CASE REPORT

Multiple Heterotopic Ossification of Scar Following Degloving Injury: A Case Report

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Introduction

Heterotopic ossification (HO) is defined as bone formation in locations where there is no skeletal system. Typically, HO occurs during regenerative or degenerative processes such as atherosclerosis within arteries¹. It is also a common complication following orthopedic operations such as total hip arthroplasty, the location of HO often being concurrent with the joint operated upon. The incidence of HO is increased in the presence of concomitant central nervous system disorders, including brain injuries and spinal cord lesions². Scar HO is an uncommon, but important, complication of burn injuries and has occasionally been reported in certain regions such as in the abdominal linea alba after abdominal surgery^{3,4}. Here, we report a case of open degloving injury in which more than one focus of HO developed. We conducted an extensive review of published reports but found no other reports of HO in patients with degloving injuries.

Case Report

A 62-year-old woman presented with non-healing ulceration that had been present on the left thigh for 3 months. Twenty-one years previously, she had been involved in a traffic accident in which a large portion, almost 5% of the surface area of the left thigh skin, had been openly degloved. The injury had healed after the avulsed skin had been replaced *in situ*. A circular scar had formed near the knee joint within 4 weeks. She had no concomitant brain or spinal cord injuries. Four years before presenting to us, she had reported feeling two contracture bands under the scar on the anterior and lateral side of the thigh. These bands had gradually manifested as pain and swelling and ulceration had subsequently developed on the lateral side of the thigh. Symptom including pain and swelling emerged 6 months ago, but she had no history of injury. A blister had developed on the anterior band 1 month previously (Fig. 1). The inferior lateral ulcer was covered by hard white plaque. The range of motion of the knee was 0°–120°. Plain radiography of the thigh

showed lateral funicular and anterior spotty opaque areas on the site corresponding to the ulceration (Fig. 2). Results of relevant blood biochemistry tests, such as serum calcium concentration, were within normal limits and wound swabs showed no microbial growth. The ulcers, together with peripheral inflammatory tissue, were excised until normal subcutaneous tissue was exposed. The excised tissue showed funicular sclerosis. The surgical incision was sutured after releasing subcutaneous tissue. Histopathological analysis revealed areas of amorphous calcification and lamellar bone in the excised tissue (Fig. 2). No recurrence of calcification was detected during an 18-month follow-up. This study was approved by the institutional review board of the Sixth Affiliated People's Hospital of Shanghai Jiaotong University (Shanghai, China) and written informed consent was obtained from the patient.

Discussion

Heterotopic ossification complicates a variety of pathologic processes and can occur in all kinds of soft tissues, including subcutaneous fat and skeletal muscle, in which undifferentiated cells with potential for osteoblastic differentiation are present. The characteristics of scar HO differ from those of HO in orthopedic surgery; HO is more commonly seen in the hip and elbow joints than in scars. Between 2%–7% of patients undergoing hip-joint surgery develop extensive HO⁵. Although the exact mechanism of development of both types of HO is unknown, it is known that the risk factors for orthopedic HO and scar HO are different. Open reduction and internal fixation, particularly of acetabular fractures, has a high incidence of subsequent HO⁴. Immobilization of a joint, multiple injuries and concomitant central nervous system injuries increase the incidence of HO. The residual portions of lower limbs can develop HO in wound scars after non-traumatic, traumatic or combat-related amputation; ossification may be induced by the residual bone, rather than by scar tissue⁶. In spite of an extensive review of published reports, we were

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Fig. 1 Macroscopic appearance of surface of HO site on the thigh. (a) There is a blister (white arrow) on the anterior scar band in which HO (0.6 cm × 1.5 cm) was identified. (b) HO (0.8 cm × 2.5 cm and 1.8 cm × 7.5 cm) posterior to the lateral ulcers (white arrow). (c) Excised scar and HO.

unable to find any systematic analysis of risk factors for the various types of scar HO. However, there is some information on the risk factors for HO development after burn injuries. Factors that may be associated with development of HO include skin grafting, active inflammation, infection, complete immobilization and over-vigorous physiotherapy⁷⁻⁹. Moreover, upper midline incisions do not seem to be particularly prone to scar HO¹⁰. Chalmers and Rush described three conditions necessary for HO formation: osteogenic precursor cells, inducing agents and a permissive environment¹¹. Each of these three conditions may be different for scar HO than for HO developing after traumatic orthopedic surgery.

Scar HO has most commonly been reported after burn injuries and abdominal surgery. Our patient, who had had a degloving injury, presented with symptoms characteristic of those of HO after burn injury rather than of HO after abdominal surgery. All three types of scar HO occur in the absence of periarticular muscle involvement. Several reports state that HO in abdominal scars has characteristics similar to those of actual bone, such as containing normal bone marrow with histological evidence of normal trilineage hematopoiesis⁴. In contrast, histological examination of the HO in another case of degloving injury showed amorphous calcification similar in structure to the HO found in post-burn cases, as well as chronic ulceration¹². However, both types of HO have the same clinical findings; they both present with chronic non-healing ulcers after trivial injuries. Interestingly, the time to emergence of non-healing ulcers, which ranges between 20 and 30 years, is also similar in both types of HO. Moreover, in both instances of HO associated with degloving injury, skin grafting or replacement of degloved skin was performed. This suggests that replacement of degloved skin, as well as skin grafts after burn excision, might contribute to the subsequent occurrence of HO⁹.

Although the precise risk factors for development of scar HO are still unclear, the process of calcification is believed to occur in two stages, hydroxyapatite crystal initiation and propagation, these stages being similar to those of normal physiological processes. According to reports on post-burn HO, consumption of large amounts of protein in burn patients has an adverse effect on calcium balance, leading to the formation of extrasosseous calcium deposits and renal stones. However, this phenomenon usually occurs in cases of full-thickness burns over 20% or more of the body surface^{10,13} and develops quickly, as early as within 2 weeks of the burn injury¹⁴. An inflammatory environment plays an important role not only in HO but also in bone formation during fracture healing¹⁵. However, in our case, we considered the inflammation to be the result of the ulceration rather than the cause of the HO, even though pathological examination showed infiltration of inflammatory cells along with calcified tissue. Blood biochemistry tests, such as C-reactive protein concentration, provided no evidence of systemic inflammation. Because scars with contracture bands have a limited blood supply, hypoxia may be involved in the pathophysiological development of HO and facilitate HO formation¹⁶. In our patient, both foci of HO were present on the scar of the contracture band; midline

Fig. 2 Plain radiograph and pathological examination (HE stain $\times 40$). (a) Plain radiographs showing spotty opacity on the anterior thigh on a lateral view of the femur (white arrows) and an opaque band laterally on an anterior-posterior view of femur (red circle). (b) Histology showing amorphous calcification and lamellar bone. (c) Calcification in adipose tissue.

abdominal scars may also lie in contracture bands. Contracture bands are susceptible to repeated trivial trauma such as stretch strain, which may initiate differentiation of undifferentiated cells into osteogenic cells¹⁷. Trivial trauma in calcified contracture bands can result in skin breakdown and formation of non-healing ulcers. Thus, in cases of degloving injury, the combination of formation of contracture bands after skin grafting and a satisfactory range of motion of the adjacent joint may facilitate HO development.

Finally, radiotherapy and administration of nonsteroidal anti-inflammatory drugs and bisphosphonates (such as etidronate disodium) are standard and useful methods for preventing development of HO after orthopedic surgery and burn injuries. However, these methods may not be useful in cases in which HO develops a very long time after injury. Therefore, total excision of all calcified tissue and taut scarring may be the most reliable method for the treatment of HO in such cases.

References

1. Liu K, Tripp S, Layfield LJ. Heterotopic ossification: review of histologic findings and tissue distribution in a 10-year experience. *Pathol Res Pract*, 2007, 203: 633–640.
2. Cadosch D, Gautschi OP, Thyer M, et al. Humoral factors enhance fracture-healing and callus formation in patients with traumatic brain injury. *J Bone Joint Surg Am*, 2009, 91: 282–288.
3. Richards AM, Klaassen MF. Heterotopic ossification after severe burns: a report of three cases and review of the literature. *Burns*, 1997, 23: 64–68.
4. Koolen PG, Schreinemacher MH, Peppelenbosch AG. Heterotopic ossifications in midline abdominal scars: a critical review of the literature. *Eur J Vasc Endovasc Surg*, 2010, 40: 155–159.

5. Vanden Bossche L, Vanderstraeten G. Heterotopic ossification: a review. *J Rehabil Med*, 2005, 37: 129–136.
6. Potter BK, Burns TC, Lacap AP, Granville RR, Gajewski DA. Heterotopic ossification following traumatic and combat-related amputations. Prevalence, risk factors, and preliminary results of excision. *J Bone Joint Surg Am*, 2007, 89: 476–486.
7. Chen HC, Yang JY, Chuang SS, Huang CY, Yang SY. Heterotopic ossification in burns: our experience and literature reviews. *Burns*, 2009, 35: 857–862.
8. Crawford CM, Varghese G, Mani MM, Neff JR. Heterotopic ossification: are range of motion exercises contraindicated? *J Burn Care Rehabil*, 1986, 7: 323–327.
9. Elledge ES, Smith AA, McManus WF, Pruitt BA Jr. Heterotopic bone formation in burned patients. *J Trauma*, 1988, 28: 684–687.
10. Kim J, Kim Y, Jeong WK, Song SY, Cho OK. Heterotopic ossification developing in surgical incisions of the abdomen: analysis of its incidence and possible factors associated with its development. *J Comput Assist Tomogr*, 2008, 32: 872–876.
11. Chalmers J, Gray DH, Rush J. Observations on the induction of bone in soft tissues. *J Bone Joint Surg Br*, 1975, 57: 36–45.
12. Ebrahim MK, Kanjoor JR, Bang RL. Heterotopic calcification in burn scars and non-healing ulcers. *Burns*, 2003, 29: 461–468.
13. Hunt JL, Arnoldo BD, Kowalske K, Helm P, Purdue GF. Heterotopic ossification revisited: a 21-year surgical experience. *J Burn Care Res*, 2006, 27: 535–540.
14. Gaffey MJ, Winston DC. Heterotopic ossification of soft tissue: a review with emphasis on ossification within abdominal surgical scars. *Anat Pathol*, 1998, 3: 195–208.
15. Blackwell KA, Raisz LG, Pilbeam CC. Prostaglandins in bone: bad cop, good cop? *Trends Endocrinol Metab*, 2010, 21: 294–301.
16. Shafer DM, Bay C, Caruso DM, Foster KN. The use of etidronate disodium in the prevention of heterotopic ossification in burn patients. *Burns*, 2008, 34: 355–360.
17. Kanno T, Takahashi T, Ariyoshi W, Tsujisawa T, Haga M, Nishihara T. Tensile mechanical strain up-regulates Runx2 and osteogenic factor expression in human periosteal cells: implications for distraction osteogenesis. *J Oral Maxillofac Surg*, 2005, 63: 499–504.