Heterotopic Ossification and Hypertrophic Scars

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KEYWORDS

• Heterotopic ossification • Hypertrophic scar • Burn injury

KEY POINTS

- Two conditions, heterotopic ossification (HO) and hypertrophic scarring, present a substantial challenge in the management of patients with large surface-area burns.
- HO is the pathologic formation of ectopic osseous lesions causing severe pain, nonhealing wounds, and restricted range of motion.
- Hypertrophic scars in contrast are nonosseous lesions caused by excessive collagen deposition.
- Current treatment strategies aimed at HO include prophylactic radiation therapy, nonsteroidal anti-inflammatory drugs, and bisphosphonates.

INTRODUCTION

Heterotopic Ossification

Heterotopic ossification (HO) is the formation of ectopic osseous lesions within soft tissue or joints. HO occurs in patients with genetic mutations in receptors responsible for bone morphogenetic protein signaling and in patients with severe trauma without any known genetic predisposition. Patients with severe trauma, including burns, musculoskeletal injury, spinal cord injury (SCI), or traumatic brain injury (TBI), represent a much larger population of patients with HO. Patients with severe burns may develop HO in sites distant from the visible burn injury. These osseous lesions may cause nerve compression, resulting in severe pain, open or nonhealing wounds, and restricted range of motion due to physical obstruction within joints. In burn patients, HO is often documented in the upper extremities, most notably the elbow,[1–3] despite burn injuries that are distant from this site. Ultimately, HO presents a substantial barrier to patient recovery after already devastating injuries; these patients have already required extensive medical, surgical, and rehabilitative care related to the original injury, only to require further surgery to remove the offending lesions.

Hypertrophic Scarring

Hypertrophic scarring is a late complication of thermal cutaneous injury that can lead to substantial functional impairment, as well as aesthetic disfigurement. Hypertrophic scars are characterized by excessive and disorganized deposition of extracellular matrix within the wound bed, leading to raised scars. These can occur in any anatomic location but have especially detrimental

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consequences in areas involving joints and other mobile regions, leading to scar contractures limiting free range of motion.[4] Reported studies estimate that hypertrophic scarring develops in up to 80% of all burn patients with greater than deep-partial-thickness burns.[5,6]

EPIDEMIOLOGY

Heterotopic Ossification

Patients with musculoskeletal injury or trauma, extensive burns, and SCI or TBI are at risk for HO. In a study of 3000 burn subjects from 6 high-volume centers, 3.5% of subjects formed HO.[7] Subjects were 18 to 64 years old with affected total body surface area (TBSA) greater than 20%; 65 years and older with affected TBSA 10% or greater; and any subjects with burn injury to face, neck, hands, or feet.[7] Subjects with the highest risk of developing HO had greater than 30% TBSA burns. Overall, elbow HO has been reported to occur in 0.1% to 3.3% of burn patients.[8–10] A systematic review of reports describing excision of HO in the elbow found that 28% (174 per 626) of cases were in burn patients, 55% (343 per 626) of cases were in trauma patients, and 17% (109 per 626) were in TBI patients.[11] Studies of burn patients have found the elbow to be the most commonly involved joint, with formation approximately 3 months after the initial injury.[1–3] Schneider and colleagues[12] have reported on a risk scoring system based on data from the Burn Model System National Database, including more than 3500 patients. This 13-point system has led to an online calculator (available at http://www.spauldingrehab.org/HOburncalculator).

Patients with non–burn-related injury are also at risk for developing HO. Notably in these patients, HO develops directly within the site of injury, thereby impeding wound healing. Patients who undergo orthopedic surgical operations (eg, total hip arthroplasty [THA]) are at risk, with studies reporting up to 58% of patients with THA developing ectopic bone.[13–16] Among trauma patients, injury severity score (ISS) is positively associated with odds of developing HO (ISS$\geq$16, odds ratio 2.2, $P<.05$).[17,18]

Hypertrophic Scarring

Several risk factors for hypertrophic scar formation have been identified and include young age, infection, skin stretch, and anatomic location (ie, axilla, neck, small finger).[19] In contrast to HO, hypertrophic scarring is a relatively common phenomenon among patients with burns, especially those with partial deep or deep burns. Although superficial burn wounds tend to heal without complications, deeper partial-thickness and full-thickness burns have a significantly increased risk to result in hypertrophic scar formation.[20] Contracture is more common when burns are allowed to heal secondarily due to the prolonged inflammation.[21] Additionally, deeper burns are also at increased risk of hypertrophic scar, even when grafted.[22]

DIAGNOSIS

Heterotopic Ossification

Examination

Signs of HO include limited range of motion, arthritis, pain, stiffness, and swelling. Diagnosis among burn patients poses a challenge to physicians because HO lesions may develop outside of the area of the burn injury. When HO develops within the burn injury site, it may go undiagnosed due to the more prominent appearance of burn scar contractures, which present with similar signs, including stiffness and pain. Plastic surgeons may diagnose HO in patients who have concomitant overlying hypertrophic scars that confound the diagnosis.

Current imaging techniques

Based on the initial examination, radiographic images may be obtained to make a conclusive diagnosis of HO. There are currently no published recommendations for obtaining radiographic images in patients who present signs concerning for HO. Spatial characterization may be performed using computed tomography (CT) imaging. Plastic surgeons can use this imaging information to assess the extent of resection that may be required. MRI may also delineate the proximity of nerves that may be compressed or encased by the offending lesion.

Experimental imaging techniques

Additional modalities for detecting HO lesions before ossification are now in preclinical and clinical investigation. Single-photon emission CT (SPECT) is able to correlate metabolic activity using radioisotope uptake with the presence of osseous lesions. Areas of early HO may be nonossified but have high metabolic activity, indicated by increased uptake of the radioisotope.[23,24] However, because HO in burn patients may develop outside of the burn sites, it may be impractical to perform imaging before the formation of an ossified lesion with its presenting signs. Ultrasonography is also able identify HO even before the development of clinical signs.[25] The changes identified by ultrasound are likely due to extracellular matrix deposition occurring during cartilage.[26] Raman spectroscopy is another modality that is