found that TBI was associated with HO, as was an increased injury severity score ($\geq$16; odds ratio, 2.2; $P<.05$).[13,14] More than 20% of patients with SCI have been reported to develop HO.[15,16] Increased systemic inflammation, local spasticity, and prolonged immobilization all place these patients at higher risk, and both preclinical and clinical studies are investigating how controlling these sequelae of trauma may reduce or eliminate HO.[17]

In addition, patients who have had elective orthopedic operations are also at risk for HO, particularly those who have had total hip arthroplasty (THA). One study cited more than 40% of patients developing some form of ectopic bone after THA.[18] More recent studies have reported HO rates ranging from 26% to 58% in THA patients.[19–21] The predictably higher rate of HO in these patients has prompted investigators to test prophylactic measures such as nonsteroidal anti-inflammatory drugs (NSAIDs) or radiation therapy to prevent HO or its recurrence, as described later.[22–33]

DIAGNOSIS

Examination

Because of the central role of the elbow in upper extremity movement, HO at this site can cause substantial disability. Signs include limited range of motion, arthritis, pain, stiffness, and swelling. Concomitant symptoms of ulnar nerve compression at the elbow can occur requiring detailed sensory and motor examination of the upper extremity in the ulnar nerve distribution. This examination should include evaluation of 2-point discrimination, documentation of Wartenberg or Froment signs, examination of the intrinsic muscles for atrophy, and testing for Tinel sign over the cubital tunnel.[34] Delayed conduction on nerve conduction studies can provide additional objective data regarding the severity of nerve compression.

Current Imaging Techniques

At present a conclusive diagnosis of HO is based on radiographic imaging. Patients may present with clinical signs or symptoms prompting radiograph imaging (**Fig. 1**). Ectopic bone on radiograph can aid in determining the appropriate approach for excision. Importantly, radiographic imaging modalities are able to detect only the ossified lesion. These imaging modalities do not identify patients who are developing early cartilage deposits that later undergo ossification, nor are they able to identify patients who are at the highest risk for developing HO before even cartilage formation. Therefore, at the time when patients have presented with clinical signs or symptoms prompting radiographic evaluation, the major therapeutic option available to patients is surgical